Downloaded from UvA-DARE, the institutional repository of the University of Amsterdam (UvA)
http://dare.uva.nl/document/107354

File ID	107354
Filename	Chapter 1: General introduction

SOURCE (OR PART OF THE FOLLOWING SOURCE):

Type	Dissertation
Title	The future health (care) burden of chronic diseases in the Netherlands
Author	J.N. Struijs
Faculty	Faculty of Medicine
Year	2008
Pages	152
ISBN	9789071433795

FULL BIBLIOGRAPHIC DETAILS:
http://dare.uva.nl/record/273766

Copyright

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other then for strictly personal, individual use.

UvA-DARE is a service provided by the library of the University of Amsterdam (http://dare.uva.nl)

Chapter 1

General introduction

Chapter 1

General introduction

1 General introduction

The overall aim of this thesis is to assess the health care burden related to chronic diseases, and to identify incentives that can curb the expected increase in the health care burden of chronic diseases. In this introductory chapter we provide a general background of the health care burden of chronic diseases. Furthermore, the aims and research questions of this thesis will be addressed. At the end an outline of this thesis is given.

1.1 Background and research issues

Chronic diseases have become one of the major challenges of this century. The health care burden of chronic diseases has increased tremendously during the last centuries as a consequence of epidemiological and demographic transitions.

The epidemiological transition addresses changes in cause-of-death patterns in a population, and consists of several stages (1-4). The first stage *(the age of pestilence and famine)* is characterized by poor conditions of sanitation and health care services, and the dominance of infectious diseases, causing high mortality rates. The life-expectancy in this stage, which lasted until about 1875, was low, varying between 20-40 years. In the next stage *(the age of receding pandemics)* improvements in the sanitary life conditions and medical conditions were achieved, which resulted in an increase of the life expectancy to 50 years and a sustained population growth (5). Although infectious and parasitic diseases were replaced by non-infectious diseases like cardiovascular diseases and cancer, infectious diseases still remained the leading cause of death. During the second half of the 20th century, the third stage *(age of degenerative and man-made diseases)* emerged in which chronic conditions gradually replaced infectious diseases as the leading cause of death, as a consequence of the elimination of infectious diseases (6). In this phase, the average life-expectancy exceeded 70 years. From 1970 onwards, a further improvement of the survival rates at older ages took place, resulting in a further increase in life-expectancy. This last stage of the epidemiological transition is called *the age of delayed degenerative diseases*. Figure 1.1 presents the increase in the life-expectancy at birth in the Netherlands for the time-period 1850 till 2004. In that time-period the life-expectancy has doubled, from 36.1 in 1850 to 76.3 years in 2004 in men, and from 38.5 to 80.7 years in women (7;8).

The demographic transition is characterized by a shift in patterns of high fertility and high mortality rates to a pattern of low fertility and delayed mortality rates in a population (3). In the first half of the 20th century the overall mortality rates declined and were followed by declines in fertility rates. The reasons for the decline in fertility rates were diverse, but most can be related to modernization processes, economic growth, increased level of education, emancipation of women and the widespread use of contraception (9;10). As a consequence of this shift in mortality and fertility rates, the proportion of elderly has increased substantially since the 1950s, and is continuing to increase in the next coming decades (Figure 1.2). The peak of the aging process of the Dutch population

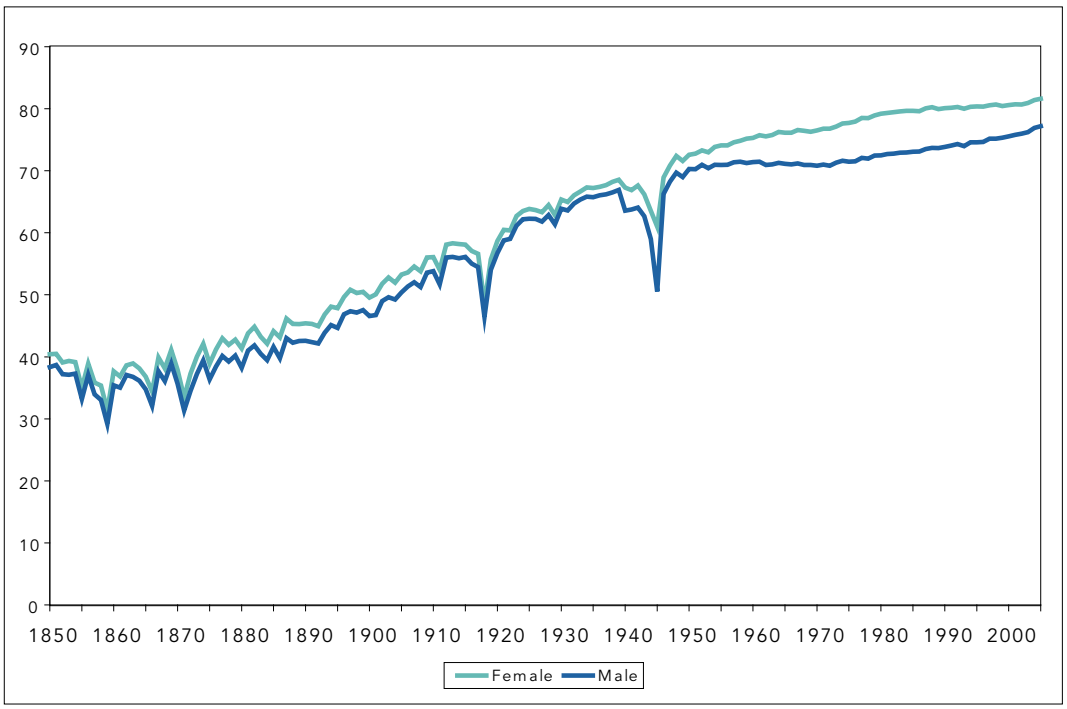

Figure 1.1: Life-expectancy at birth in the Netherlands for the period 1850-2004 (7;8)

is expected at the end of the fourth decade of this century (7). In 2039, the percentage of persons over 65 years is estimated to be 25.1% as compared with 14.5% in 2007 (11). Figure 1.2 presents the observed and predicted percentage of persons over 65 years in the Dutch population during the period 1950-2050.

A drawback of the aging process of the Dutch population is the concomitant rise in the number of chronically ill. In the Netherlands, cross-sectional prevalence estimates of chronic conditions are often estimated on the basis of general practitioners (GP) registrations. Demographic projections based on these GP registrations show an substantial increase in the prevalence figures of about 30-50% for most chronic conditions for the time period 2005-2025 (12-18). As a consequence of the increasing number of chronically ill, the health care burden will rise substantially in the coming decades, and will result in a large upward pressure on health care services and related health care costs in the future. The health care burden of chronic diseases will even be enlarged by the frequent occurrence of comorbidity (19-24). Comorbidity can be defined as the occurrence of one or more chronic conditions in the same person with an index-disease (25). It is estimated that 30% of the chronically ill have comorbidity (24). In this estimation psychiatric comorbidity is not even taken into account. Comorbidity has been shown to intensify health care utilization of the chronically ill and to increase health care costs (20;23;24;26-29).
Currently, most health care systems are insufficiently able to keep pace with the growing health care demands of the population (30). In order to sustain a high-quality health care system in the future, it becomes essential to find incentives that can curb the increasing health care burden of chronic diseases and to bridge the growing gap between demand and supply of health care.

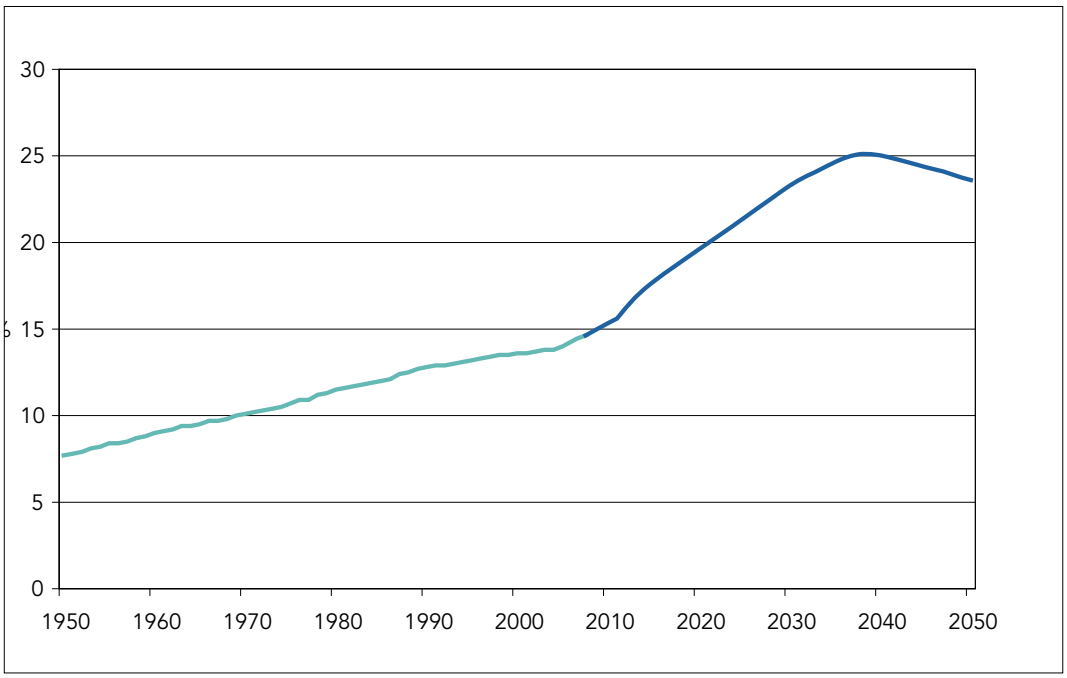

Figure 1.2: Percentage of persons over 65 years in the Dutch population 1950-2050 (7)

A strengthening of the primary prevention and a reorganization of chronic disease management in the health care system are proposed as potential solutions to curb the increasing health care burden of chronic diseases by the Ministry of Health, Welfare and Sports (31;32). The aim of prevention is to ensure that less individuals develop a chronic disease by promoting healthy life-styles, and to create awareness about the risk factors and consequences.
Organizational shifts in health care are needed to bridge the gap between demand and supply of care by improving the quality and continuity of care (33-35). Integrating services in so called disease management programs has the potential to improve the health system performance and to stimulate higher efficiency (36).
In this thesis we will assess the impact of prevention (e.g. changes in life-style) and the impact of organizational shifts in health care on the (future) health care burden of chronic diseases.

Primary prevention
Life-style behavior of individuals plays an important role in the development of chronic diseases (30;37). During the last decades, the prevalence rates of major risk factors for chronic diseases like overweight, (in)activity and smoking show unfavorable patterns. For instance, the prevalence of moderate overweight (Body Mass Index (BMI) >25.0-30.0 kg/m2) in the Netherlands has increased substantially till 57% for men and 42% for women in the period 2005- 2006, and further increases are expected (38). Also the prevalence of obesity (BMI≥ 30.0 kg/m2) has increased from 3% (men) and 6% (women) in 1981 till 12% for both men and women in 2006 (38;39). A further increase of about 50% in the prevalence of obesity is expected in the next 20 years (40). On top of that, an increasing trend is observed in the incidence of childhood overweight and obesity (41). Overweight and obesity in childhood are likely to persist resulting in increased risk for morbidity and mortality in adult life (42). Overweight and obesity will also result in the occurrence of chronic diseases earlier in life, for instance for diabetes (43).

The prevalence of physical inactivity in the Dutch population has also increased in the last decades, although a sharp decline in the prevalence of physical inactivity has been observed in the last few years (44). The Dutch guidelines of physical activity states that every adult should accumulate 30 minutes or more of moderate intense physical activity on most, preferably all days of the week (45). In 2006, about 56% of the Dutch population was active at the recommended levels of the guideline of physical activity, while in 2000 about 43% of the people adhered to the guideline of physical activity (44). Physical inactivity increases the likelihood to develop chronic diseases, for instance cardiovascular diseases or diabetes mellitus (46;47).
In contrast to the aforementioned risk factors, the prevalence of smoking declined, but only for men. The prevalence of smoking in men declined from 90% in 1958 till 31% in 2004 (48). For women the prevalence of smoking was stable during the last decades (about 28%).
The Dutch health care policy is strongly focusing on the prevention of chronic conditions and has stated that prevention has become a top-priority (31). To be able to develop and implement effective health policy, we need to gain more insight into the effects of these unfavorable trends in major risk factors on the future health care burden related to chronic diseases.

Organizational shifts in health care

Chronically ill use a wide variety of health care services and providers simultaneously or in a tight sequence. Chronic care management faces some obstacles of which a lack of coordination is the most prominent (49-53). As a solution, new health care models, so called disease management programs, have been introduced since the 1990s to improve the continuity and simultaneously the quality of care for chronically ill (52;53). Several related concepts like integrated care, managed care and shared care are formulated in the literature (54-57). All concepts share a similarity in goals, namely to improve the quality and efficiency of care by the use of management instruments (58). The main features of disease management programs are a good coordination between the different health care providers, task reallocation and responsibilities and the implementation of protocols and guidelines (58).
Disease management programs exist at a limited scale in the Netherlands (51;59). Diabetes mellitus and stroke are front runner diseases with respect to the development and implementation of disease management programs in the Netherlands (51;59). The main features of diabetes disease management programs are the introduction of diabetes control schemes, diabetes consultation hours, the implementation of joined care protocols, multidisciplinary meetings and the presence of a specialized diabetes nurse (60). Diabetes disease management programs often include multiple health care providers like GPs, specialized nurses, dieticians and medical specialists. Diabetes disease management programs have been proven to be effective in improving the quality of care (33;60;61). Numerous studies have shown to improve process measures (like percentage of patients in which Hba1c is measured annually) and patient outcomes (like HbA1c and total cholesterol levels) (62-80). However, for other patient outcomes like blood pressure, overweight and cardiovascular complications, no improvements were found. Nevertheless, it is to be expected that diabetes disease management programs will become more widespread implemented in the Netherlands in the coming years. Stroke disease management programs are currently the only disease-specific disease management programs which are already more widespread implemented in the Netherlands (59). Stroke disease management programs are delivered by so called stroke services which include multiple health care providers like GPs, medical specialists, nurses, speech therapists, etc.. The main features of these stroke services are stroke units in the hospital, early discharge procedures in the

hospital, guaranteed accessibility to a nursing home, multidisciplinary meetings, specialized nurses and an integrated (electronic) medical record that is accessible to all health care providers (81). A Dutch experiment demonstrated that stroke care organized in stroke services can achieve better health effects with the same budget (49;50;61). A clearer understanding of the effect of a widespread implementation of disease management programs on the future health care burden is of particular interest for health care providers and policymakers.

1.2 Research questions

The overall aim of this thesis is to assess the (future) health care burden related to chronic diseases in the Netherlands and to find incentives which can curb the expected increase in the health care burden of chronic diseases.
The overall aim can be subdivided into three research questions:

1. What is the impact of chronic diseases and comorbidity on the future health care burden?
2. What is the impact of trends in risk factors on the future burden of chronic diseases?
3. What is the impact of organizational shifts in health care on the future health care burden of chronic diseases?

In this thesis diabetes mellitus and stroke are used as illustrative examples. The prevalence of diabetes mellitus is estimated at 600,000 patients in the Netherlands in 2003, while 75,000 new patients are diagnosed annually (15). In 2003, about € 735 million were spent on diabetes mellitus (type 1 and 2), which corresponds to 1.3% of the Dutch health care budget (82). The cost estimates of diabetes are an underestimation, since complications of diabetes are not taken into account.
The prevalence and incidence of stroke in the Netherlands in 2000 are based on GP registrations and show a wide variety, from about 120,000 till 190,000 for stroke prevalence and from 34,000 till 41,000 for stroke incidence (14;83;84). Also the stroke cost estimates vary substantially from 2.5% till 4.3% of the Dutch health care costs (82;84).
The health care utilization of diabetes mellitus and stroke patients show different patterns. Health care utilization of diabetes patients concerns mainly the medical 'cure' sector, while stroke patients use the whole health care spectrum from cure and rehabilitation till nursing care. It is interesting to study whether these differences in health care utilization patterns lead to different outcomes and conclusions with respect to the impact of organizational shifts in health care on the future burden of chronic diseases.

1.3 Research methods

To answer the research questions, we need to combine demographic and epidemiological data and data on the health care burden of chronic diseases. Demographic data were obtained from Statistics Netherlands (7), while the epidemiological data were derived from GP registrations (85-89). Data on the health care burden of chronic diseases comprise data on health care utilization and costs data.
To quantify multidisciplinary health care utilization we used medical record linkage techniques. In addition, we opted for a modeling approach in which all data from various sources were combined, which provided us the opportunity to estimate the chronic disease burden and related costs over time.

Medical record linkage techniques
An efficient and relatively cheap manner to collect health care utilization data is to use existing health care registrations. However, the existing health care registrations were originally set up for administrative reasons rather than for a public health interest (90). As a consequence, the registrations in the Netherlands are event-oriented instead of patient-oriented and comprise data on single health care services (91). Therefore, current studies on health care utilization of chronically ill using existing health care registrations are confined to one health service and provide year-by-year analyses to monitor changes over time. No information is available about multidisciplinary health care utilization. Medical record linkage techniques enable us to reconstruct existing event-oriented registrations into patient-oriented registrations and to create longitudinal datasets needed for the quantification of longitudinal multidisciplinary health care utilization patterns of patients with chronic diseases.

Modeling approach
One of our research questions is to investigate the health care burden of chronic diseases over time. Therefore, we constructed a dynamic model, which is equipped to deal with this time-dimension. A dynamic model is able to comprise multiple states (for instance different health states or smoking and non-smoking states) so that we can estimate the effect of demographic changes and epidemiological changes over time (92). By each step in time, incidence, survival and resulting prevalence are being calculated by taken into account changes in life-style. This modeling approach provides us the opportunity to estimate the future dynamics of chronic disease occurrence and related health care costs while taking into account demographic, epidemiological and organizational shifts in health care. Such models can be helpful in gaining insight into the future health care burden and therefore contribute to a more evidence-based decision making of policy makers (93).

1.4 Outline
To answer the different research questions, we explore in **Chapter 2** the technical possibilities and the problems of linking data on GP referrals with data on hospital admissions and the usefulness of the linked data set for quantifying the health care utilization of patients with chronic conditions.
In chapter 3 and 4, we study the impact of comorbidity (research question 1) and organizational shifts in health care (research question 3) on the health care burden of diabetes mellitus.
In **Chapter 3** we estimate the impact of comorbidity on the use of GP care and hospital care in patients with diabetes mellitus, using medical record linkage techniques.
Chapter 4 investigates the impact of organizational shifts in GP practices with respect to diabetes services. We aimed to identify organizational aspects of diabetes services that reduce medical care utilization of patients with diabetes. We focused on aspects that can be considered as important building blocks of diabetes disease management programs like the presence of a specialized nurse, the implementation of diabetes control schemes and diabetes consultation hours, and the participation of GPs in multidisciplinary meetings.
In chapter 5 till 7, we study all research questions (1-3) related to stroke.
In **Chapter 5**, a model is constructed to estimate the effects of demographic changes and the trends in major risk factors (hypertension and smoking) on the future dynamics of stroke in terms of incidence, prevalence and 'Potential Years of Life Lost' (PYLL).
In **Chapter 6**, a further elaboration of the stroke model is presented. We extended the model with costs estimates for current practice and for stroke disease management programs. The modeling approach will enable us to quantify the impact of a nationwide implementation of stroke services on future costs of stroke.

Chapter 7 presents a review of stroke costs studies. In this review, we systematically compare stroke expenditures in different countries by means of a well-designed checklist. The purpose of this review is to validate the results of the model used in chapter 5 and 6. In this review, we also address the economic implications of changes caused by the rapid international spread of new innovative interventions and to interpret these implications at an international level.
Finally, in **Chapter 8**, we give a summary of the findings and we discuss some methodological issues as well as the implications of our finding for research and policy.

References

(1) Wahdan MH. The epidemiological transition. Eastern Med Health Journal 1996;2(1):8-20.
(2) Caldwell JC. Population health in transition. Bull World Health Organ 2006;2001(79):159-60.
(3) Omran AR. The epidemiologic transition. A theory of the epidemiology of population change. Milbank Mem Fund Q 1971;49(4):509-538.
(4) Omran AR. The epidemiologic transition theory. A preliminary update. J Trop Pediatr 1983; 29(6):305-316.
(5) Olshansky SJ, Ault AB. The fourth stage of the epidemiologic transition: the age of delayed degenerative diseases. Milbank Q 1986;64(3):355-391.
(6) Wolleswinkel-van den Bosch JH, Looman CW, van Poppel FW, Mackenbach JP. Cause-specific mortality trends in The Netherlands, 1875-1992: a formal analysis of the epidemiologic transition. Int J Epidemiol 1997;26(4):772-781.
(7) Statistics Netherlands (CBS). www.cbs.nl/en/statLine/index.htm.2007.
(8) van Poppel FW, Deerenberg I, Wolleswinkel-van den Bosch JH, Ekamper P. Hoe lang leefden wij? Historische veranderingen in de levensduur en het doodsoorzakenpatroon. Bevolkingstrends 2005; 3e kwartaal.
(9) Mathews TJ, Ventura SJ. Birth and Fertility Rates by Educational Attainment: United States, 1994. Monthly Vital Statistics Report 1997;45(10):1-20.
(10) Worldbank. www.worldbank.org/depweb/english/beyond/beyondco/beg_03.pdf. 2004. New York, Worldbank.
(11) Eurostat. Population projections 2004-2050. Eurostat News release 2005; 48.
(12) Hollander AEM de, Hoeijmans N, Melse JM, Oers van JAM, Polder JJ. Zorg voor gezondheid, Volksgezondheid Toekomst Verkenning 2006. [Care for health. The 2006 Dutch health status and forecasts]. RIVM rapportnr. 270061003/2006. 2006. Bilthoven, RIVM.
(13) Niessen LW, Barendregt JJ, Bonneux L, Koudstaal PJ. Stroke trends in an aging population. The Technology Assessment Methods Project Team. Stroke 1993;24(7):931-9.
(14) Blokstra A, Baan CA, Boshuizen HC, Feenstra TL, Hoogenveen RT, Picavet HSJ et al. Vergrijzing en toekomstige ziektelast. Prognose chronische ziektenprevalentie 2005-2025 [Impact of the ageing population on burden of disease. Projections of chronic disease prevalence for 2005-2025]. RIVM rapport 260401004. 2007. Bilthoven, RIVM.
(15) Poortvliet MC, Schrijvers CTM, Baan CA. Diabetes in Nederland. Omvang, risicofactoren en gevolgen, nu en in de toekomst [Diabetes in the Netherlands]. RIVM rapportnr. 260322001. 2007. Bilthoven, RIVM.
(16) Feenstra TL, van Genugten ML, Hoogenveen RT, Wouters EF, Rutten-Van Molken MP. The impact of aging and smoking on the future burden of chronic obstructive pulmonary disease: a model analysis in the Netherlands. Am J Respir Crit Care Med 2001;164(4):590-596.

(17) Hoogendoorn M, Feenstra TL, Rutten-Van Molken MP. Toekomstprojecties van het zorggebruik van en de kosten van astma en COPD in Nederland. [Projections of future resource use and the costs of asthma and COPD in the Netherlands]. Ned Tijdschr Geneeskd 2006; 150(22):1243-1250.
(18) Hoogendoorn M, Rutten-Van Molken MP, Hoogenveen RT, van Genugten ML, Buist AS, Wouters EF et al. A dynamic population model of disease progression in COPD. Eur Respir J 2005; 26(2):223-233.
(19) Van den Akker M, Buntinx F, Metsemakers JF, Roos S, Knottnerus JA. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. J Clin Epidemiol 1998;51(5):367-375.
(20) Rupp I, Boshuizen HC, Jacobi CE, Dinant HJ, van den BG. Comorbidity in patients with rheumatoid arthritis: effect on health-related quality of life. J Rheumatol 2004;31(1):58-65.
(21) Schellevis FG. Chronic diseases in general practice. Comorbidity and quality of life [thesis]. 1993. Nijmegen, University of Nijmegen.
(22) Gijsen R, Hoeymans N, Schellevis FG, Ruwaard D, Satariano WA, van den Bos GAM. Causes and consequences of comorbidity: a review. J Clin Epidemiol 2001;54(7):661-74.
(23) van Weel C, Schellevis FG. Comorbidity and guidelines: conflicting interests. Lancet 2006; 367(9510):550-551.
(24) Heijmans MJWM, Rijken PM, Schellevis FG, van den Bos GAM. Meer dan een ziekte. De gevolgen van comorbiditeit vanuit het perspectief van chronisch zieken en gehandicapten. 2003. NIVEL/RIVM/AMC.
(25) Feinstein A. Clinical judgement. New York: The Williams & Wilkins Company, 1967.
(26) Shwartz M, Iezzoni LI, Moskowitz MA, Ash AS, Sawitz E. The importance of comorbidities in explaining differences in patient costs. Med Care 1996;34(8):767-782.
(27) Cramer JA, Blum D, Fanning K, Reed M. The impact of comorbid depression on health resource utilization in a community sample of people with epilepsy. Epilepsy Behav 2004;5(3):337-342.
(28) Maddigan SL, Feeny DH, Johnson JA. Health-related quality of life deficits associated with diabetes and comorbidities in a Canadian National Population Health Survey. Qual Life Res 2005;14(5):1311-1320.
(29) Sullivan PW, Morrato EH, Ghushchyan V, Wyatt HR, Hill JO. Obesity, inactivity, and the prevalence of diabetes and diabetes-related cardiovascular comorbidities in the U.S., 2000-2002. Diabetes Care 2005;28(7):1599-1603.
(30) World Health Organization, Public Health Agency of Canada. Preventing Chronic diseases a vital investment: WHO global report. 2005. Geneve, Switzerland, WHO.
(31) Ministerie van VWS. Preventienota Kiezen voor gezond leven. PG/OGZ/2.720.104. 6-10-2006. Den Haag, Ministerie van VWS.
(32) Ministerie van VWS. Plan van aanpak 'Diabeteszorg beter'. PG/ZP 2.546.925. 17-2-2005. Den Haag, Ministerie van VWS.
(33) Steuten LMG. Evaluation of Disease Management programmes for chronically ill [thesis]. 2006. Maastricht, University Maastricht.
(34) Rosendal H, van Beekum WT, van der Linden BA, Schrijvers AJP. De effectiviteit van transmurale zorg: een literatuurstudie naar de stand van zaken van in Nederland. Tijdschrift voor Sociale Geneeskunde 2000;78(7):426-431.
(35) van der Linden BA, Spreeuwenberg C, Schrijvers AJ. Integration of care in The Netherlands: the development of transmural care since 1994. Health Policy 2001;55(2):111-120.

(36) Hofmarcher MM, Oxley H, Rusticelli E. Improved health system performance through better care coordination. OECD Health Working Paper no. 30. 2007. Paris, OECD.
(37) Gillies CL, Abrams KR, Lambert PC, Cooper NJ, Sutton AJ, Hsu RT et al. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. BMJ 2007;334(7588):299.
(38) Visscher TLS (VUmc) VARBCvdR. Hoeveel mensen hebben overgewicht of ondergewicht? In: Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid. Bilthoven: RIVM, <http://www.nationaalkompas.nl> Gezondheidsdeterminanten\ Persoonsgebonden\ Lichaamsgewicht, 4 juli 2007.
(39) Centraal Bureau voor de Statistiek (CBS). Permanent Onderzoek Leefsituatie gezondheid en welzijn (POLS). 2006. Voorburg/Heerlen, CBS.
(40) Bemelmans WJE, Hoogenveen RT, Visscher TL, Verschuren WM, Schuit AJ. Toekomstige ontwikkelingen in matig overgewicht en obesitas. Inschatting effecten op de volksgezondheid. [Future developments in overweight - Estimating effects on public health]. RIVM rapportnr. 260301003/2004. 2004. Bilthoven, RIVM.
(41) Bundred P, Kitchiner D, Buchan I. Prevalence of overweight and obese children between 1989 and 1998: population based series of cross sectional studies. BMJ 2001;322(7282):326-328.
(42) Dietz WH. Childhood weight affects adult morbidity and mortality. J Nutr 1998;128(2 Suppl): 411S-414S.
(43) Dabelea D, Snell-Bergeon JK, Hartsfield CL, Bischoff KJ, Hamman RF, McDuffie RS. Increasing prevalence of gestational diabetes mellitus (GDM) over time and by birth cohort: Kaiser Permanente of Colorado GDM Screening Program. Diabetes Care 2005;28(3):579-584.
(44) Hildebrandt VH, Ooijendijk WTM, Hopman-Rock M. Trendrapport Bewegen en gezondheid 2004/2005. TNO Kwaliteit van Leven. 2007. Leiden, TNO Kwaliteit van Leven.
(45) Kemper HGC, Ooijendijk WTM, Stiggelbout M. Consensus over de Nederlandse Norm voor Gezond Bewegen. Tijdschr Soc Gezondheidsz 2000;78:180-183.
(46) Kesaniemi YK, Danforth E Jr, Jensen MD, Kopelman PG, Lefebvre P, Reeder BA. Dose-response issues concerning physical activity and health: an evidence-based symposium. Med Sci Sports Exerc 2001;33(6 Suppl):S351-S358.
(47) Haskell WL. J.B. Wolffe Memorial Lecture. Health consequences of physical activity: understanding and challenges regarding dose-response. Med Sci Sports Exerc 1994;26(6):649-660.
(48) Willemsen MC (STIVORO). Neemt het aantal mensen dat rookt toe of af? In: Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid. 2007. Bilthoven, RIVM, <http://www.nationaalkompas.nl> Gezondheidsdeterminanten\ Leefstijl\ Roken, 16 mei 2005.
(49) van Exel JNJA, Koopmanschap M.A., van Wijngaarden JDH, Scholte op Reimer WJM. Costs of stroke and stroke services: Determinants of patient costs and and a comparison of costs of regular care and care organised in stroke services. Cost effectiveness and Resource Allocation 2003;1(2).
(50) van Exel NJ, Koopmanschap MA, Scholte op RW, Niessen LW, Huijsman R. Cost-effectiveness of integrated stroke services. QJM 2005;98(6):415-425.
(51) Baan CA, Hutten JBF, Rijken PM (red.). Afstemming in de zorg. Een achtergrondstudie naar de zorg voor mensen met een chronische aandoening. [Coordination of Care. A srudy into the care for patients with a chronic condition]. RIVM rapportnr. 282701005. 2003. Bilthoven, RIVM/Nivel.
(52) Vrijhoef HJ, Spreeuwenberg C, Eijkelberg IM, Wolffenbuttel BH, van Merode GG. Adoption of disease management model for diabetes in region of Maastricht. BMJ 2001;323(7319):983-985.

(53) Plochg T. Building a tower of Babel in health care? Theory & practice of community-based integrated care [thesis]. 2006. Amsterdam, University of Amsterdam.
(54) Rosendal H. Comparative cohort studies in transmural care. Three cases of structurally embedded practice in The Netherlands [thesis]. Utrecht, Utrecht University, 2002.
(55) Vondeling H. Economic evaluation of integrated care: an introduction. International Journal of Integrated Care 2004; 4:e20.Epub 2004.
(56) Kodner DL, Spreeuwenberg C. Integrated care: Meaning, logic, applications, and implications: A discussion paper. International Journal of Integrated Care 2002; 2.
(57) Hardy B, Mur-Veemanu I, Steenbergen M, Wistow G. Inter-agency services in England and The Netherlands. A comparative study of integrated care development and delivery. Health Policy 1999;48(2):87-105.
(58) Schrijvers AJP. Disease management in de Nederlandse context. Utrecht: Igitur, publishing and archiving services, 2006.
(59) Inspectie voor de Gezondheidszorg (IGZ). Staat van de gezondheidszorg 2003. Ketenzorg bij chronisch zieken. 2003. Den Haag, IGZ.
(60) Struijs JN, Westert GP, Baan CA. Effectevaluatie van transmurale diabeteszorg in Nederland. [Effectevaluation of transmural diabets care in the Netherlands]. RIVM rapportnr. 260402001/2004. 2005. Bilthoven, RIVM.
(61) Huijsman R, Klazinga NS, Scholte op Reimer WJM, van Wijngaarden JDH, van Exel NJA, van Putte-Boon C, et al. Beroerte, beroering en borging in de keten. [Resultsof the Edisse-studyof three regional experiments with stroke-services]. Rotterdam: Erasmus Universiteit Rotterdam, 2001.
(62) de Sonnaville JJ, Bouma M, Colly LP, Deville W, Wijkel D, Heine RJ. Sustained good glycaemic control in NIDDM patients by implementation of structured care in general practice: 2-year follow-up study. Diabetologia 1997;40(11):1334-1340.
(63) Vrijhoef HJ, Diederiks JP, Spreeuwenberg C, Wolffenbuttel BH. Substitution model with central role for nurse specialist is justified in the care for stable type 2 diabetic outpatients. J Adv Nurs 2001;36(4):546-555.
(64) Weinberger M, Kirkman MS, Samsa GP, Shortliffe EA, Landsman PB, Cowper PA et al. A nurse-coordinated intervention for primary care patients with non-insulin-dependent diabetes mellitus: impact on glycemic control and health-related quality of life. J Gen Intern Med 1995; 10(2):59-66.
(65) Peters AL, Davidson MB. Application of a diabetes managed care program. The feasibility of using nurses and a computer system to provide effective care. Diabetes Care 1998;21(7):1037-1043.
(66) De Berardis G, Pellegrini F, Franciosi M, Belfiglio M, Di Nardo B, Greenfield S et al. Quality of care and outcomes in type 2 diabetic patients: a comparison between general practice and diabetes clinics. Diabetes Care 2004;27(2):398-406.
(67) Trento M, Passera P, Tomalino M, Bajardi M, Pomero F, Allione A et al. Group visits improve metabolic control in type 2 diabetes: a 2-year follow-up. Diabetes Care 2001;24(6):995-1000.
(68) Sperl-Hillen J, O'Connor PJ, Carlson RR, Lawson TB, Halstenson C, Crowson T et al. Improving diabetes care in a large health care system: an enhanced primary care approach. Jt Comm J Qual Improv 2000;26(11):615-622.
(69) Ciardullo AV, Daghio MM, Brunetti M, Bevini M, Daya G, Feltri G et al. Changes in long-term glycemic control and performance indicators in a cohort of type 2 diabetic patients cared for by general practitioners: findings from the "Modena Diabetes Project". Nutr Metab Cardiovasc Dis 2003;13(6):372-376.

(70) Gary TL, Bone LR, Hill MN, Levine DM, McGuire M, Saudek C et al. Randomized controlled trial of the effects of nurse case manager and community health worker interventions on risk factors for diabetes-related complications in urban African Americans. Prev Med 2003;37(1):23-32.
(71) Renders CM, Valk GD, Franse LV, Schellevis FG, van Eijk JT, van der Wal G. Long-term effectiveness of a quality improvement program for patients with type 2 diabetes in general practice. Diabetes Care 2001;24(8):1365-1370.
(72) Rosendal H, Vondeling H, de Witte LP, Hutubessy RC, van Beekum WT, Heine RJ. Het instellen op insuline van patiënten met diabetes mellitus type 2: in een transmurale organisatievorm minstens even effectief als poliklinisch; een retrospectief onderzoek met 4 jaar follow-up. Ned Tijdschr Geneeskd 2002;146(4):166-171.
(73) Ho M, Marger M, Beart J, Yip I, Shekelle P. Is the quality of diabetes care better in a diabetes clinic or in a general medicine clinic? Diabetes Care 1997;20(4):472-475.
(74) Griffin S. Diabetes care in general practice: meta-analysis of randomised control trials. BMJ 1998;317(7155):390-396.
(75) McDermott RA, Schmidt BA, Sinha A, Mills P. Improving diabetes care in the primary healthcare setting: a randomised cluster trial in remote Indigenous communities. Med J Aust 2001;174(10):497-502.
(76) McClellan WM, Millman L, Presley R, Couzins J, Flanders WD. Improved diabetes care by primary care physicians: results of a group-randomized evaluation of the Medicare Health Care Quality Improvement Program (HCQIP). J Clin Epidemiol 2003;56(12):1210-1217.
(77) Goldberg HI, Neighbor WE, Hirsch IB, Cheadle AD, Ramsey SD, Gore E. Evidence-based management: using serial firm trials to improve diabetes care quality. Jt Comm J Qual Improv 2002;28(4):155-166.
(78) Wandell PE, Gafvels C. Metabolic control and quality of data in medical records for subjects with type 2 diabetes in Swedish primary care: improvement between 1995 and 2001. Scand J Prim Health Care 2002;20(4):230-235.
(79) Ilag LL, Martin CL, Tabaei BP, Isaman DJ, Burke R, Greene DA et al. Improving diabetes processes of care in managed care. Diabetes Care 2003;26(10):2722-2727.
(80) Olivarius NF, Beck-Nielsen H, Andreasen AH, Horder M, Pedersen PA. Randomised controlled trial of structured personal care of type 2 diabetes mellitus. BMJ 2001;323(7319):970-975.
(81) Langhorne P, Taylor G, Murray G, Dennis M, Anderson C, Bautz-Holter E et al. Early supported discharge services for stroke patients: a meta-analysis of individual patients' data. Lancet 2005; 365(9458):501-506.
(82) Slobbe LCJ, Kommer GJ, Smit JM, Groen J, Meerding WJ, Polder JJ. Kosten van Ziekten in Nederland 2003; Zorg voor euro's. [Cost of illness in the Netherlands 2003]. RIVM rapportnr. 270751010. 2006. Bilthoven, RIVM.
(83) Poos MJJC, Gijsen R. Achtergronden en details bij cijfers uit huisartsenregistraties. In: Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid. 2006. Bilthoven, RIVM.
(84) Raad voor de Volksgezondheid & Zorg (RVZ). Arbeidsmarkt en zorgvraag. Achtergrondstudies. 2006. Den Haag, RVZ.
(85) Lisdonk Evd, van den Bosch WJHM, Huygen FJA, Lagro-Janssen ALM. Ziekten in de huisartspraktijk. Derde herziene druk. Maarssen: Elsevier/Bunge, 1999.
(86) Meer V van der, Waal MWM de, Timmers AP, Bock GH de, Springer MP. Hoe up-to-date is het medisch dossier? Een onderzoek op vijf lokaties [in Dutch]. Huisarts en Wetenschap 2001; 44:194-197.

(87) Metsemakers JFM. Unlocking patients'records in general practice for research, medical education and quality assurance: the Registration Network Family Practices. Maastricht University, 1994.
(88) Okkes IM, Polderman GO, Fryer GE, Yamada T, Bujak M. The role of family practice in different health care systems. A comparison of reasons for encounter, diagnosis, and interventions in primary care populations in the Netherlands, Japan, Poland and the United States. J Fam Pract 2002;51:72-73.
(89) Westert GP, Schellevis FG, De Bakker DH, Groenewegen PP, Bensing JM, van der Zee J. Monitoring health inequalities through general practice: the Second Dutch National Survey of General Practice. Eur J Public Health 2005;15(1):59-65.
(90) Reitsma JB, Bonsel GJ, Heisterkamp SH. Registers in cardiovascular Epidemiology. Registers in Cardiovascular Epidemiology [thesis]. Enschede: PrintPartners Ipskamp, 1999.
(91) de Bruin A, de Bruin EI, Projectgroep ontwikkeling GezondheidsStatisch Bestand. Koppeling van LMR- en GBA gegevens: methode, resultaten en kwaliteitsonderzoek. Rapportnr. 6008703010. 2003. Voorburg/Heerlen, Centraal Bureau voor de Statistiek.
(92) Nusselder WJ. Compression or expansion of morbidity? A life-table approach [thesis]. Erasmus University Rotterdam, Rotterdam, the Netherlands, 1998.
(93) Bonneux L, Barendregt JJ, Nusselder WJ, der Maas PJ. Preventing fatal diseases increases healthcare costs: cause elimination life table approach. BMJ 1998;316(7124):26-9.