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Comorbidity of chronic diseases

EFFECTS OF DISEASE PAIRS ON PHYSICAL AND MENTAL FUNCTIONING

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ABSTRACT

Although much research has been done on the impact of chronic illness on quality of life, still relatively little is known about the role of comorbidity. Given the growing number of (older) people with multiple chronic conditions, more information is needed on the effects of specific disease combinations for preventive purposes. In a nationwide representative sample of 1673 non-institutionalized chronic disease patients (recruited in 56 general practices) in The Netherlands, we assessed the separate and joint effects of cardiovascular disease, cancer, arthritis, chronic respiratory disease, diabetes mellitus, and thyroid dysfunction on physical and mental functioning. Data on medical diagnoses were provided by the general practitioners; data on physical and mental functioning were collected by a patient survey (SF-36). Compared to reference data of the general population, physical functioning appeared to be worse in all six diagnostic groups, whereas mental functioning was more or less comparable. Patients with arthritis or those suffering from comorbidity reported the lowest levels of physical functioning. Synergistic effects of combinations of diabetes, cardiovascular disease and/or chronic respiratory disease were found, indicating that patients suffering from these disease combinations run a higher risk of physical disability than could be expected from their separate effects.

INTRODUCTION

Chronic diseases are considered major threats to the quality of life of western populations. In the Netherlands, it has been estimated that at least 10% of the total population is diagnosed with a chronic disease [1]. Since prevalence rates of most chronic diseases increase with age, a substantial part of the elderly population suffers from more than one chronic disease (e.g. [2]). Nevertheless, most studies on the consequences of chronic disease are directed to one chronic disease in particular. The presence of comorbidity complicates the question how a specific disease is related to outcome variables such as functional status or quality of life. Therefore, in clinical research patients with comorbid conditions are usually excluded from the sample. The growing number of (older) people with multiple chronic diseases urges however for more scientific knowledge of the impact of co-occurring chronic diseases on quality of life [3–5]. This paper was aimed to contribute to this knowledge, more specifically of the effects of somatic chronic disease pairs on physical and mental functioning.

Gijsen et al. reviewed studies published between 1993 and 1997 on the consequences of comorbidity [5]. Taking this period into account, they found 14 papers in which the impact of specific disease pairs on quality of life was assessed. Of these 14 papers, nine were exclusively concerned with aspects of physical functioning or disability as outcome variables, the other five also described the effects on mental and social functioning. In three studies, the presence of comorbid conditions was not related to functional status or quality of life. The other 11 studies showed that all, or at least some, comorbid conditions increased the risk for impaired functional status or poor quality of life. In the case of diabetes mellitus, Parkinson's disease or respiratory diseases, all comorbid conditions that were studied increased the risk of impaired physical functioning or quality of life. For cancer,

cardiovascular diseases and musculoskeletal disorders, the effect depended on the specific cooccurring disease that was taken into account.

More recently, Heijmans and colleagues repeated the literature search of Gijsen et al. over the period 1998–2001 [6]. They found 17 papers in which the relationships between specific disease pairs and quality of life were described. Still, in most studies (n = 10) only physical functioning was taken into account; seven studies also addressed the consequences of the comorbid conditions on mental and/or social functioning. Again, negative effects of comorbidity were found in all studies where diabetes, neurological disorders and respiratory diseases were included, whereas in the case of cancer, cardiovascular diseases and musculoskeletal disorders, the effect depended on the type of comorbid condition that was involved.

Specific combinations of chronic diseases may not only have additive effects, but also synergistic effects. Knowledge of the specific disease combinations that lead to increased deterioration is very important for individual patient care as well as for public health purposes. Gijsen et al. [5] found two studies in which synergistic effects were studied. Both papers were concerned with the functional status of patients with osteoarthritis [7, 8]. Significant exacerbating effects on physical disability were found for osteoarthritis in combination with visual impairment, hip fracture, atherosclerosis, ischemic heart disease, pulmonary disease and obesity, whereas the combination of osteoarthritis and hypertension had a damping effect on disability. A more recent study showing the surplus value of assessing synergistic effects is the study of Fried et al. [9]. Investigating a sample of 3841 women aged 65 years and older living in Baltimore, they found the following combinations of diseases to have both additive and synergistic effects on physical disability: arthritis together with visual impairment, arthritis and hypertension, heart disease and cancer, lung disease and cancer, and stroke and hypertension.

In the study of Fried and colleagues, the absence or presence of the chronic conditions in the research sample was based on self-report as was the case with the assessment of functional disability. A disadvantage of this approach is that there may be some common variance in the assessment of chronic conditions and disability that can be explained by personal or mood characteristics. This may result in an overestimation of the impact of multiple chronic conditions on functional status or quality of life.

In the study presented here, we obtained independent assessments of chronic diseases (medical diagnoses registered by general practitioners (GPs)) and functional status (self-report by patients). Based on these data, we wished to assess the separate and joint effects of co-occurring chronic diseases on both physical and mental functioning. For preventive purposes, we believe there is a strong need to further extend the knowledge on the relationship between specific somatic disease pairs and mental functioning, since chronically ill patients are known to run a higher risk of psychiatric morbidity (e.g. [10, 11]), but the psychological consequences of comorbidity are not yet clear.

METHODS

Sample

Subjects of this study were selected from a nationwide representative database of the 'Panel of Patients with Chronic Diseases', a prospective panel study on the consequences of chronic illness in the Netherlands. All patients were recruited *via* 56 general practices randomly selected from the national Register of General Practitioners. It should be noted that virtually all non-institutionalized people in the Netherlands subscribe to a general practice. These general practices can be considered the central sources of medical information, since GPs keep lifelong files of their patients which are carried over in case the patient is moving house.

In each practice, GPs screened a random sample of 36% of the patient files with the help of a trained research assistant, in order to guarantee uniform application of the selection criteria. Inclusion criteria were: a diagnosis of a somatic disease defined as chronic[1] by the Netherlands Classification and Terminology Committee for Health [12] or a diagnosis of a somatic disease not chronic by definition, but with symptoms known by the GP for at least one year. Exclusion criteria were: aged younger than

[1] According to this committee, chronic diseases can be distinguished from acute diseases by their course (irreversible, no cure), their duration (life-long, life expectancy >6 months) and their severity or burden (in terms of disability, health care utilization and self-management).

15 years, institutionalized, not yet informed about the diagnosis, terminally ill, unable to read or write (even with help), and having insufficient mastery of the Dutch language.

During the period November 1997–February 1998 a total of 53,648 patient files were screened (on average 958 per practice). In this way 5228 chronic disease patients (9.7%) were selected and invited to participate in the panel. Participation comprised filling in postal questionnaires twice a year (April and October) during three years and being interviewed by telephone incidentally. A total of 2992 (57.2%) agreed to participate. Those who agreed to participate did not differ significantly from the non-participants with regard to their health status as registered by their GP: disease types, illness duration, comorbidity, assessment of the degree in which their health status was (1) lifethreatening, (2) progressively deteriorating, (3) intercurrent, (4) controllable by medical care, (5) controllable by self-care, and the degree in which they had experienced (6) visible physical changes, (7) disability in social functioning, and (8) disability in mental functioning ($p > 0.05$). However, panel members were assessed by their GPs to have slightly more pain ($p < 0.001$) and more physical disability ($p = 0.003$). More than 90% of the panel members reported to visit their GP at least once a year; the mean number of consultations per year varied from 4.5 (95% CI: 3.4–5.5) in patients with neurological diseases to 6.3 (95% CI: 5.1–7.5) in patients with chronic digestive disorders [14].

In this paper we used data of the first survey among the patients (April 1998), in addition to the data registered by the GPs at inclusion. Net response rate to this survey was 83.1. Those who did not respond to the survey were comparable with the respondents with regard to the disease and illness characteristics as assessed by their GP (to what extent their illness was life-threatening, the course and controllability of the illness, pain, disability, etc.) ($p > 0.05$). For the purpose of this study, we selected diagnoses that occurred in at least 100 members of the panel. As a result, the sample of this study consisted of 1673 patients with a diagnosis of cardiovascular disease, cancer, arthritis, chronic respiratory disease, diabetes mellitus, and/or thyroid dysfunction (see Box 1 for diagnoses).

[BOX 1]

Measuring instruments

GPs could register up to four somatic diseases that met the above-mentioned criteria of non-curability or generally long-lasting, and coded these diseases according to the International Classification of Primary Care [15].

Physical and mental functioning was assessed by the SF-36, a generic measure of self-reported health status which contains 36 items and which was initially designed to tap eight dimensions of functioning and well-being [16, 17]. Ware and colleagues later argued that a reduction of dimensions would be useful in order to reduce the necessary statistical analyses and thus the role of chance in these analyses. For this reason, they employed statistical procedures to reduce the number of dimensions on the SF-36 to two summary scores comprising the eight dimensions: a Physical Component Summary scale (PCS) and a Mental Component Summary scale (MCS) [18, 19]. Results from the PCS and MCS have been standardized on the basis of a normative US general population data set, with the mean set at 50 (SD 10). This standardization facilitates interpretation, because when the scoring algorithms are applied to other data sets, scores above 50 indicate better health than the mean of the general population, while scores below 50 indicate worse health.

We used a Dutch version of the SF-36 that had been developed and documented by Van der Zee, et al. [20]. Results from a study performed by Aaronson et al. [21] in a representative sample of the Netherlands population showed that the mean scores and standard deviations of the various dimensions only slightly differ from the mean scores found by Ware and colleagues in their Medical Outcomes Study. For the reason of international comparability, we therefore decided to standardize our scores on the basis of the original American data set.

Data analysis

We computed the number of patients suffering from each of the six chronic diseases as well as percentages of patients with comorbidity for each disease category separately. For this purpose, comorbidity was defined in two ways: (1) the presence of any other chronic somatic disease besides the disease under study, and (2) the presence of one (or more) of the other selected diseases besides the disease under study.

Next, we computed PCS and MCS average scores and standard deviations for each of the six diseases. In the case of missing values, the series mean was imputed. The mean number of missing values replaced per item was 171 (range 14–270). By computing separate scores for patients with and without comorbidity, we assessed the impact of comorbidity on physical and mental health disregarding the nature of the co-occurring disease(s). *T*-tests for independent samples were performed in order to test the difference in PCS and MCS scores between patients with and without comorbidity.

Finally, we assessed the additive and multiplicative effects of specific combinations of diseases. Two linear regression models were assessed for each disease pair. In the first model, two chronic disease variables were entered together with their product (independent variables) in order to assess their main and interaction effects on PCS and on MCS (dependent variables). In the second model, age and gender were added as independent variables, besides the two chronic diseases and their product. By comparing the results of these two regression analyses, we were able to determine whether the separate and joint effects of chronic diseases reflected the effects of age and gender related to the occurrence of specific chronic diseases or whether these diseases were associated with physical and mental functioning above the age and gender effects.

RESULTS

Characteristics of the sample

The sample of 1673 chronic disease patients had a mean age of 58.5 years (SD 15.8 years). The minimum age was 15 years (pre-set selection criterion) and maximum age was 92 years. Fifty-four percent of the patients were female. The majority of the patients (74%) was married or cohabited. With regard to educational level, 48% had a low educational level, 39% had been moderately educated and 13% had higher vocational education or university. The average illness duration (time postdiagnosis) at inclusion was 9.8 years (SD 8.6 years).

Morbidity and comorbidity

The GPs registered on the average 1.34 (SD = 0.20) diagnoses per patient. Table 1 shows that most patients were diagnosed with chronic respiratory disease (n = 525), cardiovascular disease (n = 373), diabetes mellitus (n = 368), and/or arthritis (n = 366). Cardiovascular disease had the highest rates of comorbidity; more than half (57%) of the patients with cardiovascular disease were diagnosed with at least one other chronic somatic disease and one third (34%) was diagnosed with one or more of the other five diseases selected for this study. Among the six selected diseases, the lowest rates of comorbidity were found in patients with chronic respiratory disease and arthritis.

[TABLE 1]

Patients suffering from comorbidity (of selected diseases) were usually diagnosed with two chronic diseases (n = 207); 13 patients had three of the selected diseases and one patient suffered from four of the six selected diseases. Patients with more than two of the selected diseases (n = 14) were excluded from further analyses; thus 1659 patients were involved in the analyses of specific disease combinations. The disease pairs ‘diabetes–cardiovascular disease’ (n = 39) and ‘cardiovascular disease– chronic respiratory disease’ (n = 38) were the most common in our patient sample. Both disease pairs are well-known in chronic disease patients.

PCS and MCS scores

Table 2 shows the mean scores (and standard deviations) on PCS and MCS per disease category for patients without and with comorbidity, disregarding the specific nature of the co-occurring disease(s). Taking a score of 50 as the norm of the general US population, the table shows that patients with all selected diseases reported worse physical functioning (PCS). Patients suffering from thyroid dysfunction reported the highest scores, and those with arthritis the lowest scores on PCS. When comparing PCS scores of patients without and with comorbidity of any chronic disease, significant differences were found for cardiovascular disease, chronic respiratory disease, diabetes, and thyroid dysfunction ($p < 0.001$). When confining the comorbid conditions to the six selected diseases, the difference between cancer patients with and without comorbidity on PCS was also significant ($p <$

0.01). In all cases, average scores of patients with comorbidity were lower than of those without comorbidity.

[TABLE 2]

Table 2 also shows that MCS mean scores were close to 50, indicating that mental functioning was only slightly worse than in the general US population. Patients diagnosed with more than one chronic disease did not have lower MCS scores than patients without comorbidity.

Separate and joint effects of specific chronic diseases

Table 3 contains the results of the linear regression analyses with PCS and MCS as outcome variables.[2] Beta-coefficients (and significance levels) of age, gender and chronic diseases (main effects) and their product (interaction effect) are presented.

[TABLE 3]

Linear regression analyses with *PCS* being the dependent variable (Model 1) show that significant main effects were found for all selected diseases in at least some combinations. One has to consider that all patients in our sample suffered from chronic disease. Thus, the main effects indicate the effects of particular chronic diseases compared to other chronic diseases. Taking this into consideration, the results of Model 1 show that arthritis has the most substantial negative effect on physical functioning (betas – indicating change per year – vary from –0.20 to –0.25, $p < 0.001$). In three combinations of chronic diseases significant interaction effects were found on PCS: cardiovascular disease–chronic respiratory disease, chronic respiratory disease–diabetes, and diabetes–thyroid dysfunction (all negative interaction effects).

When age and gender are included (Model 2), the main and interaction effects of chronic diseases on PCS change quite a lot. In all analyses, age appeared to be most strongly related to physical functioning (betas vary from –0.27 to –0.31, $p < 0.001$). Gender also has significant main effects on PCS (betas vary from –0.11 to –0.16, $p < 0.001$). Thus, older and/or female patients report worse physical functioning. When we consider the effects of specific chronic disease pairs, there are four combinations of diseases in which small synergistic effects come to the fore. We will describe these four combinations in more detail below:

Cardiovascular disease–arthritis: In this disease pair, cardiovascular disease does not have a significant main effect (after inclusion of age and gender), but arthritis still has a negative main effect on physical functioning. Their joint effect is however less negative due to the small positive interaction effect. Thus, patients suffering from cardiovascular disease in combination with arthritis report less physical disability than could be expected from the effects of these two diseases separately.

Cardiovascular disease–chronic respiratory disease: In this combination, again cardiovascular disease does not have a significant main effect on PCS. Thus, in general, patients with cardiovascular disease report equal levels of physical functioning as other chronic disease patients do. However, chronic respiratory disease has a negative main effect, indicating that patients diagnosed with this disease report worse physical functioning than other chronic disease patients. In combination with cardiovascular disease, their perceived physical health is even more impaired due to the negative synergistic effect of this combination.

Diabetes mellitus–cardiovascular disease: This combination consists of a disease that does not have a significant main effect (cardiovascular disease) and a disease with a positive main effect (diabetes). These main effects suggest that patients with cardiovascular disease report equal levels of physical functioning than other chronic disease patients, whereas diabetics report relatively better physical functioning. However, patients with diabetes who also suffer from cardiovascular disease are doing less well, illustrated by the negative interaction effect.

Chronic respiratory disease–diabetes mellitus: This combination shows again the negative main effect of respiratory disease and the positive main effect of diabetes. The negative interaction effect

[2] These linear regression analyses were performed only for disease pairs that occurred together in at least ten patients. Consequently, 7 out of 15 possible disease combinations were analysed.

signifies that diabetes mellitus in combination with chronic respiratory disease more seriously affects physical functioning than could be expected from their separate effects.

The results of the linear regression analyses with *MCS* being the dependent variable (Model 1) show that, in general, mental functioning is not related to the type of chronic disease the patient is suffering from nor to the absence or presence of comorbidity. The only exception is the negative main effect of thyroid dysfunction, indicating that patients with thyroid dysfunction report worse mental health compared to other chronic disease patients.

When age and gender are included in the analyses (Model 2), the negative main effect of thyroid dysfunction, although still significant, slightly decreases. This implies that the negative effect of thyroid dysfunction on mental functioning is partly due to a negative gender effect (being female). Gender appeared to be related to mental functioning (betas vary from –0.05 to –0.06, $p < 0.05$): women with chronic diseases report lower MCS scores than men. Age is also related to mental functioning (betas vary from 0.10 to 0.11, $p < 0.001$): older chronic disease patients report better mental health than younger patients.

DISCUSSION

In this study the relationship between somatic chronic disease and physical and mental functioning was examined with special attention for the co-occurrence of chronic diseases within the same person. Before studying the impact of specific disease combinations, we first assessed the impact of chronic diseases with and without unspecified comorbidity on physical and mental functioning. Our findings show that patients with a medical diagnosis of chronic disease report worse physical functioning than the US general population regardless of the specific chronic disease under study. Furthermore, patients with comorbid conditions perceive their physical functioning as poor. Patients suffering from arthritis (with or without comorbidity) report the worst physical functioning. With regard to mental functioning, average scores on MCS were close to 50 suggesting that mental health was not much affected. The lowest scores on MCS were reported by patients suffering from thyroid dysfunction. Unspecified comorbidity was not related to more impaired mental functioning.

In general, our PCS scores were somewhat lower than the American norm scores for chronically ill patients provided by Ware et al. [18]. The average scores they report for cancer patients, patients with chronic lung disease and arthritis are 45.1, 42.3 and 43.2 respectively. In our study we found average scores of 41.8 (cancer), 40.9 (chronic respiratory disease), and 36.5 (arthritis) in patients without comorbidity and even lower scores in patients with comorbidity. One should bear in mind, however, that a medical diagnosis of a chronic disease, which was used in our study, may deviate substantially from the assessment of a chronic condition by means of self-report as had been applied by Ware and colleagues. The mean PCS score they found for diabetics ($M = 39.3$) was more comparable with ours (43.1 in patients without comorbidity and 38.3 in patients with comorbidity). In the case of diabetes, more similarity has been found between self-report and medical registration than in the case of several other diseases [22, 23]. Fanuele et al. [24] report an average PCS score of 38.4 for cancer patients [25] and 33.9 for patients with COPD (chronic obstructive pulmonary disease) [26], thus a fraction lower than the scores we found, but these studies include specialists' patients instead of primary care patients.

With regard to MCS, scores of our patients with chronic respiratory disease ($M = 47.1$) were higher than the scores found by Ware and colleagues in patients with chronic lung disease ($M = 44.5$). In the case of cancer, arthritis and diabetes mellitus the deviations between our scores and theirs were smaller. We found average scores of 47.4 (cancer), 48.0 (arthritis) and 47.3 (diabetes) in patients without comorbidity, whereas Ware et al., report 48.8, 48.8 and 47.9 respectively.

Next, we assessed the separate and joint effects of specific combinations of chronic diseases (without and with the effects of age and gender) by means of linear regression analysis. Before discussing the findings of these analyses, it should be mentioned that non-significant main and interaction effects do not mean that physical or mental functioning is not affected by chronic disease. Since our sample exclusively consisted of chronic disease patients, the effect of a particular chronic disease was assessed compared to the effect of other chronic diseases.

In general, we found several significant main effects of the selected chronic diseases on physical functioning, but not on mental functioning. With regard to the main effects on physical health, especially arthritis has a substantial negative effect on physical functioning. The main effects of

diabetes mellitus and thyroid dysfunction were positive. Thus, assuming that perceived physical health is worse in all chronic disease patients (as can be derived from the scores in Table 2), some chronic diseases are relatively 'favourable' (e.g. diabetes mellitus, thyroid dysfunction), others are more neutral (cardiovascular disease) or unfavourable (chronic respiratory disease, arthritis) with regard to physical functioning. The negative additive effect of thyroid dysfunction on mental health indicates that patients with thyroid dysfunction experience relatively unfavourable mental functioning, which may be explained by the biomedical association between thyroid dysfunction and depression [27].

The significant effects of the interaction terms in four of the seven analyses that were performed on PCS indicate that synergistic effects of chronic disease pairs do exist. With regard to physical functioning, the following disease pairs showed synergism: diabetes–cardiovascular disease, diabetes–chronic respiratory disease, cardiovascular disease–arthritis, and cardiovascular disease– chronic respiratory disease. In three of these four pairs (diabetes–cardiovascular disease, diabetes– chronic respiratory disease, cardiovascular disease– chronic respiratory disease) the interaction effect was negative, indicating an exacerbation of the bad physical health status. Since these disease pairs also occur frequently in the population, we believe that GPs as well as medical specialists should be aware of this increased risk for physical disability.

In contrast with other researchers, we did not find multiplicative effects of combinations where arthritis was involved (except for the combination cardiovascular disease–arthritis, where the interaction effect was positive). As was shown in Table 2, arthritis affected physical functioning more than all other diseases in our study regardless of the presence of comorbidity. We also reported that our patients with arthritis had lower PCS scores than the subjects with (self-reported) arthritis in the study of Ware et al. [18]. It is possible that the substantial negative main effect of arthritis in our study did not leave room for any negative interaction effect on physical functioning.

With regard to mental health, we did not find a synergistic effect of combinations of somatic chronic diseases in any of the seven regression analyses on MCS. Scores on MCS were somewhat lower than in the general US population, but a higher risk for specific chronic diseases (except for thyroid dysfunction) or specific disease pairs did not come to the fore. Other disease characteristics, such as illness duration and disease stage or activity, may be more important for mental health than the type or number of chronic diseases. It is most likely that mental health is vulnerable during the first months after the diagnosis has been established, since this situation of acute crisis (diagnosis and primary treatment) is characterized by uncertainty, threat and fear [28]. In addition, renewed disease activity or recurrence of symptoms can be considered very stressful and thus endanger mental health [29].

In our study data were available on illness duration, but not on disease stage or disease activity. Since illness duration – unlike age and gender – appeared to be not related to physical and mental functioning in our sample, we did not include this variable in our regression models. One has to consider that most patients in our study had already been ill for years (the average time postdiagnosis was 10 years) and only a very small part of them had been recently diagnosed. Disease stage and activity might have been more relevant for our research group; not only as important determinants of mental health, but naturally also of physical functioning. Future research on the effects of disease combinations should therefore incorporate appropriate measures of illness duration and disease stage or activity.

In our research the number of disease pairs that could be analysed was limited because of the relatively low rates of comorbidity in our sample. Despite the fact that we had 1673 patients who all suffered from chronic illness, only 13% of them (n = 221) were diagnosed with more than one of the six selected diseases. When all chronic diseases registered by the GPs would have been included as comorbid conditions in this study, total comorbidity would have raised to 30%. This latter percentage is equal to the 29.7% found by Van den Akker et al. [30] in a representative study population (n = 60,857) of subjects registered in Dutch general practices. Based on self-report,[3] we found – as expected – higher comorbidity percentages, ranging from 41.6 (25–44 years) to 68.1 (≥65 years) [32]. These figures show that comorbidity rates based on GP registration are in general lower than the rates based on self-reported chronic conditions. Nevertheless, we believe that the decision to start from medical diagnoses is exactly the strength of our research: data of chronic disease and functioning were

[3] Panel members filled in the Checklist Chronic conditions of the Netherlands Health Interview Survey [31] in April 1998.

obtained from different resources, which precludes the possibility of confounding by personal or mood characteristics.

We conclude that comorbidity in chronic disease patients is attended with physical disability rather than mental health problems. Not only do comorbid conditions have additive negative effects on physical functioning, but synergistic effects of some chronic disease pairs also exist. Patients suffering from combinations of diabetes, cardiovascular disease and/or chronic respiratory disease run a higher risk of physical disability than could be expected from the separate effects of these diseases. Therefore, maintaining functional capacity should be an important objective of the care for these comorbid patients.

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REFERENCES

1. Nationale Commissie Chronisch Zieken [National Committee of the Chronically Ill]. Van mogelijk naar noodzakelijk. Chronisch-ziekenbeleid in de 21e eeuw. Eindadvies. Zoetermeer, Nationale Commissie Chronisch Zieken, 1999.
2. Akker M van den, Buntinx F, Knottnerus JA. Comorbidity or multimorbidity: What's in a name. A review of literature. Eur J Gen Pract 1996; 2: 65–70.
3. Schellevis FG, Bos GAM van den, Tijssen JGP, Grobbee DE, Heinsbroek RPW. Comorbidity and chronic diseases: A report of the workshop Comorbidity and Chronic Diseases. The Hague: Council for Medical Research, The Netherlands Organization for Scientific Research, 1997.
4. Satariano WA. Comorbidities and cancer. In: Hunter CP, Johnson KA, Muss HB (eds), Cancer in the Elderly. New York: Marcel Dekker, Inc., 2000: 477–499.
5. Gijsen R, Hoeymans N, Schellevis FG, Ruwaard D, Satariano WA, Bos GAM van den. Causes and consequences of comorbidity: A review. J Clin Epidemiol 2001; 54: 661– 674.
6. Heijmans MJTM, Rijken PM, Schellevis FG, Bos GAM van den. Meer dan een ziekte. De gevolgen van comorbiditeit vanuit het perspectief van chronisch zieken en gehandicapten. Utrecht/Amsterdam/Bilthoven: NIVEL/ AMC/RIVM, 2003.
7. Ettinger WH, Davis MA, Neuhaus JM, Mallon KP. Longterm physical functioning in persons with knee osteoarthritis from NHANES I: Effects of comorbid medical conditions. J Clin Epidemiol 1994; 47: 809–815.
8. Verbrugge LM. Women, men, and osteoarthritis. Arthritis Care Res 1995; 8: 212–220.
9. Fried LP, Bandeen-Roche K, Kasper JD, Guralnik JM. Association of comorbidity with disability in older women: The Women's Health and Aging Study. J Clin Epidemiol 1999; 52: 27–37.
10. Katon W, Sullivan M. Depression and chronic medical illness. J Clin Psychiatry 1990; 51(Suppl. 6): 3–11.
11. Wells KB, Golding JM, Burnam MA. Psychiatric disorder in a sample of the general population with and without chronic medical conditions. Am J Psychiatry 1988; 145: 976–981.
12. Nationale Raad voor de Volksgezondheid [Netherlands Classification and Terminology Committee for Health]. Standaardisatie van chroniciteitsbegrippen. Vooronderzoek naar het definiëren en specificeren van chroniciteit van gezondheidsproblemen ten behoeve van classificaties. Zoetermeer: Nationale Raad voor de Volksgezondheid, 1995.
13. Schellevis F. Chronic Diseases in General Practice. Comorbidity and Quality of Care. Utrecht: Drukkerij Pascal, 1993.
14. Heijmans M, Foets M, Rijken M, Schreurs K, Ridder D de, Bensing J. Stress in chronic disease: Do the perceptions of patients and their general practitioners match? Br J Health Psychol 2001; 6: 229–242.
15. Lamberts H, Wood M (eds.), ICPC International Classification of Primary Care. Oxford: Oxford University Press, 1987.
16. Ware JE, Sherbourne CD. The RAND-36 Short-form Health Status Survey: I. Conceptual framework and item selection. Med Care 1992; 30: 473–481.
17. McHorney CA, Ware JE, Lu JF, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. Med Care 1994; 32: 40–66.
18. Ware JE, Kosinsky M, Keller SD. SF-36 Physical & Mental Health Summary Scales: A User's Manual. Boston, The Health Institute, New England Medical Center, December 1994.

19. Ware JE, Kosinski M, Bayliss MS, McHorney CA, Rogers WH, Raczek A. Comparison of Methods for the Scoring and Statistical Analysis of SF-36 Health Profile and Summary Measures: Summary of Results from the Medical Outcomes Study. Med Care 1994; 33: AS264–279.
20. Zee KI van der, Sanderman R, Heyink JW, Haes H de. Psychometric Qualities of the RAND 36-Item Health Survey 1.0: A multidimensional measure of general health status. Int J Behav Med 1996; 3: 104–122.
21. Aaronson NK, Muller M, Cohen PDA, et al. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. J Clin Epidemiol 1998; 51: 1055– 1068.
22. Kriegsman DM, Penninx BW, van Eijk JT, Boeke AJ, Deeg DJ. Self-reports and general practitioner information on the presence of chronic diseases in community dwelling elderly. A study on the accuracy of patients' self-reports and on determinants of inaccuracy. J Clin Epidemiol 1996; 49: 1407–1417.
23. Haapanen N, Miilunpalo S, Pasanen M, Oja P, Vuori I. Agreement between questionnaire data and medical records of chronic diseases in middle-aged and elderly Finnish men and women. Am J Epidemiol 1997; 145: 762–769.
24. Fanuele JC, Birkmeyer NJO, Abdu WA, Tosteson TD, Weinstein JN. The impact of spinal problems on the health status of patients. Spine 2000; 25(12): 1509–1514.
25. Anderson JP, Kaplan RM, Coons SJ, Schneiderman LJ. Comparison of the Quality of Well-Being Scale and the SF- 36 results among two samples of ill adults: AIDS and other illnesses. J Clin Epidemiol 1998; 9: 755–762.
26. Mahler DA, Mackowiak JI. Evaluation of the SF-36 Questionnaire to measure health-related quality of life in patients with COPD. Chest 1995; 107: 1585–1589.
27. Haggerty JJ, Prange AJ. Borderline hypothyroidism and depression. Ann Rev Med 1995; 46: 37–46.
28. Moos RH, Schaeffer JA. The crisis of physical illness. An overview and conceptual approach. In: Moss RM (ed.), Coping with Physical Illness, New Perspectives. New York: Plenum Press, 1984; 2: 3–39.
29. Zautra AJ. Investigations of the ongoing stressful situations among those with chronic illness. Am J Community Psychol 1996; 24: 697–717.
30. Akker M van den, Buntinx F, Metsemakers JFM, Roos S, Knottnerus JA. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occuring chronic and recurrent diseases. J Clin Epidemiol 1998; 51: 367– 375.
31. Statistics Netherlands. Netherlands Health Interview Survey 1981–1995. The Hague: SDU Publishers, 1996.
32. Rijken PM, Foets M, Peters L, Bruin AF de, Dekker J. Patiëntenpanel Chronisch Zieken. Kerngegevens 1998. Utrecht: NIVEL, 1999.

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TABLES AND BOXES

Box 1. Description of chronic disease categories (ICPC-codes)

Cardiovascular disease	Ischemic heart disease (K74–76), heart failure (K77), cerebrovascular disease (K89–90), atherosclerosis and other arterial obstructive/peripheral vascular disease (K91–92), other cardiovascular disease (K99)
Cancer	All types of malignant neoplasms, excl. skin (A79, B72–74, D74–77, K72, L71, N74, R84–85, T71, U75–76, X75–77, Y77–78)
Arthritis	Osteoarthritis of spine (L84), rheumatoid arthritis/allied conditions (L88), osteoarthritis other types (L89–91)
Chronic respiratory disease	Chronic bronchitis/bronchiectasis (R91), emphysema/COPD (R95), asthma (R96)
Diabetes mellitus	Diabetes mellitus type 1 and 2 (T90)
Thyroid dysfunction	Goiter (T81), hyperthyroidism/thyrotoxicosis (T85), hypothyroidism/myxedema (T86), other thyroid disease (T99.2)

Table 1. Number of patients with selected chronic diseases, comorbidity of any other chronic disease, and comorbidity of other selected diseases

	Diagnosed with	Comorbidity of any chronic disease		Comorbidity of selected diseases	
	N	N	%	N	%
Cardiovascular disease	373	214	57	127	34
Cancer	151	54	36	34	23
Arthritis	366	126	34	69	19
Chronic respiratory disease	525	179	34	92	18
Diabetes mellitus	368	151	41	98	27
Thyroid dysfunction	126	50	40	37	29

Table 2. PCS and MCS scores of chronic disease patients, without and with comorbidity of any chronic disease, and without and with comorbidity of selected diseases

	Any chronic disease			Selected diseases		
	N	Mean	SD	N	Mean	SD
PCS						
Cardiovascular disease	373			373		
Comorbidity absent	159	41.25***	(7.57)	246	40.29***	(7.62)
Comorbidity present	214	37.75	(7.94)	127	37.21	(8.25)
Cancer	151			151		
Comorbidity absent	97	41.82	(9.06)	117	41.78**	(8.93)
Comorbidity present	54	38.87	(8.41)	34	37.25	(8.03)
Arthritis	366			366		
Comorbidity absent	240	36.46	(8.69)	297	36.40	(8.48)
Comorbidity present	126	36.03	(8.07)	69	35.90	(8.50)
Chronic respiratory disease	525			525		
Comorbidity absent	346	40.88***	(8.64)	433	40.53***	(8.84)
Comorbidity present	179	37.03	(8.86)	92	35.00	(7.67)
Diabetes mellitus	368			368		
Comorbidity absent	217	43.08***	(7.87)	270	42.35***	(8.25)
Comorbidity present	151	38.28	(8.84)	98	37.70	(8.66)
Thyroid dysfunction	126			126		
Comorbidity absent	76	45.52***	(7.13)	89	44.39**	(8.03)
Comorbidity present	50	39.22	(8.55)	37	39.72	(8.07)
MCS						
Cardiovascular disease	373			373		
Comorbidity absent	159	48.30	(6.87)	246	47.76	(6.89)
Comorbidity present	214	46.98	(6.80)	127	47.13	(6.78)
Cancer	151			151		
Comorbidity absent	97	47.37	(6.41)	117	47.28	(6.12)
Comorbidity present	54	47.35	(5.02)	34	47.65	(5.31)
Arthritis	366			366		
Comorbidity absent	240	48.00	(7.22)	297	47.84	(7.26)
Comorbidity present	126	46.59	(7.08)	69	46.12	(6.79)
Chronic respiratory disease	525			525		
Comorbidity absent	346	47.08	(6.67)	433	47.09	(6.81)
Comorbidity present	179	47.13	(7.13)	92	47.11	(6.92)
Diabetes mellitus	368			368		
Comorbidity absent	217	47.30	(5.89)	270	47.35	(5.80)
Comorbidity present	151	47.89	(5.81)	98	48.07	(6.00)
Thyroid dysfunction	126			126		
Comorbidity absent	76	45.60	(6.64)	89	46.07	(6.70)
Comorbidity present	50	46.70	(7.04)	37	45.96	(7.12)

T-tests for independent samples: * $p < 0.05$; ** $p < 0.01$, *** $p < 0.001$.

Table 3. Results of linear regression-analyses with PCS and MCS as dependent variables

	PCS				MCS			
	Model 1		Model 2		Model 1		Model 2	
	beta	*p*	beta	*p*	beta	*p*	beta	*p*
Age (year)			−0.27	0.000			0.10	0.000
Gender (female)			−0.11	0.000			−0.06	0.01
Cardiovascular disease	−0.10	0.000	−0.04	NS	0.03	NS	−0.01	NS
Arthritis	−0.25	0.000	−0.19	0.000	0.03	NS	0.02	NS
Cardio * arthritis	0.05	NS	0.05	0.04	−0.02	NS	−0.02	NS
Age (year)			−0.31	0.000			0.11	0.000
Gender (female)			−0.14	0.000			−0.06	0.01
Cardiovascular disease	−0.01	NS	0.01	NS	0.03	NS	−0.01	NS
Chronic respiratory disease	−0.00	NS	−0.07	0.01	−0.01	NS	0.01	NS
Cardio * respiratory	−0.09	0.000	−0.06	0.02	−0.04	NS	−0.05	NS
Age (year)			−0.31	0.000			0.11	0.000
Gender (female)			−0.13	0.000			−0.06	0.01
Cardiovascular disease	−0.01	NS	0.04	NS	0.02	NS	−0.03	NS
Diabetes mellitus	0.09	0.001	0.11	0.000	0.02	NS	0.01	NS
Cardio * diabetes	−0.05	NS	−0.05	0.05	0.01	NS	0.01	NS
Age (year)			−0.30	0.000			0.10	0.000
Gender (female)			−0.11	0.000			−0.06	0.01
Arthritis	−0.24	0.000	−0.21	0.000	0.01	NS	0.02	NS
Chronic respiratory disease	−0.09	0.001	−0.14	0.000	−0.02	NS	0.00	NS
Arthritis * respiratory	−0.03	NS	0.00	NS	−0.02	NS	−0.03	NS
Age (year)			−0.28	0.000			0.10	0.000
Gender (female)			−0.11	0.000			−0.06	0.01
Arthritis	−0.20	0.000	−0.15	0.000	0.02	NS	0.02	NS
Diabetes mellitus	0.04	NS	0.06	0.02	0.02	NS	0.02	NS
Arthritis * diabetes	−0.03	NS	−0.03	NS	−0.01	NS	−0.01	NS
Age (year)			−0.31	0.000			0.10	0.000
Gender (female)			−0.14	0.000			−0.06	0.02
Chronic respiratory disease	0.02	NS	−0.05	0.04	−0.03	NS	−0.01	NS
Diabetes mellitus	0.10	0.000	0.08	0.001	−0.00	NS	0.00	NS
Respiratory * diabetes	−0.07	0.006	−0.05	0.04	0.04	NS	0.03	NS
Age (year)			−0.30	0.000			0.10	0.000
Gender (female)			−0.16	0.000			−0.05	0.04
Diabetes mellitus	0.10	0.000	0.10	0.000	0.01	NS	0.00	NS
Thyroid dysfunction	0.13	0.000	0.13	0.000	−0.07	0.01	−0.05	0.05
Diabetes * thyroid	−0.05	0.04	−0.04	NS	0.04	NS	0.03	NS