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Comorbidity of chronic cardiovascular disorders

A cross-sectional analysis in a large general practice population in the Netherlands

by

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Abstract

Aim: *Comorbidity is of increasing interest because of the rising prevalence of chronic disease in the next years due to the aging of the population and the development of medical possibilities. Cardiovascular disorders are particularly important because of their high prevalence, especially among older persons. We studied the prevalence and co-occurrence of chronic cardiovascular disorders and other chronic disorders.*

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Materials and Methods: *Data were obtained from the Registration Network Family Practices (RNH) in the Netherlands. The population studied consisted of 73,254 persons and resembled the general Dutch population. Six groups of chronic cardiovascular disorders were analyzed for their comorbidity with 30 other groups of chronic disorders involving all body systems. Logistic regression analyses were performed to obtain odds ratios describing their relations, adjusted for age and sex.*

Results and conclusions: *Cardiovascular disorders proved to be a disease category with a high amount of comorbidity in various body systems. This is especially true for ischaemic heart disease. Many people suffer from cardiovascular disease and additional conditions. It is therefore recommended that the nature and direction of these relations are studied more in detail to increase insight in the possibilities of prevention and therapy.*

Keywords

comorbidity, cardiovascular disorders, general practice, chronic disorders

Introduction

Comorbidity is defined as the occurrence of medical conditions additional to an index disease (1). Chronic diseases play an important role, especially in the elderly. The prevalence of chronic diseases has increased in the past few decades because of the shift from acute to chronic diseases, due to life-saving but not curing medical interventions, and the aging of the population. The percentage of people aged 65 years or older in the Dutch population for example, is expected to rise from 14% in 1995 to 17% in 2015 and will increase even more in the years thereafter (2).

Especially general practitioners often are confronted with patients suffering from more than one chronic condition. In previous studies on multi-morbidity two or more conditions at the same time were reported in 3,6% to 70%, depending on the number of conditions and the age categories under study (3, 4, 5, 6, 7). While the number of chronic conditions a patient is suffering from rises, the level of disability increases as well (8). It can result in more pain and suffering, loss of independence and loss of quality of life (9, 7). In elderly patients with cardiovascular disease comorbidity was found to be related to a high level of complications of

diagnostic and therapeutic procedures, and comorbidity added to more frequent and serious adverse drug reactions (10). The co-existence of a second disease may influence the course and the effect of therapeutic interventions for the initial disease. Medical care, however, is still based on single-disease trials.

Multi-morbidity not only influences a patient's fate. People near to them, such as family and friends, are concerned as well. This is called 'social prevalence' (11). Taking care of someone with multiple chronic conditions may take a lot of time and energy and carers may be forced to change their life style, e.g. forgo job opportunities. The economic impact on society increases when patients live longer with multiple chronic conditions: there's a greater need for social services and the cost to society rises with higher medical and health care expenses and loss of productivity (9).

For all those reasons the study of comorbidity is of increasing importance. This paper is part of a series of exploratory studies in which comorbidity of different groups of chronic diseases is analysed.

Cardiovascular disease is the major cause of death and disability, especially in the elderly. Atherosclerotic coronary heart disease and hypertensive cardiovascular disease are the most prevalent cardiovascular problems (10). In the general Dutch population the prevalence of chronic ischaemic heart disease was 5/1000 and the prevalence of hypertension was 52/1000 (12).

Patients with cardiovascular diseases report significantly poorer well-being than healthy people, and have a lower quality of life, as is reflected in not being fit, having less energy and complaining more about physical symptoms (13, 14, 15). Any additional chronic condition may worsen the well-being even more (7).

In this exploratory study the comorbidity of chronic cardiovascular diseases is addressed. Therefore the co-occurrence of the 6 cardiovascular diseases with each of the 30 other chronic disease groups is identified and tested for statistical significance.

Materials and Methods

Patients

In this study data of the Registration Network Family Practices (Registratienet Huisartspraktijken = RNH) were used. This registration network was established in the Netherlands in 1988. The goal was to establish a computerized anonymous database containing basic background

characteristics of all patients as well as all relevant health problems. On September the 1st 1998 it consisted of 55 participating general practitioners working in 22 general practices, mainly situated in the south of Limburg, a province of the Netherlands. The population covered by these practices counted approximately 100.000 patients (16). The patient population resembles the general population of the Netherlands with respect to age, sex, and level of education (17).

On a daily basis, the general practitioners record all new relevant health problems in a problem list of the patient, as well as certain patient characteristics (including sex, date of birth, type of health insurance, type of household and level of education). Problems are recorded if they are permanent, chronic (duration longer than six months) or recurrent (recurring at least three times within six months). [16] All problems are coded using the 'International Classification of Primary Care' (ICPC) and are diagnosed using the inclusion criteria of the 'International Classification of Health Problems in Primary Care' (ICHPPC-2-defined) (18, 19). Four times a year the data are read into a central database (16).

To guarantee the quality of the data several strategies are used. The software provides the general practitioner with an automated thesaurus for the ICPC-codes. To check the representativeness of the database the age and sex distribution of the patients that are registered is compared with that of the practice population. Furthermore, six consensus groups are formed who discuss aspects of problem definition and coding on a regular basis. Finally, the Center for Data and Information Management reports omissions, inconsistencies and mistakes to the general practitioners and to the staff of the network (16).

As the RNH-database covers a large population resembling the general population of the Netherlands and contains descriptive data on all relevant health problems as well as certain patient characteristics, it can be used to study incidence, prevalence and comorbidity of specific diseases.

This study was based on the entire population included in the database of the registration network of family practices in December 1997. At the time of this study the population consisted of 73,254 persons of which 35,696 (48.7%) were males and 37,553 (51.3%) were females. The age distribution is presented in table 1.

Definitions

In order to study the comorbidity specific groups of chronic cardiovascular disorders were selected. Only disorders with a chronic character and affecting either the heart, the arteries or both were included, hereby leaving out disorders of the venous system.

TABLE 1
Distribution of the RNH population among age and sex categories (N=73,254) Numbers and percentages

Age category	Male	Female	Total
0-25	10438 (29.2%)	10230 (27.2%)	20668 (28.2%)
26-65	20784 (58.2%)	20788 (55.4%)	41572 (56.8%)
>65	4474 (12.6%)	6535 (17.4%)	11009 (15%)
Total	35696 (100%)	37553 (100%)	73254 (100%)

The selected chronic cardiovascular disorders were grouped into six categories. In order to study the comorbidity of chronic cardiovascular categories, thirty categories of additional chronic disorders were selected. These disorders have common symptomatology or pathophysiologic mechanisms, and are based on a previous selection of chronic diseases, which was used by Knottnerus et al. for their study of chronic illness in the community (11). For this study only disorders coded as a disease entity in the International Classification of Primary Care (ICPC) were used.

Statistical analysis

Interrelations between each couple of cardiovascular disorder and each of the others of the same group, adjusted for age (0-25, 26-65, >65 years) and sex, were studied, using logistic regression and expressing the results in odds ratios with their 95% confidence interval. To study the comorbidity of chronic cardiovascular disorders, the relation between each of the 30 groups of chronic disorders and each of the cardiovascular disorders was analysed by means of logistic regression, adjusting for age and sex. The presence of one of the chronic disorders, age and sex served as independent variables, the presence of one of the cardiovascular disorders served as the dependent variable. The results of these analyses are expressed in odds ratios with their 95% confidence intervals.

Additional analyses were performed to study some of the relations more closely. So, the relation between hyperthyroidism/thyrotoxicosis and each of the cardiovascular disorders was examined separately for each age category. To get insight in the direction of some of the relations, the dates of diagnosis of several conditions were compared.

Results

Table 2 represents the relations within the group of cardiovascular disorders. High and significant odds ratios are found for all combinations except for pulmonary embolism, which only relates significantly with ischaemic heart disease.

The relations between the occurrence of cardiovascular disorders and the other chronic disease categories are shown in table 3.

Chronic lung disease is related positively and significantly to all categories. Diabetes mellitus and retinopathy are related to all groups but pulmonary embolism.

TABLE 2

Co-occurrence of diseases within the group of cardiovascular disorders, adjusted for age and sex. Reported are odds ratios with their 95% confidence interval.

	Ischaemic heart disease	Heart failure	Hypertension with organ involvement	Cerebrovascular disease	Peripheral arterial disease	Pulmonary embolism
Ischaemic heart disease	-	3.96 (3.21-4.87)	4.30 (3.56-4.87)	2.00 (1.62-2.46)	3.72 (3.22-4.30)	2.91 (1.61-5.23)
Heart failure	*	-	3.58 (2.55-5.03)	2.66 (1.84-3.83)	2.22 (1.63-3.03)	2.13 (0.66-6.89)
Hypertension with organ involvment	*	*	-	6.62 (5.08-8.61)	4.06 (3.18-5.17)	**
Cerebrovascular disease	*	*	*	-	4.41 (3.50-5.57)	1.81 (0.56-5.85)
Peripheral arterial disease	*	*	*	*	-	1.38 (0.49-3.84)
Pulmonary disease	*	*	**	*	*	-

* Exchanging dependent and independent variables in the analyses revealed similar odds ratios.
** Patient count in this disorder combination was low, therefore odds ratios couldn't be computed.

TABLE 3

Co-occurrence of cardiovascular disorders and other chronic disorders, adjusted for age and sex. Odds ratios with their 95% confidence interval

	Ischaemic heart disease	Heart failure	Hypertension with organ involvement	Cerebrovascular diseases	Peripheral arterial disease	Pulmonary embolism
Osteoarthritis	**1.24** (1.10-1.40)	**1.29** (1.01-1.66)	1.17 (0.92-1.49)	**1.31** (1.04-1.65)	1.16 (0.97-1.39)	**2.16** (1.19-3.94)
Acquired deformities of llimbs	1.04 (0.86-1.25)	1.12 (0.73-1.70)	1.02 (0.70-1.49)	0.94 (0.63-1.40)	**1.56** (1.23-1.99)	0.62 (0.15-2.53)
RA, allied conditions	**1.94** (1.55-2.43)	**1.80** (1.13-2.86)	**1.72** (1.12-2.64)	1.08 (0.64-1.82)	1.19 (0.81-1.75)	**3.44** (1.37-8.62)
Osteoporosis	**1.60** (1.27-2.01)	1.18 (0.73-1.92)	0.99 (0.59-1.65)	1.32 (0.84-2.08)	**1.49** (1.05-2.12)	1.68 (0.51-5.48)
Chronic lung disease	**1.56** (1.35-1.79)	**2.75** (2.14-3.54)	**1.46** (1.10-1.94)	**1.40** (1.06-1.85)	**2.11** (1.75-2.54)	**2.57** (1.28-5.17)
Asthma	**1.34** (1.10-1.63)	1.39 (0.88-2.20)	0.82 (0.51-1.32)	0.73 (0.44-1.23)	1.16 (0.86-1.57)	1.72 (0.63-4.74)
Phlebitis and thrombophlebitis	**2.05** (1.38-3.05)	3.25 (1.73-6.11)	1.96 (0.95-4.03)	**3.01** (1.65-5.49)	1.65 (0.91-3.01)	**24.07** (11.57-50.04)
Hyperthyroidism/ thyrotoxicosis	**1.84** (1.35-2.51)	**4.30** (2.80-6.58)	1.66 (0.94-2.93)	1.71 (0.97-3.02)	**1.83** (1.17-2.85)	**3.35** (1.03-10.88)
Hypothyroidism/ myxedema	**1.88** (1.40-2.52)	1.15 (0.59-2.27)	0.76 (0.36-1.63)	1.03 (0.53-2.03)	1.48 (0.93-2.34)	0.94 (0.13-6.82)
Diabets mellitus	**2.56** (2.27-2.89)	**3.43** (2.74-4.30)	**3.34** (2.72-4.11)	**2.58** (2.08-3.21)	**2.73** (2.31-3.22)	1.75 (0.86-3.59)
Gout	**2.07** (1.63-2.62)	**2.51** (1.55-4.06)	**4.71** (3.35-6.63)	**2.21** (1.43-3.43)	1.01 (0.66-1.56)	2.99 (0.92-9.78)

	Ischaemic heart disease	Heart failure	Hypertension with organ involvement	Cerebrovascular diseases	Peripheral arterial disease	Pulmonary embolism
Lipid metabolism disorder	**6.42** (5.72-7.21)	**1.42** (1.02-1.97)	**3.78** (3.06-4.69)	1.30 (0.96-1.76)	2.56 (2.14-3.08)	1.83 (0.83-4.03)
Dementia,other organic psychosis	1.07 (0.75-1.54)	**2.37** (1.39-4.05)	1.41 (0.74-2.67)	**2.38** (1.43-3.94)	0.82 (0.45-1.52)	1.25 (0.17-9.13)
Psychosis, incl. Schizophrenia	0.67 (0.35-1.28)	1.51 (0.48-4.82)	0.92 (0.29-2.89)	**2.49** (1.15-5.37)	0.50 (0.16-1.57)	0.02 (0.00-252,079,599)
Neurotic or personality disorder, mental retardation, suicide attempt	1.20 (0.96-1.51)	1.52 (0.93-2.50)	0.90 (0.55-1.49)	**1.60** (1.06-2.40)	1.26 (0.91-1.75)	1.54 (0.48-4.92)
Depressive disorder	**1.39** (1.09-1.77)	0.96 (0.52-1.77)	1.36 (0.86-2.14)	**2.34** (1.61-3.40)	1.02 (0.69-1.53)	1.77 (0.55-5.66)
Atopic dermatitis, eczema	0.66 (0.41-1.05)	0.97 (0.36-2.62)	0.74 (0.31-1.80)	0.19 (0.03-1.19)	1.07 (0.62-1.88)	1.31 (0.18-9.51)
Retinopathy	**1.82** (1.38-2.41)	**3.77** (2.49-5.69)	**15.13** (11.62-19.69)	**3.01** (1.99-4.56)	**3.77** (2.77-5.14)	1.98 (0.48-8.17)
Macular degeneration blindness all types	1.19 (0.91-1.55)	1.11 (0.62-1.99)	**1.75** (1.12-2.75)	**1.68** (1.07-2.64)	**1.68** (1.19-2.37)	0.72 (0.10-5.25)
Otosclerosis, deafness (partial or complete)	**1.23** (1.03-1.47)	1.40 (0.96-2.05)	0.85 (0.56-1.30)	1.10 (0.75-1.60)	1.15 (0.87-1.52)	2.19 (0.94-5.12)
Malignant neoplasms	**1.35** (1.16-1.57)	1.22 (0.88-1.69)	1.14 (0.83-1.56)	**1.66** (1.27-2.18)	**1.50** (1.21-1.86)	**2.30** (1.12-4.71)
Congenital anomalies urinary tact	1.55 (0.85-2.82)	1.35 (0.33-5.57)	**3.10** (1.34-7.13)	1.03 (0.25-4.20)	1.70 (0.74-3.91)	4.43 (0.61-32.27)
Glomerulonephritis/ Nephrosis	**4.70** (2.83-7.79)	**5.16** (2.17-12.27)	**14.80** (8.59-25.50)	1.82 (0.57-5.86)	**4.04** (2.09-7.80)	*

- table 3 continued

- table 3 continued

	Ischaemic heart disease	Heart failure	Hypertension with organ involvement	Cerebrovascular diseases	Peripheral arterial disease	Pulmonary embolism
Benign prostatic hypertrophy	**1.38** (1.07-1.78)	1.14 (0.61-2.14)	1.17 (0.66-2.07)	1.29 (0.78-2.15)	1.20 (0.82-1.74)	0.88 (0.12-6.62)
Migraine/cluster headache/trigeminus neuralgia	0.97 (0.69-1.37)	0.34 (0.08-1.36)	1.23 (0.69-2.20)	0.82 (0.38-1.73)	0.91 (0.54-1.53)	0.84 (0.12-6.09)
Poliomyelitis/enterovirus	2.44 (0.77-7.75)	*	*	**5.23** (1.17-23.48)	1.30 (0.17-9.90)	*
Congenital anomalies CNS	0.64 (0.15-2.70)	*	1.51 (0.21-11.10)	**5.52** (1.65-18.43)	1.67 (0.40-7.01)	* *
Multiple sclerosis	0.45 (0.06-3.34)	*	1.92 (0.26-14.16)	2.19 (0.29-16.39)	2.32 (0.55-9.84)	*
Parkinsonism	1.51 (0.98-2.31)	0.75 (0.24-2.36)	0.46 (0.11-1.86)	**2.08** (1.05-4.13)	**1.90** (1.08-3.34)	* *
Epilepsy, all types	**1.49** (1.03-2.15)	1.27 (0.52-3.11)	**3.31** (2.01-5.47)	**8.35** (5.74-12.16)	**2.58** (1.68-3.97)	*
Esophageal disease	**1.86** (1.54-2.24)	1.04 (0.65-1.66)	1.29 (0.87-1.90)	1.22 (0.82-1.81)	**1.49** (1.13-1.98)	2.28 (0.91-5.72)
Peptic ulcer	**1.69** (1.33-2.16)	0.91 (0.47-1.79)	0.87 (0.47-1.59)	1.55 (0.96-2.48)	**1.68** (1.20-2.37)	1.64 (0.40-6.77)
Diverticular disease	**1.57** (1.28-1.92)	1.37 (0.90-2.07)	1.40 (0.95-2.05)	1.44 (0.99-2.09)	**1.51** (1.13-2.01)	**3.54** (1.58-7.92)
Inflammable bowel disease	1.25 (0.74-2.10)	1.46 (0.46-4.66)	1.58 (0.64-3.88)	1.02 (0.32-3.23)	1.58 (0.80-3.13)	*
Irritable bowel syndrome	1.29 (0.96-1.75)	0.25 (0.06-1.01)	0.85 (0.44-1.65)	1.01 (0.54-1.91)	1.02 (0.63-1.64)	*

* Patient count in these disorder combinations was 0, therefore odds ratios couldn't be computed.

Ischaemic heart disease

All but one musculoskeletal conditions, glomerulonephritis/nephrosis, phlebitis and thrombophlebitis and all endocrine disorders were positively and significantly associated with ischaemic heart disease. Of the latter, lipid metabolism disorders had the strongest association (OR 6.42, 95% CI 5.72-7.21). Out of the psychological disorders only depressive disorder was positively related to ischaemic heart disease. Furthermore, associations with asthma, otosclerosis/deafness, malignant neoplasms, benign prostatic hypertrophy and epilepsy were found.

Heart failure

Significant positive associations were found with osteoarthritis, rheumatoid arthritis and allied conditions, phlebitis and thrombophlebitis, dementia/other organic psychosis and glomerulonephritis/nephrosis. Out of the endocrine disorders relations were identified with hyperthyroidism/thyrotoxicosis, gout and lipid metabolism disorder.

Hypertension with organ involvement

Glomerulonephritis/nephrosis was strongly related to hypertension. Furthermore, rheumatoid arthritis and allied conditions, gout, lipid metabolism disorder, macular degeneration/blindness, congenital anomalies of the urinary tract and epilepsy showed positive relations.

Cerebrovascular diseases

All psychological disorders and all but one neurological disorders were positively and significantly related to cerebrovascular diseases. Of the latter epilepsy showed the strongest association. Furthermore, positive associations were found for osteoarthritis, phlebitis/thrombophlebitis, gout, macular degeneration/blindness and malignant neoplasms.

Peripheral arterial disease

Acquired deformities of the limbs and osteoporosis were positively and significantly associated with peripheral arterial disease. Furthermore, hyperthyroidism/thyrotoxicosis, lipid metabolism disorder, macular degeneration/blindness, malignant neoplasms and glomerulonephritis/nephrosis, parkinsonism and epilepsy showed a significant association.

Pulmonary embolism

Phlebitis and thrombophlebitis turned out to be very strongly associated with pulmonary embolism. Additional significant associations were found for osteoarthritis, rheumatoid arthritis and allied conditions, hyperthyroidism/thyrotoxicosis and malignant neoplasms.

Additional analyses

After stratification within age categories the separate relations between hyperthyroidism/thyrotoxicosis and cerebrovascular diseases were not statistically significant anymore (table 4). The relations with ischaemic heart disease, heart failure, hypertension with organ involvement and pulmonary embolism however, were more pronounced in the age category 26-65 years, compared to the other age groups. Pulmonary embolism was stronger related to hyperthyroidism/thyrotoxicosis in the age category 66 years and older. The association with ischaemic heart disease and heart failure turned out to be less in the highest age category. In 23 out of 26 cases heart failure preceded hyperthyroidism/thyrotoxicosis with 2 months to 28 years. The combination of pulmonary embolism and hyperthyroidism/thyrotoxicosis was found in 3 cases only.

Discussion

All cardiovascular conditions proved to be disease categories with a high amount of comorbidity. Especially ischaemic heart disease was associated with a high number of chronic diseases.

There may be different explanations for an association detected in a cross-sectional study:

1. As a considerable number of analyses were performed in this exploratory study, some of the significant relations may result from coincidence.
2. The relations may be confounded by an external factor that we did not control for. However, as all relations are adjusted for age and sex, at least these variables are excluded as possible confounders.
3. Any identified disease may result in an increase in medical attention. More frequent and more extensive examinations can be expected and a larger number of diagnosed disorders (detection bias).

TABLE 4

Co-occurrence of cardiovascular disorders and hyperthyroidism/thyrotoxicosis in different age categories, adjusted for sex. Odds ratios with their 95% confidence interval.

Age categories		Ischaemic heart disease	Heart failure	Hypertension with organ involvement	Cerebrovascular diseases	Peripheral arterial disease	Pulmonary embolism
Hyperthyroidism/ Thyrotoxicosis	26-65 n=209	**4.83** (2.72-8.59)	**10.39** (2.47-43.64)	**4.93** (2.00-12.16)	1.33 (0.19-9.61)	**2.89** (1.18-7.08)	**
	>65 n=202	**1.45** (1.02-2.06)	**4.06** (2.61-6.32)	1.15 (0.56-2.35)	1.75 (0.97-3.17)	1.62 (0.98-2.69)	**4.06** (1.23-13.39

* In the age category 0-25 years, the prevalences of the cardiovascular disorders were almost zero.

** Patient count in this disorder combination was low, therefore odds radios couldn't be computed.

4. The direction of the relation can never be detected from a cross-sectional study. In some of the relations, the direction is straightforward. In some others (e.g. the relation with thyroid disorders) we examined the direction by examining the data of diagnosis of both related disorders. In most cases, however, additional research is needed to decide on a possible direction.
5. If a comorbid relation is detected, additional information in needed to determine the nature of that relation. Both diseases may result from a common pathogenic pathway, either known (e.g. atherosclerosis) or not. Alternatively, there may be a cause and effect relation (e.g. ischaemic heart disease may result in heart failure). Homogeneity of the associations over age and sex strata can be in favor of such causal relations.

We discuss some of the associations that were identified in this study within the framework of these possible explanations.

Finding strong associations between disease categories of which the relation was expected, based on previous studies, provides the other associations found in this study with more confidence. Examples of expected associations are the strong relation between pulmonary embolism and phlebitis or thrombophlebitis and between hypertension and retinopathy or glomerulonephritis/nephrosis (5,12,14,19,32). Also, a strong association between diabetes mellitus and a large number of cardiovascular diseases was expected and found (20). All of them are examples of an association based on a cause and effect relation.

The association between chronic lung disease and all cardiovascular disorder categories may result from confounding by smoking. We were not able to adjust for smoking.

Unlike the other categories, pulmonary embolism showed little comorbidity. Apart from the known relation between pulmonary embolism and phlebitis/thrombophlebitis or malignant neoplasms, both known risk factors, associations were found for osteoarthritis, rheumatoid arthritis and allied conditions and hyperthyroidism/thyrotoxicosis (21, 22, 23,). Possible explanations are an increased risk due to surgery and immobilization after surgery in osteoarthritis, immobilization in rheumatoid arthritis and allied conditions and the occurrence of complications in late-detected hyperthyroidism in older people for hyperthyroidism (24, 25).

The initial analysis showed significant positive associations between hyperthyroidism/thyrotoxicosis and four of the cardiovascular diseases. We hypothesized that especially in old-age people the

diagnosis of hyperthyroidism might have been made relatively late, because at high age the differentiation from other disorders can be especially difficult (25). Therefore cardiovascular complications might develop and even be detected before the diagnosis and adequate treatment of the thyroid disorder. The hypothesis was strengthened by the finding that in 23 out of 26 cases heart failure was diagnosed before hyperthyroidism/thyrotoxicosis, of which 9 shortly before the diagnosis of hyperthyroidism/thyrotoxicosis. Additional analyses however, showed stronger positive relations for the combinations with ischaemic heart disease, heart failure, hypertension and peripheral arterial disease in the age category 26-65 years compared to people aged 65 and older. These findings don't support the hypothesis mentioned before.

A remarkable finding was that all disorders in the psychopathology group were associated with the group of cerebrovascular diseases. Several relations have been described before (26, 27, 28, 29, 30, 31, 32). The risk of (vascular) dementia is known to be increased in patients with a history of stroke (30, 31). Anxiety disorders and depression are found to occur frequently after acute stroke, often in combination with each other. The explanation for the association between cerebrovascular diseases and these disorders is not clear. Various explanations have been proposed, ranging from a psychological response to stroke or disability to cognitive and emotional effects related to neurophysiological changes (27, 26, 28, 33, 29, 32).

A surprising finding was the strong positive association between poliomyelitis/enterovirus and cerebrovascular disease. A Medline search (1966-1998) using the MeSH-terms 'Poliomyelitis' and 'Cerebrovascular-Disorders' didn't result in any additional information with respect to this relation. The association was based however, on only two patients having both cerebrovascular disease and poliomyelitis/enterovirus.

Based on previous studies on migraine and stroke described in the literature, we expected cerebrovascular diseases to be positively associated with the category of migraine/cluster headache/trigeminus neuralgia (34, 35). This association turned out to be negative and not significant. This may be due to differences between this study and the other studies: in the RNH, migraine is mixed with other types of headache, whereas in the other studies the association found was based on classic migraine only.

Macular degeneration and blindness were found to be associated with hypertension, cerebrovascular disease and peripheral arterial disease.

The prevalence of this disorder is low (total prevalence 0.86%) and increases with age. The association may result from detection bias, as fundoscopy tends to be performed more easily in patients with these cardiovascular diseases.

Gout was found to have strong associations especially with heart failure and hypertension with organ involvement. Overdiagnosis of gout (e.g. by classifying all patients with increased serum values of uric acid) might attribute to these findings. A small survey among a number of general practitioners of the RNH however, indicated that the diagnostic criteria are used fairly strictly. In these cardiovascular diseases, drug therapy often includes diuretics. One of the possible adverse effects of these drugs is hyperuricaemia, which is seen often. Development of gout due to hyperuricaemia that only results from diuretic treatment however, is not common (36).

Concluding, this study made clear that cardiovascular disorders are associated with a large number of chronic diseases. Because of the high prevalences of the cardiovascular diseases, many people suffer from a cardiovascular disease as well as from an additional chronic disease. It is important to get more insight into the direction and nature of these relations and in possible preventive interventions or adaptations of therapy. Longitudinal studies on the direction of relations are recommended in order to obtain such insight.

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Appendix

Prevalence of chronic diseases stratified for age and sex categories.
Percentages and total numbers.

Part A: Non-cardiovascular diseases.

Chronic disease	Male	Female	0-25	26-65	>65	Total
Osteoarthritis	3.44% (1228)	5.11% (1917)	0.04% (8)	2.87% (1198)	17.19% (1939)	4.29% (3145)
Acquired deformities of limb	2.91% (1039)	3.39% (1272)	1.63% (330)	3.33% (1388)	5.26% (593)	3.16% (2311)
Rheumatoid arthritis, allied conditions	0.87% (310)	1.28% (479)	0.12% (24)	1.04% (434)	2.93% (331)	1.08% (789)
Osteoporosis	0.22% (80)	1.27% (475)	0.00% (0)	0.25% (105)	4.01% (450)	0.76% (555)
Chronic lung disease	3.47% (1237)	2.00% (750)	0.82% (166)	1.78% (743)	9.56% (1078)	2.71% (1987)
Asthma	5.13% (1830)	4.19% (1575)	7.13% (1482)	3.74% (1557)	3.25% (366)	4.65% (3405)
Phlebitis and thrombophlebitis	0.22% (79)	0.33% (122)	0.00% (2)	0.22% (92)	0.95% (107)	0.27% (201)
Hyperthyroidism/ throtoxicosis	0.18% (64)	0.94% (209)	0.03% (6)	0.50% (209)	1.79% (202)	0.57% (417)
Hypotyroidism/ myxedema	0.17% (62)	1.15% (432)	0.05% (11)	0.63% (261)	1.97% (222)	0.67% (494)
Diabetes mellitus	2.82% (1005)	3.45% (1297)	0.16% (32)	2.37% (987)	11.37% (1283)	3.14% (2302)
Gout	1.3% (465)	0.28% (104)	0.00% (0)	0.79% (328)	2.14% (241)	0.78% (569)
Lipid metabolism disorder	3.25% (1160)	2.62% (985)	0.05% (10)	3.06% (1276)	7.62% (859)	2.93% (2145)
Dementia, other organic disorder	0.27% (97)	0.42% (156)	0.02% (4)	0.12% (48)	1.78% (201)	0.35% (253)
Psychosis, incl. Schizophrenia	0.51% (181)	0.45% (167)	0.14% (28)	0.65% (271)	0.43% (49)	0.48% (348)
Neurotic disorder, personality disorder, mental retardation, suicide attempt	2.47% (882)	2.58% (967)	1.04% (210)	3.24% (1351)	2.55% (288)	2.52% (1849)
Depressive disorder	0.99% (353)	2.05% (770)	0.13% (27)	1.89% (786)	2.75% (310)	1.53% (1123)
Atopic dermatitis, eczema	2.34% (836)	2.71% (1019)	5.55% (1126)	1.53% (639)	0.80% (90)	2.53% (1855)

Retinopathy	0.46% (163)	0.68% (255)	0.00% (0)	0.43% (180)	2.11% (238)	0.57% (418)
Macular degeneration, blindness all types	0.84% (300)	0.88% (331)	0.32% (64)	0.60% (249)	2.82% (318)	0.86% (631)
Otosclerosis, deafness (partial or complete)	2.44% (870)	1.94% (730)	0.78% (159)	1.93% (805)	5.64% (636)	2.18% (1600)
Malignant neoplasms	2.15% (768)	2.71% (1018)	0.13% (27)	1.80% (751)	8.93% (1008)	2.44% (1786)
Congenital anomalies urinary tract	0.23% (83)	0.28% (106)	0.15% (31)	0.28% (118)	0.36% (40)	0.26% (189)
Glomerulonephritis/ Nephrosis	0.18% (64)	0.14% (52)	0.05% (10)	0.17% (69)	0.33% (37)	0.16% (116)
Benign prostatic hypertrophy	1.13% (403)	0.00% (0)	0.00% (0)	0.23% (94)	2.74% (309)	0.55% (403)
Migraine/cluster headache/trigeminus neuralgia	095% (340)	2.36% (886)	0.71% (144)	2.26% (943)	1.23% (139)	1.67% (1226)
Poliomyelitis/enterovirus	0.03% (11)	0.04% (15)	0.00% (0)	0.04% (16)	0.09% (10)	0.04% (26)
Congenital anomalies CNS	0.18% (63)	0.13% (49)	0.23% (47)	0.13% (55)	0.09% (10)	0.15% (112)
Multiple sclerosis	0.05% (19)	0.10% (37)	0.00% (1)	0.11% (47)	0.07% (8)	0.08% (56)
Parkinsonism	0.16% (57)	0.22% (82)	0.00% (0)	0.05% (20)	1.06% (119)	0.19% (139)
Epilepsy, all types	0.76% (270)	0.69% (259)	0.51% (103)	0.77% (320)	0.94% (106)	0.72% (529)
Part B: Cardiovascular disorders						
Ischaemic heart disease	4.67% (1668)	2.99% (1124)	0.00% (2)	2.16% (900)	16.76% (1890)	3.81% (2792)
Heart failure	0.52% (186)	0.67% (251)	0.03% (5)	0.14% (58)	3.32% (374)	0.60% (437)
Hypertension with organ involvement	0.83% (297)	0.88% (332)	0.00% (0)	0.57% (237)	3.48% (392)	0.86% (629)
Cerebrovascular disease	0.81% (289)	0.80% (301)	0.00% (1)	0.40% (165)	3.76% (424)	0.81% (590)
Peripheral arterial disease	1.80% (641)	1.33% (498)	0.04% (8)	0.96% (398)	6.50% (733)	1.56% (1139)
Pulmonary embolism	0.08% (28)	0.11% (42)	0.00% (0)	0.07% (27)	0.38% (43)	0.10% (70)