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Health care utilization of patients with multiple chronic diseases in the Netherlands: Differences and underlying factors ☆

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ABSTRACT

Purpose

To examine health care utilization of people with multiple chronic diseases in The Netherlands compared to people with a single chronic disease, and to identify subgroups of multimorbid patients according to health care utilization.

Methods

All patients diagnosed with one or more chronic diseases in 2008–2009 (N = 54,051) were selected from the nationwide NIVEL Primary Care Database, and data on their GP contacts and medication in 2010 were retrieved. Data on hospital admissions, household size and income were added. Chi-square-tests and multivariate regression analyses were performed to analyze differences between multimorbid patients and patients with a single chronic disease, and between subgroups of multimorbid patients derived from cluster analysis.

Results

Multimorbid patients (37% of all patients) had more GP contacts, prescribed medications, and hospital admissions (all $p < .0001$) than patients with a single chronic disease. The largest cluster of multimorbid patients (57%) had a relatively low level of health care utilization, a smaller cluster (36%) had higher levels of health care utilization, and 7.6% of patients were heavy health care users ($p < .0001$ for all variables). The latter were older, more often female, had a lower income, lived in a smaller household, had more chronic diseases, and more often had specific chronic diseases such as COPD, diabetes and heart failure.

Conclusions

The majority of multimorbid patients have only slightly higher health care utilization than patients with a single chronic disease. Extensive health care utilization among multimorbid patients seems to be related to patient characteristics as well as chronic disease numbers and patterns.

1. INTRODUCTION

Due to rapid aging and greater longevity of the population as well as increasing improvement of medical care, a growing number of people are living with a chronic disease [1]. Thirty percent of the population of the European Union (EU) is living with a chronic disease [2] and this percentage is expected to further increase in the next decades [3]. An increasing proportion of people with a chronic illness suffers from multimorbidity [4] and [5], which refers to the co-occurrence of multiple chronic diseases within a person [6] and [7]. The total number of people with multimorbidity in the EU is conservatively estimated at about 50 million [8]. Especially among older people the prevalence of multimorbidity is very high: among people over age 65 the proportion of individuals with multiple chronic diseases is estimated at about 65%; among people over age 85 at about 85% [9] and [10].

Multimorbidity is associated with a poor functional status [11], poor quality of life [12], [13] and [14], more psychological distress [15], and mortality [16]. Multimorbidity may also be associated with higher levels of health care utilization, not only in comparison to people without a chronic disease but also to people with a single chronic disease [12]. Since health care systems are under pressure (not the least as a result of the growing number of people with [multiple] chronic diseases and the consequential burden on financial and human resources), the innovation of chronic illness care/management in order to provide good quality care (with limited resources) is urgently needed. Integrated care has the potential to meet the complex needs of people with multiple chronic conditions, while making more efficient use of resources [8]. To allocate resources as efficiently as possible, it may be helpful to identify the subgroup of multimorbid patients who are most care and support demanding. This would allow the health system to better respond to the needs of specific subgroups of multimorbid patients, for instance by developing targeted integrated care programs [17], [18] and [19].

It is, however, hard to identify multimorbid patients with extensive or complex health care needs merely based on particular combinations of chronic conditions. Sinnige and colleagues, who studied multimorbidity patterns in an elderly general practice population, argued that multimorbidity is “far more complicated than merely the presence of two co-occurring diseases within a person”, and that the knowledge on comprehensive disease patterns should be taken into account when providing care for multimorbid patients. [20] Moreover, apart from illness-related factors, needs might also relate to individual patient characteristics such as socio-demographic and social characteristics (e.g. age, gender, education level, and living situation). The identification of profiles of groups of multimorbid patients with extensive health care needs will allow the health and social care system to better respond to their needs, for example by developing and implementing integrated care programs, or providing case management [8], [17], [18] and [19].

The aim of this study was therefore to gain more insight into the (differences in) health care utilization of multimorbid patients. More specifically, the current research addresses the following research questions:

1. How does health care utilization of patients with multimorbidity differ from health care utilization of patients with a single chronic disease?
2. Which subgroups of multimorbid patients can be distinguished on the basis of their health care utilization?
3. Which patient and illness characteristics are associated with these subgroups of multimorbid patients?

2. METHODS

To answer these research questions we combined data on morbidity, health care utilization and personal characteristics of three databases.

2.1. Databases

2.1.1. NIVEL Primary Care Database

NIVEL Primary Care Database (formerly known as LINH) is a nationally representative database that holds longitudinal data derived from patients' electronic medical records (EMR) on consultations, morbidity, drug prescriptions, and referrals. [21] In 2010, about 130 Dutch general practices provided data [22]. General practitioners (GPs) code diagnoses using the International Classification of Primary Care (ICPC-1) [23].

2.1.2. Dutch Hospital Data

The Dutch Hospital Data (DHD) database contains information on all day care and inpatient admissions for approximately 88% of all hospitals in the Netherlands [24].

2.1.3. Integrated Income Data — Households database

The Integrated Income Data — Households database, from Statistics Netherlands, contains information on the disposable income and size of each household in the Netherlands [25]. This is mainly derived from tax administration.

2.1.4. Linkage

Data from the three databases were linked using postal code, gender, and date of birth. Linkage was performed by a Trusted Third Party (TTP) and researchers only had access to anonymized data. To perform this linkage, patients had to be uniquely identifiable, i.e. no other persons with the same combination of date of birth, gender, and postal code should be present.

2.2. Study population

From the NIVEL Primary Care Database, we selected patients aged 18 years and older who had at least one chronic disease according to their medical record. For this study, we used a list of 29 chronic diseases which had been selected for previous studies based on their high prevalence among the general Dutch population and their chronic and severe character [26] and [20] (see Appendix A). In the Netherlands, all non-institutionalized inhabitants are listed in a general practice, and all consultations with the GP are fully reimbursed by the mandatory health insurance. The GP is usually the first professional to be consulted for health problems, and acts as a gatekeeper to secondary care. As medical records in primary care practice are generally complete and representative of the entire population, these are especially suitable for estimating prevalence of chronic diseases.

To be included in this study, patients were required to be registered in the same practice during the full period 2008–2010. By using a minimal period of three years, diagnoses were determined more accurately, as for some chronic diseases patients do not necessarily visit their GP each year. The data quality was assessed at practice level. Patient data were only used from practices who met the quality criteria for recording morbidity data in 2008–2009 and for health care utilization data in 2010.

This study was executed according to the precepts of the Dutch legislation on privacy and the regulations of the Dutch Data Protection Authority. According to Dutch legislation, studies using this kind of observational data do not require medical ethical approval, or informed consent.

2.3. Patient and illness-related characteristics

Data about age, gender, number and type(s) of chronic diseases were derived from NIVEL Primary Care Database. Disposable income (in Euros, over the year 2010) and household size (in the year 2010) were derived from the Integrated Income Data — Households database. Disposable income is defined as gross income minus: inter-household transfers paid, income insurance premiums, health insurance premiums, and capital income and gain taxes.

2.4. Health care utilization

2.4.1. GP care utilization

Data on the number of GP contacts in the year 2010 were derived from NIVEL Primary Care Database. Based on this number, we calculated an additional variable ‘having had ≥ 1 GP contact in 2010’ (yes = 1, no = 0).

2.4.2. Medication use

Data on the number of prescribed medications in the year 2010 were derived from NIVEL Primary Care Database. The number of different medications was calculated at ATC3-level. Based on this number, we calculated an additional variable

‘polypharmacy’ (yes = 1, no = 0), which reflects whether patients were prescribed ten or more different types of medications in 2010 on ATC3-level.

2.4.3. Hospital admission

Data on the number of *day care* and *inpatient* admissions to Dutch hospitals in 2010 were derived from the Dutch Hospital Data (DHD) database. Based on these numbers, we calculated two additional variables: ‘with ≥ 1 *day care* admission (yes = 1, no = 0) to the hospital in 2010’ and ‘with ≥ 1 one *inpatient* admission (yes = 1, no = 0) to the hospital in 2010’ (both: yes = 1, no = 0). Outpatient hospital care was not included in the analyses.

2.5. Data analysis

First, we compared patients diagnosed with a single chronic disease with those diagnosed with more than one chronic disease (multimorbidity) on the aforementioned patient and illness-related characteristics and health care utilization (research question 1). Differences between the two groups were tested with logistic regression analysis and Chi-square-tests, except for the number of GP contacts, which was tested using multivariate negative binomial regression analyses [27]. We chose this type of regression analysis since the number of GP consultations is a rate and this type of regression analysis predicts the rate of an event.

Next, to investigate differences in health care utilization among multimorbid patients (research question 2), cluster analysis was conducted [28]. We performed both hierarchical cluster analysis (complete linkage) and kmeans clustering. We first tested the stability of the analyses by performing several analyses with a random 95% sample. The Calinsky–Harabasz ratio was used as a stopping rule to determine the number of clusters. Based on the results we determined which type best suited the data. Cluster analysis was performed with the following clustering variables: number of GP contacts in 2010, number of prescribed medications in 2010, having had at least one day care admission to a hospital in 2010, and having had at least one inpatient admission to a hospital in 2010.

Finally, we performed a series of regression analyses (multiple, logistic) and Chi-square-tests in which we tested for differences in patient and illness characteristics between the groups identified by the cluster analysis (research question 3). Groups were added as dummy variables and dependent variables were prevalence of each of the listed chronic diseases, gender, age, household size, and income.

3. RESULTS

3.1. Patients with multimorbidity versus a single chronic disease compared

3.1.1. Patient characteristics and morbidity

The total sample consisted of 54,051 patients with one or more medically diagnosed chronic diseases. Sixty-three percent of them ($N = 33,844$) had a *single chronic disease*, and 37% ($N = 20,167$) were multimorbid. Compared to the subgroup of

patients with a single chronic disease (55.1%), the subgroup of multimorbid patients consisted of a somewhat higher proportion of women (58.2%; $\chi^2 [1] = 48.51$, $p < .0001$). Also, multimorbid patients were older ($M = 65.0$ years, $SD = 14.7$) than patients with a single chronic disease ($M = 53.6$ years, $SD = 16.5$; $LR\chi^2 [1] = 5299.80$, $p < .0001$). The five most prevalent chronic diseases among the sample of multimorbid patients were hypertension (55.4%), diabetes mellitus (30.0%), coronary artery disease (16.4%), chronic back/neck pain (15.8%), and osteoarthritis (14.6%). Among the group with a single chronic disease hypertension (26.1%), asthma (9.9%), chronic back/neck pain (9.2%), diabetes mellitus (8.6%), and depression (and psychosis; 6.9%) were most prevalent. Appendix B provides a full overview.

Data on household size and income were available for 46,011 patients (85%). Compared to patients with a single chronic disease ($M_e = 36,442$, $SD_e = 24,604$), patients with multiple chronic diseases had on average a lower annual disposable income ($M_e = 30,737$, $SD_e = 19,316$; $F[1, 46,009] = 682.77$, $p < .0001$). Also, multimorbid patients lived in a smaller household ($M = 2.00$, $SD = 1.01$) than patients with a single chronic disease ($M = 2.44$, $SD = 1.24$; $F[1, 46,009] = 1508.31$, $p < .0001$).

3.1.2. Healthcare utilization

3.1.2.1. GP contacts

As Table 1 shows, the proportion of patients with *at least one* GP visit in 2010 is higher among multimorbid patients than among patients with a single chronic disease ($\chi^2 [1] = 791.90$, $p < .0001$). On average, multimorbid patients visited the GP more than eight times in 2010, which is more frequent than patients with a single chronic disease who visited the GP somewhat more than five times ($LR\chi^2 [1] = 3641.68$, $p < .0001$).

3.1.2.2. Prescribed medications

On average, multimorbid patients had a higher number of prescribed different medications ($M = 7.07$, $SD = 4.32$) than patients with a single chronic disease ($M = 3.90$, $SD = 3.26$; $LR\chi^2 [1] = 7848.62$, $p < .0001$). The proportion of patients with polypharmacy is higher among multimorbid patients (24.95%) than among patients with a single chronic disease (6.36%; $\chi^2 [1] = 3800$, $p < .0001$).

3.1.2.3. Hospital admissions

The proportion of patients with *at least one* day care admission in 2010 is higher among multimorbid patients (14.23%) than among patients with a single chronic disease (8.78%; $\chi^2 [1] = 311.04$, $p < .0001$). Also, a greater proportion of multimorbid patients (15.82%) had at least one inpatient admission compared to patients with a single chronic disease (8.75; $\chi^2 [1] = 499.43$, $p < .0001$).

3.2. Subgroups of multimorbid patients on the basis of health care utilization

Of the 20,167 multimorbid patients, data on health care use, hospitalizations, income, and household size were available for 16,482 patients (82%). Kmeans clustering resulted in the most robust results. Cluster analysis revealed a three-cluster solution as the optimal number of clusters that could explain the profile structure of health care utilization of multimorbid patients (see Table 2).

[TABLE 2]

As shown in Table 2, Cluster 1 is the largest cluster ($n = 9385$; 57%), characterized by relatively low levels of health care utilization. Ninety percent of the patients in this cluster visited the GP at least once in 2010; the average number of visits was 3.8 ($SD = 2.4$). Patients in Cluster 1 were prescribed on average somewhat less than five different types of medications, and 5.5% of the patients had polypharmacy. With regard to hospital admissions, 10% had at least one day care admission and 9.2% had at least one inpatient admission in 2010.

Cluster 2 comprises a smaller though substantial number of patients ($n = 5847$; 36%), and is characterized by higher levels of health care utilization. All people in Cluster 2 visited the GP at least once in 2010, and the average number of visits was 11.8 ($SD = 3.5$). Patients in Cluster 2 were prescribed on average somewhat more than nine different types of medications, and 44.0% of the patients had polypharmacy. With regard to hospital admissions, 18.7% had at least one day care admission and 21.8% had at least one inpatient admission in 2010.

Cluster 3 comprises only 7.6% ($n = 1250$) of the multimorbid patients, and is characterized by very high levels of health care utilization. All these people visited the GP at least once in 2010, and the average number of visits was 28.0 ($SD = 9.6$). Patients in Cluster 3 were prescribed on average more than thirteen different types of medications, and almost eight out of ten patients had polypharmacy. With regard to hospital admissions, more than a quarter of the patients in Cluster 3 had at least one day care admission and almost four out of ten had at least one inpatient admission in 2010. Clusters differed significantly ($p < .0001$) on all health care utilization measures.

3.3. Characteristics of subgroups of multimorbid patients

3.3.1. Patient characteristics

As shown in Table 3, the cluster associated with relatively low levels of health care utilization (Cluster 1) contains somewhat more women than men (54% vs. 46%), and the average age is about 63 years. The yearly disposable income of these people was 33,306 Euros and they lived in a household of 2.1 persons on average. The cluster associated with higher (but not the highest) levels of health care utilization (Cluster 2) contains more women than men (62% vs. 38%) and the average age is 68 years. The yearly disposable income of people in Cluster 2 was 28,930 Euros, and they lived in a household of 1.9 persons on average. The cluster associated with the

highest levels of health care utilization (Cluster 3) contains more than twice as many women as men (70% vs. 30%) and the average age is almost 72 years, which is almost ten years older than people in Cluster 1. The yearly disposable income of people in Cluster 3 was 25,030 Euros, which is only 75% of the yearly disposable income of people in Cluster 1. People in Cluster 3 lived in a household of 1.7 persons on average. Clusters differed significantly ($p < .0001$) on all patient characteristics.

[TABLE 3]

3.3.2. Clinical characteristics

People in the cluster that is associated with relatively low levels of health care utilization (Cluster 1) had 2.4 ($SD = 0.7$) chronic diseases on average. The five most prevalent chronic diseases among patients in Cluster 1 were hypertension (54.8%), diabetes mellitus (26.2%), chronic back/neck pain (16.3%), coronary artery disease (14.2%), and osteoarthritis (13.9%). People in Cluster 2 had 2.7 ($SD = 1.0$) chronic diseases on average, and the five most prevalent chronic diseases among them were hypertension (60.1%), diabetes mellitus (33.4%), coronary artery disease (19.6%), COPD (16.6%), and osteoarthritis (16.2%). People in the cluster that is associated with the highest levels of health care utilization (Cluster 3) had 3.1 ($SD = 1.2$) chronic diseases on average. The five most prevalent chronic diseases among these patients were hypertension (55.9%), diabetes mellitus (43.5%), COPD (23.9%), coronary artery disease (20.8%), and osteoarthritis (17.5%).

On average, people in clusters that are associated with higher health care utilization had more chronic diseases ($LR\chi^2 [2] = 311.28, p < .0001$). When looking at individual chronic diseases, for 13 out of 17 diseases the presence varied across the three clusters (see Table 3 and Appendix C). Of these 13 chronic diseases, 11 were more common in the cluster(s) with the highest health care utilization. Especially heart failure, COPD, anxiety disorder, and diabetes mellitus were more common in the cluster with the highest health care utilization. Migraine, in contrast, was more common in the cluster with the lowest health care utilization. Anxiety disorder was (slightly) more common in the clusters with the highest and the lowest health care utilization, but less common in the middle cluster. The prevalence of asthma, depression, hearing disorder and chronic back or neck pain did not differ between the three clusters (χ^2 - and p -values in Table 3).

4. DISCUSSION

Health care utilization is higher among multimorbid patients than among patients with a single chronic disease, but there is a large subgroup of multimorbid patients (about 60%) in which healthcare utilization is only slightly higher compared to patients with a single chronic disease, suggesting that these people, with the right support, are fairly able to provide in their own care and manage their conditions. A smaller group (however more than one third of all multimorbid patients) utilizes health care services or medications considerably more often, suggesting that these people have greater difficulty in managing their conditions, and might therefore benefit from disease management provided by multidisciplinary teams of health care

providers. A relatively small subgroup of multimorbid patients (7.6%) makes extensive use of healthcare, suggesting that their care is disproportionately complex and difficult to manage for themselves as well as for the health care system. These people might therefore benefit most from integrated care and case management.

Multimorbid patients with high health care utilization are thus most likely to benefit from integrated care. In order to optimally meet their comprehensive needs, it is important to identify the patients with more complex needs. With respect to patient-related characteristics, and in line with previous research [29] and [30] our findings show that these patients are older (i.e. patients with the most complex needs were over 70 years on average), more often female (i.e. seven out of ten patients with extensive health care use), have a lower disposable income (on average, the disposable income of the most complex patients is only 75% of that of patients with a single chronic disease), and they have a smaller household size, which implies that they are relatively often living alone. Interestingly, a recent Canadian study did not find a relationship between income and primary health care use of older multimorbid patients, which they attributed to the relatively small variation in SES and universal access to health care [31].

With respect to clinical or illness characteristics it is also possible to draw a profile of multimorbid patients with more complex health care needs. Not only do they suffer from *more* chronic diseases than multimorbid people with a lower health care utilization, they also differ considerably with respect to the *types* of chronic diseases they suffer from. Especially heart failure, COPD, and diabetes mellitus are relatively common among multimorbid patients with a high use of primary and hospital care. Heart failure, COPD and diabetes have also proven to be strong predictors in several risk stratification models predicting negative health outcomes [32] and high health care costs [33], and synergistic negative effects on physical functioning and high health care costs have been found for disease pairs consisting of chronic respiratory disease, diabetes and/or cardiovascular disease [12] and [34].

The prevalence of anxiety disorder was remarkable as well since this disease was, in a relative way, especially prevalent among multimorbid patients with an *extensive* health care use and somewhat more prevalent (than could be expected based on the distribution of patients among the three clusters) among multimorbid patients with a *low* health care use, whereas the prevalence of anxiety disorder was relatively low among patients with a *heightened* (but not the highest) health care use. Possibly, anxiety symptoms or complaints arise from the burden of suffering from multiple diseases and the difficulty (or inability) to cope with and control these diseases. However, no research is known examining the relation of (somatic) multimorbidity and anxiety disorder. Further research might provide more insight into this matter.

4.1. Strengths and limitations

A strength of our study is that it was not susceptible to the potential recruitment bias often associated with studies focusing on patients recruited through hospitals or clinics. Data (of a large sample) of patients with one or more chronic disease were available, and selection bias was minimal since almost all Dutch inhabitants are

listed in a general practice. Recording in EHRs is most likely accurate since practices used these files for reimbursement claims with insurance companies.

A limitation might be incompleteness of the DHD database: in 2010 14% of the hospitals did not provide data [24]. This might have led to an underestimation of the actual number of admitted persons as well as the actual number of admissions per person, but there is no reason to expect that this underestimation is more pronounced in specific patient groups (i.e. within multimorbid patients or patients with a single chronic disease, or within specific clusters of multimorbid patients) thereby affecting the study outcomes.

Possible mistakes in ICPC recording (i.e. typing errors or incorrect coding) could have been made, but it is unlikely that coding errors would differ systematically between the different clusters of multimorbid patients, or between multimorbid patients and patients with a single chronic disease.

5. CONCLUSION

Health care utilization among multimorbid patients is higher compared to patients with a single chronic disease, but a large proportion of the people with multimorbidity (about 60%) has only a slightly higher health care utilization. Compared to multimorbid patients with polypharmacy, multimorbid patients *without* polypharmacy have a relatively low level of health care utilization suggesting that these people – with the right support – are fairly able to provide in their own care and manage their conditions. Heightened (or extensive, applying to almost 8% of the patients) health care utilization among patients with multimorbidity is related to a higher number of chronic diseases as well as to specific types of diseases, such as heart failure, COPD, and diabetes mellitus. Patient characteristics such as age, household size, and income also impact on healthcare use among multimorbid patients. This should be taken into account, when identifying target groups for integrated care programmes.

It would be interesting to study patients with characteristics that seem to be connected with higher health care use before they develop multimorbidity or polypharmacy, to develop strategies to affect the clinical evolution with primary or secondary prevention policies. Finally, it would be important to collect prospective data for the three subgroups on outcomes, such as mortality. Results could be used to plan effective actions to improve patients' quality of life as well as health and economical resource utilization.

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Conflict of interest

The authors have no competing interests to report.

Appendix A. ICPC codes of the 29 examined chronic diseases

	Chronic disease	ICPC-code(s)
1	Anxiety disorder	P74
2	Asthma	R96
3	Cancer	A79, B72-B74, D75-D77, L71, N74, R84, R85, S77, T71, U75-U77, W72, X75-X77, Y77, Y78
4	Cardiac dysrhythmia	K78-K80
5	Chronic alcohol abuse	P15
6	Chronic back or neck disorder	L83, L84, L86
7	Congenital cardiovascular anomaly	K73
8	COPD	R91, R95
9	Coronary artery disease	K74-K76
10	Dementia (incl. Alzheimer's disease)	P70
11	Depression (and psychosis)	P73, P76
12	Diabetes mellitus	T90
13	Epilepsy	N88
14	Hearing disorder	H84-H86
15	Heart failure	K77
16	Heart valve disorder	K83
17	HIV/AIDS	B90
18	Hypertension	K86, K87
19	Mental retardation	P85
20	Migraine	N89
21	Neuraesthesia/surmenage/burn-out	P78
22	Osteoarthritis	L89-L91
23	Osteoporosis	L95
24	Parkinson's disease	N97
25	Personality disorder	P80
26	Rheumatoid arthritis	L88
27	Schizophrenia	P72
28	Stroke	K90
29	Visual disorder	F83, F84, F92-F94

APPENDIX B. PREVALENCE OF 29 CHRONIC CONDITIONS AMONG A SAMPLE OF PEOPLE WITH MULTIMORBIDITY AND AMONG A SAMPLE OF PEOPLE WITH ONE CHRONIC CONDITION (2010)

	Multimorbidity (N = 20,167; 37.3%)		One chronic condition (N = 33,884; 62.7%)	
	<i>n</i>	%	<i>n</i>	%
Hypertension	11,168	55.4	8829	26.1
Diabetes mellitus	6053	30.0	2900	8.6
Coronary artery disease	3307	16.4	1029	3.0
Chronic back/neck pain	3187	15.8	3110	9.2
Osteoarthritis	2948	14.6	1294	3.8
COPD	2793	13.9	915	2.7
Asthma	2780	13.8	3347	9.9
Cancer	2541	12.6	1506	4.5
Depression (and psychosis)	2474	12.3	2335	6.9
Visual disorder	1926	9.6	647	1.9
Cardiac dysrhythmia	1638	8.1	622	1.8
Osteoporosis	1223	6.1	401	1.2
Heart failure	1198	5.9	166	0.5
Stroke	1030	5.1	246	0.7
Migraine	1029	5.1	1733	5.1
Hearing disorder	1022	5.1	527	1.6
Anxiety disorder	1013	5.0	1084	3.2
Neurasthenia/surmenage/burn-out	830	4.1	1246	3.7
Rheumatoid arthritis	635	3.2	394	1.2
Chronic alcohol abuse	453	2.3	348	1.0
Heart valve disorder	399	2.0	129	0.4
Epilepsy	331	1.6	336	1.0
Dementia	329	1.6	108	0.3
Personality disorder	257	1.3	208	0.6
Parkinson's disease	178	0.9	73	0.2
Schizophrenia	87	0.4	137	0.4
Mental retardation	64	0.3	71	0.2
Congenital cardiovascular anomaly	33	0.2	49	0.1
HIV/AIDS	29	0.1	54	0.2

APPENDIX C. THE DISTRIBUTION OVER THE THREE CLUSTERS OF PATIENTS WITH A CERTAIN CHRONIC DISEASE; GREEN IMPLIES FEWER PATIENTS (THAN AVERAGE) IN THAT CLUSTER, AND RED IMPLIES MORE PATIENTS (THAN AVERAGE) IN THAT CLUSTER

	Cluster 1 (n = 9385;56.9%)	Cluster 2 (n = 5847;35.5%)	Cluster 3 (n = 1250;7.6%)	p
Heart failure	33.2%	47.5%	19.2%	<0.0001
COPD	44.2%	42.7%	13.2%	<0.0001
Osteoporosis	47.3%	42.4%	10.4%	<0.0001
Cardiac dysrhythmia	48.1%	41.6%	10.4%	<0.0001
Stroke	48.6%	41.0%	10.4%	<0.0001
CAD	48.7%	41.8%	9.5%	<0.0001
Diabetes mellitus	49.6%	39.4%	11.0%	<0.0001
Osteoarthritis	52.8%	38.4%	8.9%	<0.0001
Visual disorder	53.1%	37.4%	9.5%	<0.0001
Hypertension	55.0%	37.5%	7.5%	<0.0001
Cancer	55.7%	35.3%	8.9%	0.049
Asthma	56.3%	36.3%	7.4%	0.64
Depression	56.4%	34.9%	8.7%	0.14
Hearing disorder	58.5%	35.8%	5.7%	0.09
Chronic back/neck pain	58.7%	34.3%	7.0%	0.11
Anxiety disorder	58.7%	29.9%	11.4%	<0.0001
Migraine	64.4%	30.7%	4.9%	<0.0001

REFERENCES

- [1] van Oostrom SH, Gijsen R, Stirbu I, Korevaar JC, Schellevis FG, Picavet HSJ, et al. Rise in the prevalence of chronic diseases and multimorbidity from 2001 to 2011 in the Dutch population; 2014[Manuscript submitted for publication].
- [2] Eurostat.
http://epp.eurostat.ec.europa.eu/portal/page/portal/health/public_health/data_public_health/database. [Table people having a long-standing illness or health problem, by sex, age and income quintile, year] 2010.
- [3] Busse R, Blümel M, Scheller-Kreinsen D, Zentner A. Tackling chronic disease in Europe. Strategies, interventions and challenges. Observatory studies series no. 20. World Health Organization, on behalf of the European Observatory on Health Systems and Policies series; 2010.
- [4] Boyd C, Fortin M. Future of multimorbidity research: how should understanding of multimorbidity inform health system design? *Public Health Rev* 2010;32:451–74.

- [5] Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. *Eur J Gen Pract* 2008;14(1):28–32. <http://dx.doi.org/10.1080/13814780802436093>.
- [6] Bower P, Macdonald W, Harkness E, Gask L, Kendrick T, Valderas JM, et al. Multimorbidity, service organization and clinical decision making in primary care: a qualitative study. *Fam Pract* 2011;28(5):579–87. <http://dx.doi.org/10.1093/fampra/cmr018>.
- [7] Smith SM, Soubhi H, Fortin M, Hudon C, O'Dowd T. Managing patients with multimorbidity: systematic review of interventions in primary care and community settings. *Cochrane Database Syst Rev* 2012;2012(4). <http://dx.doi.org/10.1002/14651858.CD006560.pub2>.
- [8] Rijken M, Struckmann V, Dyakova M, Melchiorre MG, Rissanen S, van Ginneken E. ICARE4EU: improving care for people with multiple chronic conditions in Europe. *Eurohealth* 2013;19(3):29–31.
- [9] Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: a systematic review of the literature. *Aging Res Rev* 2011;10: 430–9. <http://dx.doi.org/10.1016/j.arr.2011.03.003>.
- [10] Vogeli C, Shields AE, Lee TA, Gibson TB, Marder WD, Weiss KB, et al. Multiple chronic conditions: prevalence, health consequences, and implications for quality, care management, and costs. *J Gen Intern Med* 2007;22(Suppl. 3):391–5. <http://dx.doi.org/10.1007/s11606-007-0322-1>.
- [11] Kadam UT, Croft, P. R. North Staffordshire GP Consortium group. Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice. *Fam Pract* 2007;24(5):412–9. <http://dx.doi.org/10.1093/fampra/cmm049>.
- [12] Rijken M, Kerkhof Mv, Dekker J, Schellevis FG. Comorbidity of chronic diseases: effects of disease pairs on physical and mental functioning. *Qual Life Res* 2005;14(1):45–55. <http://dx.doi.org/10.1007/s11136-004-0616-2>.
- [13] Fortin M, Bravo G, Hudon C, Lapointe L, Almirall J, Dubois MF, et al. Relationship between multimorbidity and health-related quality of life of patients in primary care. *Qual Life Res* 2006;15:83–91. <http://dx.doi.org/10.1007/s11136-005-8661-z>.
- [14] Hopman P, Schellevis FG, Rijken M. Health-related needs of people with multiple chronic diseases: differences and underlying factors. *Qual Life Res* 2016;25(3): 651–60. <http://dx.doi.org/10.1007/s11136-015-1102-8>.
- [15] Fortin M, Bravo G, Hudon C, Lapointe L, Dubois MF, Almirall J. Psychological distress and multimorbidity in primary care. *Ann Fam Med* 2006;4(5):417–22. <http://dx.doi.org/10.1370/afm.528>.
- [16] Menotti A, Mulder I, Nissinen A, Giampaoli S, Feskens EJ, Kromhout D. Prevalence of morbidity and multimorbidity in elderly male populations and their impact on 10-year all-cause mortality: the FINE study (Finland, Italy, Netherlands, elderly). *J Clin Epidemiol* 2001;54:680–6. [http://dx.doi.org/10.1016/S0895-4356\(00\)00368-1](http://dx.doi.org/10.1016/S0895-4356(00)00368-1).
- [17] de Bruin SR, Heijink R, Lemmens L, Struijs JN, Baan CA. Impact of disease management programs on healthcare expenditures for patients with diabetes, depression, heart failure or chronic obstructive pulmonary disease: a systematic review of the literature. *Health Policy* 2011;101:105–21. <http://dx.doi.org/10.1016/j.healthpol.2011.03.006>.
- [18] Boulton C, Green AF, Boulton LB, Pacala JT, Snyder C, Leff B. Successful models of comprehensive care for older adults with chronic conditions: evidence for the institute of medicine's "retooling for an aging America" report. *J Am Geriatr Soc* 2009;57: 2328–37. <http://dx.doi.org/10.1111/j.1532-5415.2009.02571.x>.
- [19] Hopman EPC, de Bruin SR, Forjaz J, Rodriguez Blazquez C, Tonnara G, Lemmens LC, et al. Effectiveness of comprehensive care programs for patients with multiple chronic conditions or frailty: a systematic literature review. *Health Policy* 2016. <http://dx.doi.org/10.1016/j.healthpol.2016.04.002> [Advance online publication].
- [20] Sinnige J, Korevaar JC, Westert GP, Spreeuwenberg P, Schellevis FG, Braspenning JC. Multimorbidity patterns in a primary care population aged 55 years and over. *Fam Pract* 2015;32(5):505–13. <http://dx.doi.org/10.1093/fampra/cmz037>.
- [21] <http://www.nivel.nl/en/dossier/nivel-primary-care-database>. [22] Verheij RA. Over NIVEL zorgregistraties: geschiedenis en achtergrond. Uit: NIVEL zorgregistraties eerste lijn. www.nivel.nl/node/3464; 2013. [Last update March 10, 2014. Accessed March 20, 2014].

- [23] Lamberts H, Wood M. The birth of the international classification of primary care (ICPC). Serendipity at the border of Lac Léman. *Fam Pract* 2002;19:433–5. <http://dx.doi.org/10.1093/fampra/19.5.433>.
- [24] Statistics Netherlands/Centraal Bureau voor de Statistiek, Centrum voor Beleidsstatistiek. Documentatierapport Landelijke Medische Registratie (LMR) 2011V1. 2013 [Retrieved from] <http://www.cbs.nl/NR/rdonlyres/AA18B546-CA6E-40C6-8B17-1BB976F1C4E5/0/lmrmicrodata.pdf>. [on March 31, 2014].
- [25] Statistics Netherlands/Centraal Bureau voor de Statistiek, Centrum voor Beleidsstatistiek. Documentatierapport Woononderzoek Nederland (WoON) 2012. 2013 [Retrieved from] <http://www.cbs.nl/NR/rdonlyres/9EAD3408-D873-465EA0F5-38C810832FBA/0/woonmicrodata.pdf>. [on May 13, 2014].
- [26] van Oostrom SH, Picavet HS, van Gelder BM, Lemmens LC, Hoeymans N, Verheij RA, et al. Multimorbidity and comorbidity in the Dutch population—data from general practices. *BMC Public Health* 2012;12:715. <http://dx.doi.org/10.1186/1471-2458-12-715>.
- [27] Lawless JF. Negative binomial and mixed Poisson regression. *Can J Stat* 1987;15(3): 209–25.
- [28] Stata.com. Cluster analysis. 2014 [Retrieved from] <http://www.stata.com/features/luster-analysis/>. [on December 12, 2014].
- [29] van Oostrom SH, Picavet HSJ, de Bruin SR, Stirbu I, Korevaar JC, Schellevis FG, et al. Multimorbidity of chronic diseases and health care utilization in general practice. *BMC Fam Pract* 2014;15:61. <http://dx.doi.org/10.1186/1471-2296-15-61>.
- [30] Bähler C, Huber CA, Brüngger B, Reich O. Multimorbidity, health care utilization and costs in an elderly community-dwelling population: a claims data based observational study. *BMC Health Serv Res* 2015;15(23).
- [31] Lane NE, Maxwell CJ, Gruneir A, Bronskill SE, Wodchis WP. Absence of a socioeconomic gradient in older adults' survival with multiple chronic conditions. *EBioMedicine* 2015; 2(12):2094–100. <http://dx.doi.org/10.1016/j.ebiom.2015.11.018>.
- [32] Alonso-Morá E, Nuño-Solinis R, Onder G, Tonnara G. Multimorbidity in risk stratification tools to predict negative outcomes in adult population. *Eur J Intern Med* 2015; 26:182–9. <http://dx.doi.org/10.1016/j.ejim.2015.02.010>.
- [33] Eckardt M, Brettschneider C, van den Bussche H, König HH. MultiCare Study Group. Analysis of health care costs in elderly patients with multiple chronic conditions using a finite mixture of generalized linear models. *Health Econ* 2016. <http://dx.doi.org/10.1002/heal>.
- [34] Zulman DM, Pal Chee C, Wagner TH, Yoon J, Cohen DM, Holmes TH, et al. Multimorbidity and healthcare utilisation among high-cost patients in the US veterans affairs health care system. *BMJ Open* 2015;5. <http://dx.doi.org/10.1136/bmjopen-2015-007771>.

TABLES

Table 1. Health care utilization in the year 2010 of people with multimorbidity versus one chronic condition ($N = 54,051$).

	Multimorbidity ($n = 20,167$; 37.3%)		One chronic condition ($n = 33,884$; 62.7%)		(LR) χ^2, p
	<i>n</i>	%	<i>n</i>	%	
GP contact					
≥ 1 GP contact	18,952	93.98	29,163	86.17	χ^2 (1)=791.90, $p < 0.0001$
Number of GP contacts (M, SD)	8.54 (7.90)		5.13 (5.36)		LR χ^2 (1)=3641.68, $p < 0.0001$
Prescribed medication					
Number of prescribed different medications (M, SD)^a	7.07 (4.32)		3.90 (3.26)		LR χ^2 (1)=7848.62, $p < 0.0001$
Polypharmacy^b	5031	24.95	2153	6.36	χ^2 (1)=3800, $p < 0.0001$
Hospital admission ($n=42,776$)^c					
≥ 1 day care admission	2346	14.23	2308	8.78	χ^2 (1)=311.04, $p < 0.0001$
≥ 1 inpatient admission	2608	15.82	2300	8.75	χ^2 (1)=499.43, $p < 0.0001$

- a) Different types, on ATC3-level.
- b) ≥ 10 prescriptions (different types, on ATC3-level).
- c) Calculation by NIVEL based on micro data files on Dutch Hospital Data, made available by Statistics Netherlands.

Table 2. Description of multimorbidity clusters according to health care utilization in the year 2010 ($N = 16,482$).

	Cluster 1 ($n = 9385$; 56.9%)		Cluster 2 ($n = 5847$; 35.5%)		Cluster 3 ($n = 1250$; 7.6%)		(LR) χ^2 , p
	n	%	N	%	n	%	
GP contact							
≥ 1 GP contact ^a	8435	89.9	5847	100	1250	100	χ^2 (2)=762.34, $p < 0.0001$
Number of GP contacts (M, SD)	3.8 (2.4)		11.8 (3.5)		28.0 (9.6)		LR χ^2 (2)=19,959.85, $p < 0.0001$
Prescribed medication							
Number of prescribed different medications (M, SD) ^b	4.8 (2.7)		9.3 (3.6)		13.3 (4.7)		LR χ^2 (2)=8280.67, $p < 0.0001$
Polypharmacy (M, SD) ^c	513	5.5	2573	44.0	978	78.2	χ^2 (2)=5000, $p < 0.0001$
Hospital admission ^d							
≥ 1 day care admission	934	10.0	1093	18.7	319	25.5	χ^2 (2)=366.62, $p < 0.0001$
≥ 1 inpatient admission	861	9.2	1272	21.8	475	38.0	χ^2 (2)=927.49, $p < 0.0001$

- This variable was not used in the cluster analysis since it was directly derived from the variable 'Number of GP contacts' (which was included in the analysis).
- Different types, on ATC3-level.
- ≥ 10 prescriptions (different types, on ATC3-level). This variable was not used in the cluster analysis since it was directly derived from the variable 'Number of prescribed different medications' (which was included in the analysis).
- Calculation by NIVEL based on micro data files on Dutch Hospital Data, made available by Statistics Netherlands.

Table 3. Patient and illness-related characteristics (in the year 2010) of people within the multimorbidity clusters ($N = 16,482$).

	Cluster 1 ($n = 9385$; 56.9%)		Cluster 2 ($n = 5847$; 35.5%)		Cluster 3 ($n = 1250$; 7.6%)		(LR) χ^2, p
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Patient characteristics							
Gender							
- Male	4336	46.2	2206	37.7	371	29.7	$\chi^2 (2)=189.73$, $p<0.0001$
- Female	5049	53.8	3641	62.3	879	70.3	
Age (M, SD)	63.1 (14.0)		68.0 (13.8)		71.7 (14.2)		F (2, 16,479)=353.53, adj R2=0.04, $p<0.0001$
Disposable income (€) in the year 2010 (M, SD) ^a	33,306 (21,212)		28,930 (16,887)		25,030 (12,921)		F (2, 16,478)=161.10, adj R2=0.02, $p<0.0001$ ^b
Household size (M, SD) ^{a/c}	2.1 (1.0)		1.9 (1.0)		1.7 (0.8)		F (2, 16,478)=126.21, adj R2=0.02, $p<0.0001$
Illness-related characteristics							
Number of chronic diseases (M, SD)	2.4 (0.7)		2.7 (1.0)		3.1 (1.2)		LR $\chi^2 (2)=311.28$, $p<0.0001$ ^d
Chronic disease ^e							
- Hypertension	5144	54.8	3511	60.1	699	55.9	$\chi^2 (2)=40.64$, $p<0.0001$
- Diabetes mellitus	2457	26.2	1954	33.4	544	43.5	$\chi^2 (2)=206.28$, $p<0.0001$
- Coronary artery disease	1333	14.2	1146	19.6	260	20.8	$\chi^2 (2)=92.78$, $p<0.0001$
- Chronic back/neck pain	1532	16.3	895	15.3	182	14.6	$\chi^2 (2)=4.43$, $p=0.11$
- Osteoarthritis	1306	13.9	949	16.2	219	17.5	$\chi^2 (2)=21.81$, $p<0.0001$
- COPD	1004	10.7	970	16.6	299	23.9	$\chi^2 (2)=221.91$, $p<0.0001$
- Asthma	1263	13.5	815	13.9	165	13.2	$\chi^2 (2)=0.90$, $p=0.64$
- Cancer	1131	12.1	717	12.3	181	14.5	$\chi^2 (2)=6.05$,

	Cluster 1 (n = 9385; 56.9%)		Cluster 2 (n = 5847; 35.5%)		Cluster 3 (n = 1250; 7.6%)		(LR) χ^2 , p
	n	%	n	%	n	%	
							p=0.049
- Depression (and psychosis)	1088	11.6	673	11.5	168	13.4	χ^2 (2)=3.97, p=0.14
- Visual disorder	868	9.3	612	10.5	155	12.4	χ^2 (2)=15.29, p<0.0001
- Cardiac dysrhythmia	659	7.0	570	9.8	142	11.4	χ^2 (2)=51.53, p<0.0001
- Osteoporosis	473	5.0	424	7.3	104	8.3	χ^2 (2)=42.86, p<0.0001
- Heart failure	316	3.4	452	7.7	183	14.6	χ^2 (2)=321.88, p<0.0001
- Stroke	402	4.3	339	5.8	86	6.9	χ^2 (2)=27.18, p<0.0001
- Migraine	512	5.5	244	4.2	39	3.1	χ^2 (2)=21.46, p<0.0001
- Hearing disorder	506	5.4	310	5.3	49	3.9	χ^2 (2)=4.86, p=0.09
- Anxiety disorder	458	4.9	233	4.0	89	7.1	χ^2 (2)=23.50, p<0.0001

- Calculation by NIVEL based on micro data files on Integral Household Incomes, made available by Statistics Netherlands.
- The difference in average disposable income between clusters remains when corrected for age and gender.
- Including the patient him/herself.
- One patient with nine different comorbidities was deleted, as the model would not converge with this observation.
- Diseases that were present in less than 5.0% of the sample with multimorbidity are not displayed here.