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Multimorbidity and hospital admissions in high-need, high-cost elderly patients

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Abstract:	Objectives The aim was to clarify which pairs or clusters of diseases predict the hospital-related events and death in a population of patients with complex-health-care-needs (PCHCN). Methods Subjects classified in 2012 as PCHCN in a local health unit by ACG® System were linked with hospital discharge records in 2013 to identify those who experienced any of a series of hospital admission events and death. Number of comorbidities, comorbidities dyads and latent classes were used as exposure variable. Regression analyses were applied to examine the associations between dependent and exposure variables. Results Besides the fact that larger number of chronic conditions is associated with higher odds of hospital admission or death, we showed that certain dyads and classes of diseases have a particularly strong association with these outcomes. Discussion Unlike morbidity counts, analyzing morbidity clusters and dyads reveals which combinations of morbidities are associated with the highest hospitalization rates or death.

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Introduction

Patients with complex health care needs (PCHCN) have numerous and costly health issues that place a heavy burden on health care resources (Hayes, et al., 2016). Efforts in the US to better classify PCHCN have shown that such patients are mainly frail elderly people, or individuals with multiple chronic conditions (multimorbidity). Targeting the needs of these patients, and particularly of those at high risk of specific health-related events, has raised interest in designing health care systems that can improve patients' health outcomes while reducing the related costs (Hochman & Asch, 2017). Multimorbidity in PCHCN poses new challenges to health care services (Marengoni, et al., 2011). Various approaches have been used to elucidate the complexity of multimorbidity, based on the fundamental assumption that health outcomes in patients with multimorbidity are influenced not only by their single diseases, but also by the additional effects of interactions between them (Fortin, et al., 2012). Identifying patterns in how chronic conditions occur in combinations in patients needing the most care and support is important to the efficient allocation of resources. Understanding how chronic conditions cluster together, and clarifying the impact of these disease patterns on health outcomes is essential to funding medical care and planning prevention and treatment services. Most research on multimorbidity has focused on measures adopting simple disease counts, but such approaches fail to capture specific combinations or patterns, and few studies have associated different chronic disease clusters in PCHCN with different demands on health care services with a view to better targeting these services to their needs.

Collerton and colleagues (Collerton, et al., 2016) used cluster analysis to identify patterns in the burden of morbidity for a given patient, also exploring associations with their use of medication and health care. They found differences between comorbidity clusters that concerned the numbers of medicines, hospital admissions, general practitioner consultations, and general practice nurse consultations. Another study (Olaya, et al., 2017) identified multimorbidity patterns using latent class analysis, finding associations between these patterns and several outcomes, including hospital admissions. The authors found two latent classes - cardiovascular/mental/arthritis and metabolic/stroke - and the former was significantly associated with more medical consultations and more hospital admissions.

A recently-published review of studies on patterns of multimorbidity (Prados-Torres, et al., 2014) concluded for an urgent need to conduct further research of this type, essentially for the purpose of orienting future health policies, developing case management programs, and designing clinical practice guidelines to help professionals respond to the special needs of people with multimorbidity. The aim of the present study was to ascertain which disease clusters are associated with a greater need for hospital services, and with a higher mortality in a population of elderly patients with numerous health care needs, with a view to better organizing health care for these PCHCN.

Methods

Context

The Italian National Health System (NHS) is a public service financed mainly by general taxation. It is grounded on values of universality, free access, freedom of choice, pluralism in provision, and equity. Regional authorities plan and organize health care facilities and activities through their regional health departments in accordance with a national health plan designed to assure an equitable provision of comprehensive care throughout the country. The regional authorities coordinate and control local health units (LHU), each of which is a separate geographically-based public company delivering public health promotion and community health services, primary care and hospital care, either with their own facilities and personnel or through outside contractors. The Veneto Regional Health Service had 21 such LHUs serving a population of about five million. The LHU involved in the present study was the "Azienda ex-ULSS4-Veneto", which served a population of about 190,000 in the province of Vicenza, in north-east Italy.

To see which multimorbidity patterns in PCHCN are associated with particular demands for hospital services, our analysis was developed as follows:

- a cohort of PCHCN was identified;
- patients were characterized by their multimorbidity, identifying the number of chronic conditions, diseases dyads (or pairs) and clusters for each patient;
- an association was sought between different multimorbidity patterns and different demands for hospital services (measured as: at least one hospital admission; at least two hospital admissions; at least one preventable admissions; total number of admissions, total days in hospital), or death.

The ACG® System: identifying the sample

The ACG® (Adjusted Clinical Groups) System was implemented in the Veneto Region in 2012 as a tool for population risk stratification. The ACG® System is a method used internationally to characterize multimorbidity on the strength of routinely-collected administrative data (e.g. hospital discharge records, pharmaceutical prescriptions, access to emergency departments, prescription charge exemptions) gathered using record linkage (The Johns Hopkins University, 2014). It relies on an algorithm that starts from individual-level diagnoses and is based on clinical judgements of likelihood (persistence or recurrence over time, demand for specialist services, hospitalization, disability or decline in quality of life, expected need for, and use of diagnostic or therapeutic procedures), and is then adjusted for age and sex, to group a population by 93 mutually-exclusive combinations of conditions. The ACG define clinically logical categories of patients expected to need similar levels of health care. Based on their health care resource usage, the ACG® System automatically collapses the different ACG into six Resource Utilization Bands (RUBs), which are defined as follows: 0, nonuser or invalid diagnosis; 1 healthy user; 2 low morbidity; 3 moderate morbidity; 4 high morbidity; 5 very high morbidity.

For the purposes of the present study, only people over 65 years old in 2012, residing in the area served by the LHU "Azienda ULSS4-Veneto", and characterized as patients with complex health care needs (PCHCN), classified as RUBs 4 and 5 were considered.

The ACG® System: identifying chronic conditions

For each individual included in the study, we extracted the *EDC (Expanded Diagnosis Clusters)*, which coincide with the clinical diagnosis that the ACG system assigns to single patients by combining different information flows. To improve the sensitivity of our model, patients with chronic conditions were also identified by means of the information available from the Pharmacy (RX)-based Morbidity Marker Groups (Rx-MGs™), which is a drug-related diagnostic approach. A dichotomous variable was assigned to each chronic disease (taking into account either the EDC or the Rx-MGs diagnosis). Cases of neoplastic disease, Alzheimer's disease, cardiac arrhythmia and cerebrovascular disease were only available from the ECD codes, while cases of hyperlipidemia could only be obtained from the Rx-MGs diagnoses.

Unfortunately, there is no standard way to measure multimorbidity, so decisions concerning which morbidities to include, and how to define them are bound to be subjective to some degree, and depend strictly on the data available. This study focused on a subset of conditions including: cancer, congestive heart failure (CHF), ischemic heart disease, high blood pressure (HBP), cardiac arrhythmia, cerebrovascular disease, Alzheimer's disease, depression, asthma/bronchitis, diabetes, chronic obstructive pulmonary disease (COPD), osteoporosis, hypothyroidism, and chronic renal disease.

Identifying outcomes

The subjects classified in 2012 as PCHCN (as explained above) were linked with the hospital discharge records in 2013 to identify patients who experienced any of the following:

- at least one hospital admission;
- at least two hospital admissions;

- at least one preventable admission among the ones used to identify quality of care for "ambulatory care sensitive conditions", defined as all discharges with any of the following ICD-9-CM principal diagnostic codes: bacterial pneumonia, hypovolemia, urinary tract infection, angina, CHF, hypertension, asthma, COPD, uncontrolled diabetes, short-term complications of diabetes, and long-term complications of diabetes (see Appendix A);
- total number of hospital admissions;
- annual days in hospital.

The subjects were also linked to a mortality registry to identify patients who died in or before 2013 in order to assess the last outcome:

- overall mortality.

Statistical methods

Descriptive analyses were run by estimating the mean number of morbidities by sex and age group (“65-69”, “70-74”, “75-79”, “80-84” and “85+” years old), and reporting the corresponding frequencies.

A previous study conducted an exploratory latent class analysis (LCA) to place patients in a number (K) of clinically meaningful classes of chronic diseases, (Buja, et al., 2017) and it has been reported in Appendix B. The number of classes was defined a priori using the Bayesian information criterion (BIC), a model selection approach that balances fit with parsimony (Schwarz, 1978). Ten different models were delineated, characterized by increasing numbers of chronic disease classes (from one to ten). Then the model with five latent classes was chosen because it had the lowest BIC index. This result was confirmed by applying the Bootstrap LRT criterion (McLachLan, 1987) with 999 iterations: this latter method showed evidence in favor of the 5-class model as opposed to the 4-class model (p-value=0.0099) or the 6-class model (p-value=0.0275).

Appendix B shows the class-conditional probabilities for each disease. Patients with ischemic heart disease, diabetes, hypertension, and hyperlipidemia seemed to be prevalent in Class 1 (which could be labelled as *Metabolic-ischemic heart disease*), while Class 2 was characterized by higher probabilities of Alzheimer's disease, cerebrovascular disease and depression (and was called *Neurological*). Congestive heart failure and fibrillation revealed higher class-conditional probabilities related to Class 3 (*Heart impairment*), and Class 4 included the majority of patients with asthma and chronic obstructive pulmonary disease (*Cardio-respiratory diseases*). Patients with neoplasms were only prevalent in the Class 5 (which was consequently labelled as *Cancer*). Hypertension clearly showed high class-conditional probabilities in all five classes, and this was because its prevalence in our dataset was high (87.8%). Logistic regression analyses were used to examine the associations between dichotomous dependent variables (e.g. at least one hospital admission, at least two hospital admissions, at least one preventable hospital admission, and death) and exposure variables (e.g. number of chronic conditions, or specific dyads, or latent classes). We defined dyads as pairs of diseases affecting the same patient. The results of the latent class analysis were adopted here to shed light on the complex patterns of morbidity in our dataset. Each model was adjusted for age and sex.

A negative binomial model and a Tobit regression model, applied to censored dependent variables (Tobin, 1958), were used to study the associations between the continuous outcomes "number of hospital admissions" or "annual days in hospital" (total number of days spent in hospital in a given year) and the exposure variables (each disease dyad, or number of chronic conditions, or latent classes), respectively. Each model was adjusted for age and sex.

In the case of the “number of chronic conditions” exposure variable, for dichotomous dependent variables trends in the proportions of the events were sought with the Cochran-Armitage test, while for continuous variables the trend in the mean values of the outcomes was examined with a Mann-Kendall test.

Since we were drawing a large number of comparisons, there being 91 possible dyads (14*13/2), it became essential to correct the significance levels: we opted to do so by applying the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995).

Ethical considerations

blinded

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Results

We analyzed data on a population of 190,000 residents served by the LHU: 2,028 of these people were over 65 years old, classified as high-need, high-cost elderly according to the ACG system, and alive at the end of 2012. Table 1 shows the characteristics of this study population. More than 65% of these patients had four or more of the chronic diseases considered in this study.

Number of chronic conditions

Table 2 shows that the adjusted odds ratio for a range of adverse outcomes increases in a dose-response fashion with increasing numbers of chronic conditions. As regards outcomes in terms of at least one hospital admission, and at least two admissions, a significantly higher adjusted odds ratio only emerged for the groups of patients with four or more diseases vis-à-vis the reference group with two. The number of chronic conditions was strongly associated with the outcome concerning one or more preventable hospital admissions: all the odds ratios were significantly higher than 1.0, and ranged from 3.28 (for patients with three diseases) to 10.62 (for those with seven or more). A significant trend emerged for each of these outcomes in relation to patients grouped by number of diseases.

Table 3 shows that having more chronic diseases coincided with a higher likelihood of spending more days in hospital per year, and of having a greater number of hospital admissions.

Dyads

Figure 1a shows the disease dyads associated with the outcome "at least one hospital admission", including the adjusted odds ratio and the relative confidence interval. The strongest associations with this outcome were for the dyads chronic kidney disease and asthma (OR=3.02, CI: 1.54-6.09), and coronary heart disease and chronic kidney disease (OR=2.66, CI: 1.48-4.86). The two dyads showing a negative association with this outcome (adjusted odds ratio less than 1.0) both included Alzheimer's disease. Figures 1b and 1c show that chronic kidney disease, osteoporosis and diabetes mellitus were involved in the dyads most strongly associated with the outcomes "at least two hospital admissions", and "at least one preventable hospital admission". In particular, the odds ratios for the dyad chronic kidney disease and depressive disorder were 4.11 (CI: 2.16-7.58) for the former, and 3.50 (CI: 1.78-6.54) for the latter, while for the dyad COPD and osteoporosis, they were 3.50 (CI: 1.85-6.37), and 4.98 (CI: 2.69-8.92), respectively. Figure 1d shows that chronic kidney disease was strongly associated with "death", since it was included in all six disease dyads most strongly associated with this outcome.

As shown in Figures 1e and 1f, the analyses on the outcomes "number of hospital admissions" and "annual days in hospital" essentially confirmed the previous results: Alzheimer's disease was part of all the disease dyads showing a negative association with these outcomes.

Latent classes

Table 4 shows that the analysis of the associations between the five latent classes and the outcomes "at least two hospital admissions", "at least one preventable hospital admission", and "death" did not differ significantly for patients in the Neurological and Cancer classes, while the other classes showed a stronger association with these outcomes (taking the Neurological class for reference). Patients classed as Heart impairment, Metabolic-ischemic, Cardio-respiratory, or Cancer carried a higher risk of being hospitalized more than once than patients in the Neurological class. There was strong evidence of patients in the Heart impairment, Ischemic or Cardio-respiratory disease groups being significantly more likely to spend more days in hospital too.

Discussion

This study confirms that multiple chronic conditions are associated with higher odds of hospitalization or death. More intriguingly, our analyses also showed that certain disease dyads are more strongly associated with the need for hospital services than others. LCA also identified some classes of patients as being characterized by statistically significant higher odds of hospitalization or death.

In particular, the high-need, high-cost population studied here showed a statistically significant rising trend in the odds of being admitted to hospital (“at least one admission”, “at least two or more admissions”, and “at least one preventable admissions”) associated with more numerous chronic diseases. Several studies have found that having more chronic conditions is associated with a significantly greater recourse to health care services. Notably, the number of comorbidities is weakly associated with the number of hospital admissions but strongly associated with the total number of days spent in hospital, probably because it takes longer to stabilize patients with several comorbidities once they have arrived in hospital. One study (Hernandez, et al., 2009) showed that the number of chronic conditions correlated with hospital admissions irrespective of age, and that each chronic condition added to the risk of hospitalization. Our findings indicate that the risk of “at least one preventable admission” rose steadily and significantly with the number of diseases in a given patient. The connection between multimorbidity and preventable hospital admission is well known. For example, a study by Wolff and colleagues (Wolff, Starfield, & Anderson, 2002) found that the numbers of avoidable hospital admissions and of inpatients’ preventable complications increased dramatically for patients with larger numbers of chronic conditions.

Our present results also point to a significant association between the number of chronic diseases and mortality in patients with high health care needs. This result confirms a previous report of chronic conditions having a particularly significant association with the likelihood of death, even if the study focused on inpatient mortality (Iezzoni, et al., 1994). In contrast, Marengoni et al. (Marengoni, et al., 2009) found that it was not multimorbidity, but chronic disability that emerged as the strongest negative prognostic factor for functionality and survival in a population-based cohort of older adults in Sweden. They reported that the hazard ratio for death was the same whether people had only one or as many as four chronic diseases.

Our study identified different probabilities of hospitalization depending on the type(s) of chronic disease. To our mind, it is intriguing that the "Neurological" class of conditions taken for reference coincided with significantly lower odds of being hospitalized than any of the other classes considered. Analyzing disease dyads confirmed as much, since the dyads with the lowest odds of hospital admission always included Alzheimer's disease. This could be partly because people with dementia are more frequently institutionalized - in the Veneto Region this is true of almost 28% of dementia sufferers (DGR Regione Veneto 653, 28/4/2015) – and this makes them less likely to be hospitalized than patients with high health care needs who live at home (Smith, et al., 2015). This is a novel finding, as previous population studies compared the hospital admission rates of institutionalized versus non-institutionalized general populations, not within a selected high-need population (Godden & Pollock, 2001).

On the other hand, some studies identified a different usage of health care resources for different multimorbidity patterns. For instance, one (Collerton, et al., 2016) found five clusters of patients that differed in terms of number of medicines, hospital admissions, and consultations with general practitioners and general practice nurses, but their clusters were not characterized by type of chronic disease, so a comparison with our results was not possible. The authors concluded that clustering patients by similar morbidity profiles can help to inform future health care provision. As in the present study, another report (Dong, Wressle, & Marcusson, 2013) on multimorbidity patterns in relation to the use of health services again found five clusters (vascular; cardiopulmonary; cardiac; somatic-mental; malignancy), and showed that clusters involving cardiac and pulmonary conditions were more strongly associated with hospitalization than any single morbidity. Our findings confirm as much, since our cardiopulmonary group had higher odds of all outcomes regarding the need for hospitalization. These findings are relevant for the purposes of developing an up-to-date, valid approach to population health management that is capable of identifying subpopulations and predicting their health care service needs. In addition, identifying subgroups of PCHCN at higher risk of needing certain kinds of health care enables the use of "impactibility models" (Lewis, 2010). Such models can help to identify subsets of patients at risk most likely to benefit from preventive care. In fact, the most often-mentioned way to increase the impact of predictive risk models has been to give priority to patients with certain diagnoses, known to be particularly amenable to upstream care. These are diseases for which prompt, high-quality primary or outpatient care can reduce the risk of hospitalization (Billings, et al., 1993). More broadly, some authors (Billings & Mijanovich, 2007) claim that the "business case" for population health management lies in that the welfare of potentially high-cost patients is offset by savings deriving from reducing their future hospitalizations. As our study shows, existing data resources can be used to predict with a reasonable degree of accuracy which comorbidities make patients most likely to need hospitalizing. These data point to the importance of a highly functional, high-value, proactive primary care model for individuals with multiple chronic conditions.

The main strength of our study lies in that it was population-based, thus minimizing selection bias and relying on independently collected data. The study also suffers from some limitations, however, because administrative health care records are unable to accurately register some highly-prevalent chronic health conditions that may be associated with a heavy health care burden, such as chronic pain, or visual or hearing impairments. Administrative records also do not track economic and social factors that might independently influence the demand for health care services.

In conclusion

In terms of hospitalization, our results are consistent with those of other studies investigating the association between multimorbidity and recourse to hospital services. The advantage of our approach lies in that analyzing morbidity clusters or dyads provides more detailed information about the risk of hospitalization events. Unlike morbidity counts (in which all morbidities are scored equally, irrespective of the relationships between them), analyzing morbidity clusters and dyads reveals which combinations of morbidities are associated with the highest hospitalization rates. In our sample, cardiopulmonary diseases were the chronic conditions most strongly associated with hospitalization.

Conflict of interest statement

The authors have no conflict of interest to declare.

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Table 1: Description of the sample's characteristics

	N (%)
ALL PATIENTS	2028 (100.00%)
SEX	
Female	1054 (51.97%)
Male	974 (48.03%)
AGE	
65-69	238 (11.74%)
70-74	367 (18.10%)
75-79	476 (23.47%)
80-84	415 (20.46%)
85+	532 (26.23%)
NUMBER OF COMORBIDITIES	
0	3 (0.15%)
1	50 (2.47%)
2	204 (10.06%)
3	427 (21.06%)
4	468 (23.08%)
5	461 (22.73%)
6	242 (11.93%)
7	125 (6.16%)
8	36 (1.78%)
9	11 (0.54%)
10	1 (0.05%)

Table 2: Association between the number of chronic conditions and the binary outcomes as measured with the adjusted odds ratio and 95% confidence interval. Odds ratios highlighted in bold are significantly greater than 1.0.

Number of diseases (ref=2)	At least one admission	At least two admissions	At least one preventable admission	Death
3	1.32 (0.91, 1.93)	1.37 (0.78, 2.52)	**3.28 (1.37, 9.71)**	1.41 (0.82, 2.55)
4	**1.62 (1.12, 2.36)**	**2.02 (1.18, 3.63)**	**3.92 (1.67, 11.50)**	1.21 (0.70, 2.18)
5	**1.99 (1.38, 2.89)**	**2.22 (1.29, 3.99)**	**6.78 (2.95, 19.65)**	**2.04 (1.21, 3.62)**
6	**2.04 (1.36, 3.10)**	**2.78 (1.54, 5.19)**	**7.46 (3.12, 22.10)**	**2.20 (1.25, 4.03)**
>= 7	**2.70 (1.75, 4.22)**	**2.72 (1.44, 5.27)**	**10.62 (4.40, 31.69)**	**2.84 (1.58, 5.30)**
*Significant trend in proportions (Cochran-Armitage test)	*	*	*	*

Table 3: Effects of the number of chronic conditions and the outcomes "Number of hospital admission" and "Annual days in hospital".

Number of comorbidities	N (%)	Number of hospital admissions (IRR)	Annual days in hospital (Marginal coefficients)
Ref = 2	204 (10.33%)		
3	427 (21.62%)	**1.35 (1.00 - 1.84)**	1.62 (-0.96 - 4.21)
4	468 (23.70%)	**1.54 (1.15 - 2.08)**	3.46 (0.93 - 5.99)
5	461 (23.34%)	**1.77 (1.32 - 2.39)**	**4.59 (2.07 – 7.12)**
6	242 (12.25%)	**1.99 (1.45 - 2.75)**	**4.88 (2.06 – 7.70)**
>=7	173 (8.76%)	**2.12 (1.51 - 3.00)**	**7.01 (4.02 – 9.99)**
* Significant trend in mean values (Mann-Kendall test)		*	*

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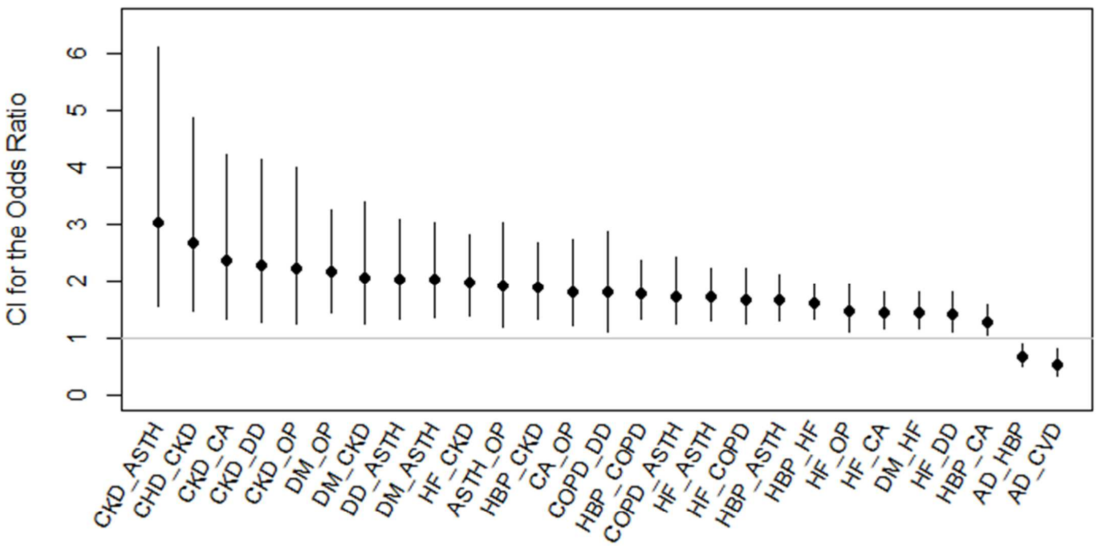
Table 4: Associations between latent classes and different outcomes (reference class "Neurological").

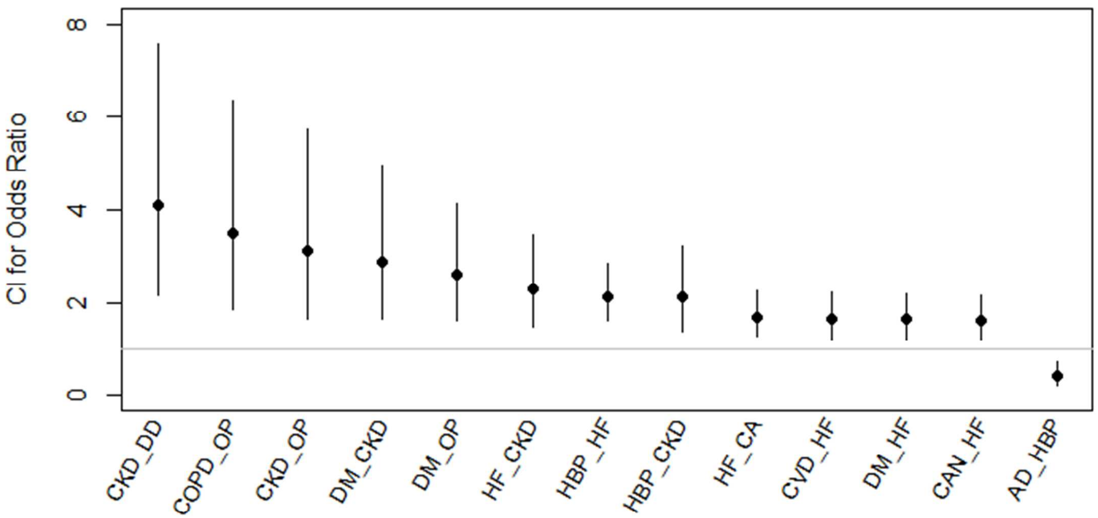
Logistic regression	Latent class	Odds ratio	95% confidence interval	P value
At least one hospital admission	Cancer	**1.58**	**1.13 - 2.20**	0.007
	Heart impairment	**1.66**	**1.24 - 2.24**	<0.001
	Metabolic-ischemic	**1.82**	**1.34 - 2.46**	<0.001
	Cardio-respiratory	**2.46**	**1.71 - 3.54**	<0.001
At least two hospital admissions	Cancer	1.48	0.84 - 2.55	0.151
	Heart impairment	**2.29**	**1.41 - 3.77**	<0.001
	Metabolic-ischemic	**2.04**	**1.35 - 3.37**	0.004
	Cardio-respiratory	**2.86**	**1.66 - 5.00**	0.001
At least one preventable hospital admission	Cancer	0.71	0.36 - 1.35	0.299
	Heart impairment	**2.17**	**1.36 - 3.57**	0.002
	Metabolic-ischemic	**1.74**	**1.07 - 2.94**	0.031
	Cardio-respiratory	**3.55**	**2.10 - 6.14**	<0.001
Death	Cancer	1.10	0.73 - 1.68	0.640
	Heart impairment	1.12	0.79 - 1.60	0.514
	Metabolic-ischemic	0.70	0.46 - 1.04	0.081
	Cardio-respiratory	**1.73**	**1.13 - 2.64**	0.011
Negative binomial regression	**Latent class**	**IRR**	**95% confidence interval**	**P value**
Number of hospital admissions	Cancer	**1.44**	**1.11 - 1.88**	0.006
	Heart impairment	**1.69**	**1.34 - 2.15**	<0.001
	Metabolic-ischemic	**1.75**	**1.37 - 2.23**	<0.001
	Cardio-respiratory	**1.86**	**1.40 - 2.46**	<0.001
Tobit regression	**Latent Class**	**Marginal coefficients**	**95% confidence interval**	**P value**
Annual days in hospital	Cancer	1.44	-0.87 - 3.75	0.222
	Heart impairment	**2.57**	**0.53 - 4.61**	0.014
	Metabolic-ischemic	**2.52**	**0.42 - 4.62**	0.019
	Cardio-respiratory	**5.04**	**2.53 - 7.56**	<0.001

Fig 1a: Odds ratios and relative confidence intervals (CI) for regressions between disease dyads and the outcome “at least one hospital admission”.



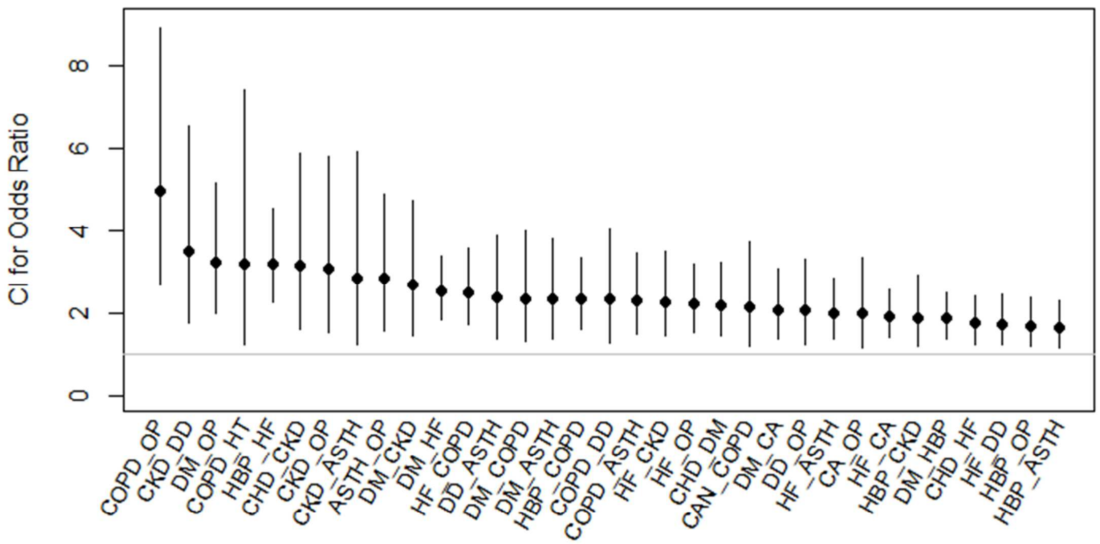
CHD=coronary heart disease; AD=Alzheimer’s disease; CVD=cerebrovascular disease; DM=diabetes mellitus; HBP=high blood pressure; HF=heart failure; COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease; DD=depressive disorder; CA=cardiac arrhythmia; ASTH=asthma; OP=osteoporosis.

Fig 1b: Odds ratios and relative confidence intervals (CI) for regressions between disease dyads and the outcome “at least two hospital admissions”.



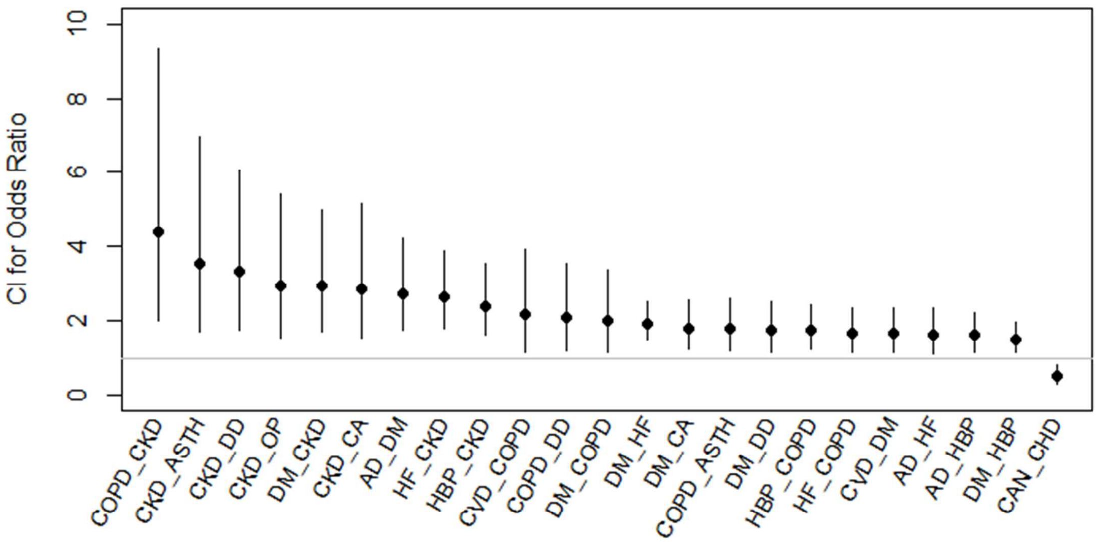
CAN=cancer; AD=Alzheimer’s disease; CVD=cerebrovascular disease; DM=diabetes mellitus; HBP=high blood pressure; HF=heart failure; COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease; CA=cardiac arrhythmia; OP=osteoporosis.

Fig 1c: Odds ratios and relative confidence intervals (CI) for regressions between disease dyads and the outcome “at least one preventable admission”



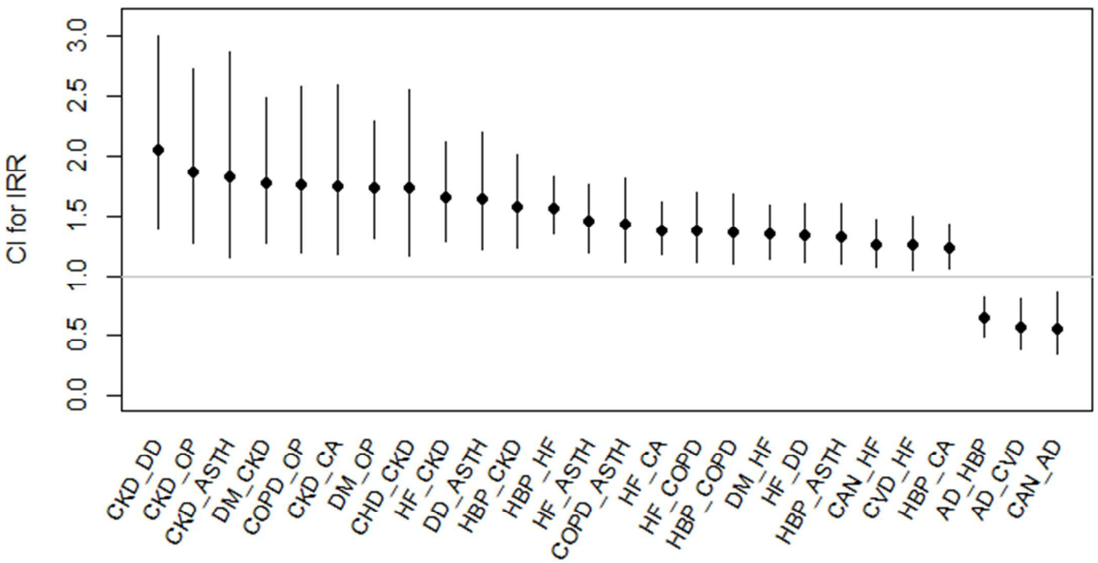
CAN=cancer; CHD=coronary heart disease; DM=diabetes mellitus; HBP=high blood pressure; HF=heart failure; COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease; DD=depressive disorder; CA=cardiac arrhythmia; ASTH=asthma; OP=osteoporosis; HT=hypothyroidism.

Fig 1d: Odds ratios and relative confidence intervals (CI) for regressions between disease dyads and the outcome “death”



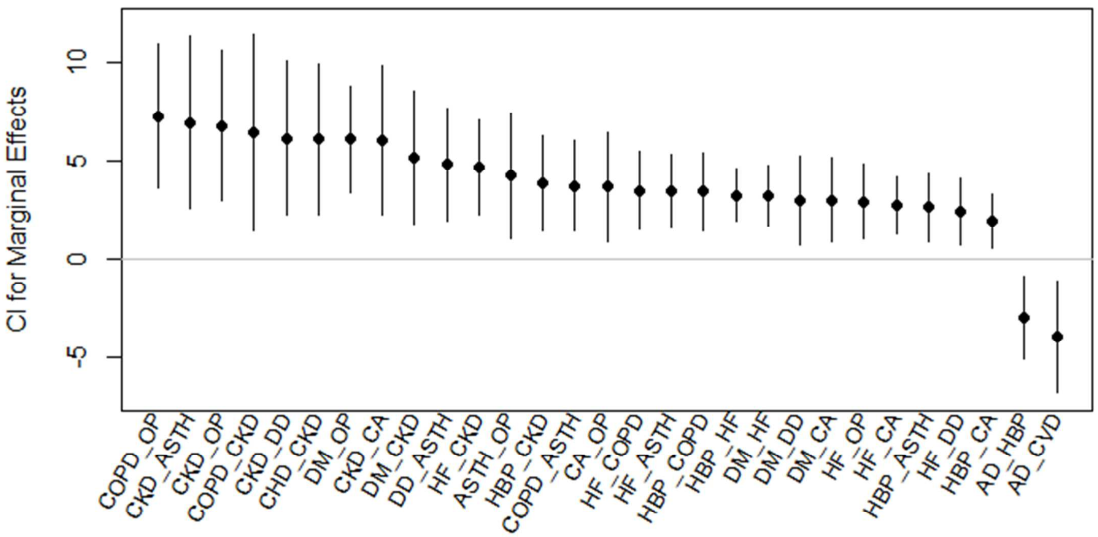
CAN=cancer; CHD=coronary heart disease; AD=Alzheimer’s disease; CVD=cerebrovascular disease; DM=diabetes mellitus; HBP=high blood pressure; HF=heart failure; COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease; DD=depressive disorder; CA=cardiac arrhythmia; ASTH=asthma; OP=osteoporosis.

Fig 1e: Incidence risk ratios (IRR) and relative confidence intervals (CI) for regressions between disease dyads and the outcome “number of hospital admissions”



CAN=cancer; AD=Alzheimer’s disease; CHD=coronary heart disease; CVD=cerebrovascular disease; DM=diabetes mellitus; HBP=high blood pressure; HF=heart failure; COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease; DD=depressive disorder; CA=cardiac arrhythmia; ASTH=asthma; OP=osteoporosis.

Fig 1f: Tobit marginal effects and relative confidence intervals (CI) for regressions between disease dyads and the outcome “annual days in hospital”



AD=Alzheimer’s disease; CHD=coronary heart disease; CVD=cerebrovascular disease; DM=diabetes mellitus; HBP=high blood pressure; HF=heart failure; COPD=chronic obstructive pulmonary disease; CKD=chronic kidney disease; DD=depressive disorder; CA=cardiac arrhythmia; ASTH=asthma; OP=osteoporosis

Appendix A: ICD-9-CM diagnostic codes used to define the ambulatory care sensitive conditions

	ICD-9-CM codes to be included	ICD-9-CM codes to be excluded
Bacterial pneumonia	481, 4822, 48230, 48231, 48232, 48239, 4829, 4830, 4831, 4838, 485, 486	28260, 2861, 28262, 28263, 28269
Dehydration	2765	-
Urinary tract infection	59000, 59001, 59010, 59011, 5902, 5903, 59080, 59081, 5909, 5950, 5959, 5990	-
Perforated appendix	5400, 5401, 5409, 541	-
Angina	4111, 41181, 41189, 4130, 4131, 4139	-
Congestive heart failure	39891, 40201, 40211, 40291, 40401, 40403, 40411, 40413, 40491, 40493, 4280, 4281, 4289	3601, 3602, 2605, 3606, 3610, 3611, 36,12, 3613, 3614, 3615, 3616, 3617, 3619, 375, 3770, 3771, 3772, 3773, 3774, 3775, 3776, 3777, 3778, 3779
Hypertension	4010, 4019, 40200, 40210, 40290, 40300, 40310, 40390, 40400, 40410, 40490	3601, 3602, 3605, 3606, 3610, 3611, 3612, 3613, 3614, 3615, 3616, 3617, 3619, 375, 3770, 3771, 3772, 3773, 3774, 3775, 3776, 3777, 3778, 3779
Adult asthma	49300, 49301, 49302, 49310, 49311, 49312, 49320, 49321, 49322, 49390, 49391, 49392,	-
Chronic obstructive pulmonary disease	4660, 490, 4910, 4911, 49120, 49121, 4918, 4919, 4920, 4928, 494, 4940, 4941, 496	-
Uncontrolled diabetes	25002, 25003	-
Diabetes short-term complications	25010, 25011, 25012, 25013, 25020, 25021, 25022, 25023, 25030, 25031, 25032, 25033	-
Diabetes long-term complications	25040, 25041, 25042, 25043, 25050, 25051, 25052, 25053, 25060, 25061, 25062, 25063, 25070, 25071, 25072, 25073, 25080, 25081, 25082, 25083, 25090, 25091, 25091, 25093	-

Appendix B: Class-conditional probabilities for each disease estimated with the five latent classes model. The higher class-conditional probabilities are highlighted in bold.

Disease	Latent classes				
	Class 1 ***(Metabolic-ischemic heart disease)***	**Class 2** ***(Neurological)***	**Class 3** ***(Heart impairment)***	**Class 4** ***(Cardio-respiratory)***	**Class 5** ***(Cancer)***
% of respondents in each class	**23**	**19**	**30**	**10**	**18**
Cancer	41	17	**50**	28	**78**
Coronary heart disease	**64**	8	22	21	8
Alzheimer's disease	5	**46**	14	16	8
Cerebrovascular disease	35	**61**	30	17	16
Diabetes mellitus	**44**	22	33	30	26
High blood pressure	**100**	**82**	**95**	**84**	75
Heart failure	**67**	41	**99**	**92**	20
Chronic obstructive pulmonary disease	4	4	4	**100**	5
Chronic kidney disease	11	2	16	12	3
Depressive disorder	26	**34**	25	28	18
Cardiac arrhythmia	34	23	**53**	37	16
Asthma	12	4	15	**70**	12
Osteoporosis	20	16	19	19	19
Hypothyroidism	12	7	8	9	12
Hyperlipidemia	**99**	10	4	14	12