

# Patterns Of Multimorbidity Of Patients In Geriatric Care – A Register-Based Cohort Study In Sweden

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## Research Article

**Keywords:** Multimorbidity, geriatrics, Adjusted Clinical Groups®, visualisation

**Posted Date:** February 21st, 2022

**DOI:** <https://doi.org/10.21203/rs.3.rs-1315408/v1>

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# Abstract

**Background:** Patients in geriatric care display a high degree of multimorbidity. We aimed to explore and visualise various patterns of multimorbidity in a person-oriented way. We used a register-based closed cohort (n=8104) of patients admitted to geriatric care in Region Stockholm, Sweden, from the year 2016.

**Methods:** Patients were grouped by their degree of multimorbidity according to the Johns Hopkins Adjusted Clinical Groups<sup>®</sup> system. Exploration was made using the Expanded Diagnosis Groups, embedded in the system. Statistical analysis was conducted in “R” and results were visualised in Excel.

**Results:** For half of all patients in the cohort, there were at least twelve diagnoses and at least thirteen active ingredients per patient. The quartile of patients with the highest level of multimorbidity were younger than the quartile of those with the lowest level. Patients with combinations of clusters of diagnoses showed various degrees of multimorbidity. Clusters of diagnoses with administrative character and cardiovascular diseases were present among nearly 80% each of all patients, followed by clusters of neurologic and musculoskeletal disorders with about 70% each. Comparisons between patients’ main diagnosis and all their diagnoses showed a shift to more of musculoskeletal disorders and less of cardiologic clusters when using main diagnoses. The morbidity status of patients measured by registered diagnoses was completed by including data on drugs, and revealed depression, persistent asthma and disorders of lipid metabolism.

**Conclusions:** Grouping patients by their degree of multimorbidity, based on all their registered concurrent diagnoses and drugs, could illustrate various patterns of mixed multimorbidity, which in turn might lead to a better understanding of the essence of multimorbidity from a patient’s perspective.

## Background

### Multimorbidity

The phenomenon of multimorbidity has gathered more and more attention during the last three decades. In the beginning, the focus was on chronic diseases and the combination of those.<sup>1</sup> With a shift to put the patient more in focus, multimorbidity has later been described as the presence of multiple diseases in one individual.<sup>2</sup> Still, the exploration of multimorbidity has focused more on diseases, than on patients with diseases.

A systematic review of the literature addressing prevalence, determinants, and patterns of multimorbidity, showed prevalence ranging from 12.9–95.1%.<sup>3</sup> Other studies have observed associations between age, lower socioeconomic status and multimorbidity<sup>4,5</sup>. The increased prevalence of multimorbidity among older people has been confirmed in many other studies, exploring the roles of ageing, functional decline and frailty, for an increased understanding of the clinical complexity<sup>6–8</sup>.

Most current methods to explore the phenomenon of multimorbidity aim at finding associations between diseases and trying to cluster them based on the frequency of combinations of diseases. Various statistical analyses have been used, mostly based on exploratory factor analysis, resulting in groups with various clusters of diagnoses<sup>9-13</sup>. This strategy has resulted in many types of clusters, making the full spectrum of multimorbidity difficult to illustrate<sup>14</sup>.

In the last decade, the interest of multimorbidity has increased worldwide, and several international networks have emerged. One is based in Canada, 'CIRMo/IRCMo', trying to keep track on all publications in this area<sup>15</sup>. The efforts have been broadened from just the understanding and definition of the concept to how to tackle the consequences of the phenomenon in the fields of diagnosis, care, rehabilitation and prevention, and how to work out guidelines within this field<sup>16</sup>.

During the last three decades there have been some interesting shifts, in terms of the definition of multimorbidity as well as in terms of the methods used to explore the phenomenon. Still, the most common definition, is that multimorbidity means two or more co-existing diseases in the same person<sup>15</sup>. The epithet 'chronic disease' has sometimes been changed to 'Long Term Condition' and discussed further<sup>17</sup>. The earlier focus on the combination and clustering of diagnoses has been complemented by a more patient-centred approach, and the trajectory of the multimorbid situation has become of greater interest<sup>18</sup>.

Furthermore, taking account of the treatment burden<sup>19</sup> and the patient's own experience of the care process,<sup>20</sup> other consequences will be of interest and will give a wider view of the awareness of multimorbidity and how to handle it. Patient-centred care is becoming more and more highlighted and concepts and models such as the Chronic Care Model<sup>21</sup> and Minimally Disruptive Medicine<sup>22</sup> have been developed.

## **Patients in geriatric care**

Patients in geriatric care tend to display a high degree of multimorbidity<sup>4,5</sup>. In Sweden geriatric medicine has been a recognised speciality for 50 years. Specialised geriatric inpatient care is offered to all individuals with acute or chronic conditions relating to higher age. Some research regarding patients in geriatric care has focused on the overlap of multimorbidity, frailty and functional impairment<sup>6,8</sup>. A Swedish study of a cohort of older people showed how the trajectories of the patients in various clusters changed over a 12-year period<sup>18</sup>.

This study is part of a larger project with the aim to analyse reasons and drivers for readmission after discharge from geriatric care<sup>23,24</sup>. Due to the prevalence of multimorbidity in elderly populations, the phenomenon of multimorbidity needs to be explored and analysed more rigorously, contributing to a profound ground for analyses of reasons for readmission.

## **Aim**

The aim of this study was to explore and visualise patterns of multimorbidity among patients in geriatric care from a patient's perspective.

## Methods

Patients admitted to any of three geriatric departments in Region Stockholm during the year 2016 have been followed up during that year and up to six months after their last discharge.

### *Data collected and data sources*

Data was collected from two sources. Firstly, the electronic health records system, "TakeCare", at the geriatric departments, and secondly, the healthcare data warehouse at Region Stockholm, "VAL", with data on health care utilisation from all publicly financed health care providers within the region, including primary, secondary and tertiary care. Diagnoses, according to the Swedish version of the WHO International statistical Classification on Diseases and related health problems, the tenth version (ICD-10-SE), were collected at the four-digit level from both sources. Data on drugs was collected at the seven-digit level according to the WHO international Anatomic Therapeutic Chemical classification system (ATC).

### *The Adjusted Clinical Groups<sup>®</sup> (ACG<sup>®</sup>)*

Drawing on a person-oriented perspective of multimorbidity, we have used a grouping instrument where the subject of the grouping is the patient; the ACG case-mix system<sup>25</sup>. Its origin stems from the awareness that diseases tend to cluster in some patients<sup>26</sup>. The ACG system takes on a person-centred approach by capturing each individual's concurrent registrations of diagnoses. The system is grouping every individual into one out of about 100 mutually exclusive patient categories depending on each patient's combined simultaneous diseases, sometimes split into more groups depending on the age and/or sex of the patient. The combination of diseases follows an algorithm taking account of what type of morbidity is involved; altogether 32 different morbidity types. The ACG system has been evaluated for use in primary care in Sweden<sup>27,28</sup>. Today ACG is used by most regions in Sweden, as one component, together with others, in the allocation of resources to health care centres in primary care.

All data on the patients' age, sex, diagnoses and drugs were grouped and analysed by the ACG system, latest version 12.1<sup>29</sup>. The outcome of the grouping procedure can be monitored and analysed in detail. In this study the following outcome measures have been used:

- A) Number of diagnoses per patient. Unique to each patient, no doubles.
- B) Number of active ingredients per patient. Unique to each patient, only medications with different active substance are counted.

C) Diagnosis cluster affiliation, “Expanded Diagnosis Cluster” (EDC), also merged into major groups, (MEDC). Each diagnosis is classified as belonging to a cluster of similar diagnoses, in total 286 EDCs, grouped into 27 MEDCs.

D) Drug group affiliation, (Rx-MG), merged into major groups, (Major Rx-MG). In total 84 Rx-MGs, are collapsed into 20 Major Rx-MGs.

E) Condition marker, a marker of any of 21 specified conditions if the patient’s condition was registered by a diagnosis (“ICD”), by a drug (“Rx”) or by both (“BTH”)

The origin and rationale for clustering diagnoses into Expanded Diagnosis Clusters is shown in Supplement A, where a complete list of all 286 EDCs is given with full descriptions (Additional File 1).

### *Statistics and Visualisation*

Besides the descriptive and analysis tools embedded in the ACG system, we have used the software Excel. Cross tabulations were conducted using R Software for Windows version 4.0.5<sup>30</sup>.

### *Ethical aspect*

The study was approved by the Regional Ethical Review Board in Stockholm (Dnr: 2013/1620-31/2; Dnr 2018/247-32; Dnr 2018/915-32).

## Results

### Study population characteristics

The study population consisted of 8104 patients. The age and sex distributions are displayed as quartiles based on age, in Table 1. As seen, women were older than men in all quartiles.

Table 1  
Distribution of age and sex by quartiles based on age.

Quartile	Female		Male		All	
	(n)	Age	(n)	Age	(n)	Age
Q1	(1347)	48–79	(758)	53–76	(2156)	48–78
Q2	(1239)	80–85	(865)	77–83	(1956)	79–84
Q3	(1257)	86–90	(677)	84–88	(1899)	85–89
Q4	(1230)	91–107	(727)	89–102	(2090)	90–107

## Diagnoses and Drugs

The proportion of patients having ten or more diagnoses per patient was 65.5%, measured by all diagnoses registered during the study period. The proportion of patients having ten or more unique drugs was 72%, measured by all drugs prescribed and dispensed at discharge and up to six months thereafter, including drugs for both regular and temporary use. The distribution in quartiles is shown in Table 2. About 2/3 of all patients had between 7 and 17 drugs per patient.

Table 2  
Distribution of diagnoses and drugs in quartiles.

Quartile	Diagnoses		Drugs	
	(n)	No. of diag.	(n)	No. of drugs
Q1	(2215)	1–8	(2268)	0–9
Q2	(1632)	9–11	(1781)	10–12
Q3	(2262)	12–17	(1950)	13–16
Q4	(1995)	18–66	(2105)	17–49

## Patterns of Expanded Diagnosis Clusters

The clusters of diagnoses in terms of EDC and MEDC, were used to illustrate the pattern of multimorbidity from a clinical perspective, as shown in Table 3. The top five MEDCs were “Administrative” (present in 79.3% of all patients), “Cardiovascular” (78.6%), “Neurologic” (68.5%), “Musculoskeletal” (68.4%) and “Respiratory” (41.7%). Within each of these MEDCs the numbers of the three most frequent EDCs are listed. The overall five most frequent EDCs were “Administrative concerns and non-specific laboratory abnormalities”, present in 69.4% of all patients, “Hypertension, w/o major complications” (52.3%), “Musculoskeletal signs and symptoms” (44.3%), “Cardiac arrhythmia” (39.4%) and “Neurologic signs and symptoms” (39.4%). Within the group of “Administrative” most diagnoses originated from the Z-chapter in ICD-10, and among them a very common registration was prescribed anticoagulants.

Table 3  
 Top-5 Major Expanded Diagnosis Groups (MEDC) and Top-3  
 Expanded Diagnosis Groups (EDC) in each MEDC for all patients (n  
 = 8104).

<b>MEDC</b>	<b>Description</b>	<b>%</b>
<b>ADM</b>	Administrative	<b>79.3</b>
	Adm concerns and non-spec lab abnormalities	69.4
	Preventive care	19.9
	Surgical aftercare	10.5
<b>CAR</b>	Cardiovascular	<b>78.7</b>
	Hypertension, w/o major complications	52.3
	Cardiac arrhythmia	39.4
	Congestive heart failure	30.0
<b>MUS</b>	Musculoskeletal	<b>68.4</b>
	Musculoskeletal signs and symptoms	44.3
	Musculoskeletal disorders, other	23.5
	Fractures (excluding digits)	17.2
<b>NUR</b>	Neurologic	<b>68.4</b>
	Neurologic signs and symptoms	35.2
	Cerebrovascular disease	18.4
	Dementia	17.5
<b>RES</b>	Respiratory	<b>41.7</b>
	Emphysema, chronic bronchitis, COPD	15.0
	Acute lower respiratory tract infection	14.6
	Aspiration and bacterial pneumonias	12.7

## Morbidity patterns based on both diagnoses and drugs

Embedded in the ACG system there are twentyone markers of specified conditions. Of those, in a Swedish context, fourteen conditions are able to capture if the patient has this condition, notified either by a diagnosis, or by a registered drug or by both a diagnosis and a drug. Table 4 shows how the specific markers were distributed among the patients for each of the conditions. Some conditions, like glaucoma, depression, persistent asthma and disorders of lipid metabolism were rarely registered as a diagnosis,

while chronic renal failure was identified by a diagnosis in up to 90% of the patients. Diabetes condition was captured by both a diagnosis and a drug among about 70% of all patients.

Table 4  
Patients with specified conditions, marked either by a diagnosis, a drug or by both (n = 8104).

Specified conditions	Diagnosis	Drug	Both	Patients
Hypertension	10.2%	31.2%	58.6%	6195
Disorders of lipid metabolism	3.3%	85.1%	11.6%	2514
Depression	9.6%	70.8%	19.6%	2119
Ischemic heart disease	17.8%	40.0%	42.3%	2030
Diabetes	27.3%	2.4%	70.4%	1640
Chronic obstr. pulm. disease	21.5%	22.0%	56.5%	1556
Persistent asthma	3.0%	80.4%	16.6%	1537
Chronic renal failure	91.4%	1.9%	6.7%	1496
Hypothyroidism	2.4%	39.9%	57.6%	1412
Osteoporosis	33.5%	46.7%	19.9%	1344
Glaucoma	8.1%	52.1%	39.8%	923
Seizure disorders	15.3%	51.0%	33.7%	608
Parkinsons disease	8.7%	36.4%	55.0%	404
Rheumatoid arthritis	37.4%	26.6%	36.0%	286

## Multimorbidity patterns based on patients' range of multimorbidity

The degree of multimorbidity can be measured by the 'Rescaled Concurrent Risk' algorithm embedded in the ACG system, ranking each patient's risk of need for resources delivered by the health care system, depending on the combination of diagnoses. Based on this metric, the population was grouped into quartiles. For each quartile the top thirty EDCs was listed. The order of the EDC for the total population changed substantially in the various groups. For instance, congestive heart failure, cardiac arrhythmia and deficiency anemias were uncommon in the quartile with the lowest risk. On the opposite, the presence of musculoskeletal disorders was much higher in the lowest risk quartile compared to the highest risk quartile. Figure 1 illustrates the difference in complexity by top ten EDCs for the quartiles with the highest risk (Q1) and the lowest risk (Q4).

The same four quartiles, grouped by the 'Rescaled Concurrent Risk' of the patients, have been used to group the patients' prescribed and dispensed drugs. The difference between the patterns in those quartiles were not as great as in terms of Expanded Diagnosis Clusters. (Data not shown.)

## Visualisation of morbidity patterns

To explore the patterns of multimorbidity we analysed the quartiles of patients, based on the ranking of their concurrent risk, in terms of patterns of EDCs. The result of the analysis in each risk quartile, performed by the R program, is visualised through radar graphs by the Excel program. The matrix from the analysis of patient risk quartile 1 is shown by Supplement B (Additional File 2). In Fig. 2, the distribution of the most frequent EDCs in combinations with each other are visualised by their proportion of numbers of EDC in each patient risk quartile. As seen, musculoskeletal disorders are most evenly distributed among the quartiles, while problems with deficiency anemias are less frequent in the lowest risk groups.

## Discussion

The numbers of diagnoses and drugs per patient were extremely high in this cohort of geriatric care patients, with at least twelve diagnoses and at least thirteen active ingredients per patient in half of the population. Cardiovascular, psychosomatic and musculoskeletal diseases were most common. However, our study took on a patient's perspective in terms of grouping patients with diseases and not the diseases themselves. Patients were grouped by ranking their concurrent risk of need for health care resources. Thus, we were not aiming at grouping diseases together into clusters. Instead, we aimed at grouping patients together depending on their combinations of clusters of diagnoses.

We found that the multimorbidity pattern varied substantially between as well as within each of the four patient risk categories. The order of the EDCs differed a great deal across the various patient groups. No specific clinical meaningful clusters of diagnosis could be found in either of the four patient groups.

## Comparisons with other studies

Most multimorbidity studies so far have used factor analysis as a method to explore correlations between diagnoses, and quite often just chronic conditions. In a Spanish study using exploratory factor analysis three, partly overlapping, groups were identified; cardiometabolic, mechanical and psychogeriatric patterns, which then were stratified in age and gender groups.<sup>9</sup> In another study from Spain, multimorbidity patterns were identified by first using multiple correspondence analysis followed by k-means clustering, yielding six distinct patterns: five organ specific as musculoskeletal, endocrine-metabolic, digestive/digestive-respiratory, neurological, and cardiovascular patterns, and one pattern not corresponding to any specific organ<sup>10</sup>. In a study from Germany, factor analysis with a tetrachoric correlation matrix was used in order to separate random comorbidity from significantly associated comorbidity, resulting in three, partly overlapping, groups; cardiovascular/metabolic disorders, anxiety/depression/somatoform disorders and pain and neuropsychiatric disorders. The authors

concluded that different multimorbidity patterns did influence each other and overlap in a large part of the population.<sup>11</sup> In a study from Singapore the researchers conducted both exploratory factor analysis, and identified patterns of multimorbidity by latent class analysis, reporting eight classes, composed by chronic conditions and demographics, for example class 2: “Chinese male patients with cardiometabolic diseases and unspecified chronic ischemic heart disease, and class 3: “Younger Chinese patients with cardiometabolic diseases and obesity”.<sup>12</sup> By exploratory factor analysis an Australian study identified six clinically meaningful clusters of multimorbid health conditions that did not fall neatly into organ or body systems, and many conditions appeared in more than one of the clusters. As an example, cluster 3 contained back/neck pain, migraine, other chronic pain, and arthritis.<sup>13</sup>

Just a few studies have illustrated the multimorbidity patterns graphically. One attempt was made in Germany showing which diseases were associated with each other in their data set, which multimorbidity clusters the diseases were assigned to, and which diseases were responsible for overlapping multimorbidity clusters. The figure showed that chronic lower back pain had the highest number of associations and was the most important mediator between diseases. The bridges between the metabolic syndrome and musculoskeletal disorders were most prominent.<sup>14</sup>

Our study was confined to a cohort of patients in geriatric departments and had a cross-sectional design. A Swedish study of a cohort of older adults settled in a geographic area identified five clinically meaningful multimorbidity clusters for about half of the cohort and the remaining half of the population formed an unspecific cluster.<sup>18</sup> The five well-characterised clusters were psychiatric and respiratory diseases, heart diseases, respiratory and musculoskeletal diseases, cognitive and sensory impairment, and eye diseases and cancer. All six clusters were tracked throughout their evolution and the authors traced the clinical trajectories of the about 3 000 individuals over 12 years. One of the findings in their study was the high proportion of migration of participants from one cluster to another. In-depth analysis of the transitions between multimorbidity clusters over time provided hints on the underlying mechanisms. In contrast to our study their ambition was to show the trajectories of clinically meaningful clusters. However, as in our study, a person-centred approach was maintained in their study.<sup>18</sup>

Quite a few studies have been trying to disentangle the concepts multimorbidity, frailty and ageing, and sometimes even functional impairment.<sup>32</sup> Other studies have focused on the overlap of concepts.<sup>33–35</sup> A Swedish study, recently published, found the yearly prevalence of multimorbidity to be 21.6%, and of polypharmacy to 24.6%, comprising all the 2.3 million inhabitants in Region Stockholm.<sup>36</sup> In contrast to our study, data on diagnoses was limited to chronic conditions, and the resulting displayed clusters were disease oriented. In Oklahoma State in the U.S. a study of multimorbidity was performed, where the patterns of various ethnic groups were displayed and illustrated with locations on and around the shape of a body.<sup>37</sup> Compared to our study with data from about one year’s period, in their study every diagnosis during the individual’s whole lifetime was used.

Aiming at providing a nuanced picture of multimorbidity in old age, we used a database where all the patients' all diagnoses were registered. By that we were not confined to the main diagnoses of the patients, which is one restriction in our national patient register of today. To show the expected vast difference in terms of both numbers of diagnoses and groups of diagnoses, we performed a grouping of the total population, resulting in 1.31 diagnoses per patient if using just main diagnoses, compared to 14.12 diagnoses per patient when considering all registered diagnoses during the period. The diagnostic pattern shifted to more of musculoskeletal disorders when using main diagnoses, as well as a lower part of administrative and cardiologic clusters. Hypertension and cardiac infarction diagnoses were then not even among the 30 most frequent ones. The results are displayed in Supplement C (Additional File 3).

Our study has yielded an insight into the phenomenon of multimorbidity. Another serious attempt to tackle this phenomenon was a symposium during 2018.<sup>33</sup> To our knowledge the latest efforts to scrutinise and manage the consequences of multimorbidity are reported by The Academy of Medical Sciences in UK,<sup>38</sup> working in close collaboration with the Canadian based international research network CIRMo/IRCMo mentioned earlier.<sup>15</sup>

## **Strengths and Limitations**

Our study has explored and illustrated the prevalence and patterning of multimorbidity among geriatric patients. The time window in this study was between six and eighteen months, depending on the time of each patient's discharge from the geriatric department. The multimorbidity measured was based on all registered diagnoses during the period, not just chronic or long-term diseases. Many other studies have been using episodes, and thereby focussing more on diseases than patients. In some cases, information about a disease, not registered as a diagnosis, could be found through the prescription of a drug.

The ACG system has been used in other studies of multimorbidity.<sup>5,19,25</sup> However, this is the first example where the complexity of combinations of clusters has been explored and visualised in a person-centred way. The use of the ACG system also enabled us to use all diagnoses registered so we were not confined to just the main diagnoses of the patients.

Of course, our study also has some limitations. The population in the cohort was confined, including about a quarter of all patients at geriatric departments in the region. Moreover, no trajectories over time have been studied.

## **Further research**

In a forthcoming study, using the same cohort, completing data on readmission by patients will be examined by the ACG instrument. The aim is to analyse how complex illness might be an important factor for readmission independently, or together with other components.

## **Conclusions**

Patients in geriatric care display a high burden of multimorbidity. Patterns of complex morbidity have so far often been shown by combination of diagnoses, and mostly by chronic conditions. By grouping patients by their degree of multimorbidity, based on all their simultaneous diagnoses and drugs, more patient-oriented patterns of complex morbidities can be elucidated and visualised. This might lead to a better understanding of the essence of multimorbidity from a patient's perspective.

## **Declarations**

### **Ethics approval and consent to participate**

This research has been performed in accordance with the Declaration of Helsinki as well as the Swedish ethical guidelines for research that are based on The Swedish Act for Ethics in research and The European Code of Conduct for Research Integrity: <https://www.vr.se/english/mandates/ethics/ethics-in-research.html>

Ethical permissions were approved by the Regional Ethical Board in Stockholm (Dnr 2013/1620–31/2; 2018/247–32). The organization of ethical boards was re-organized in Sweden during 2019. The present name is Swedish Ethical Review Authority (<https://etikprovningsmyndigheten.se/om-myndigheten/>). Due to the register-based design of the study, informed consent was not collected, a procedure that was approved by the Regional Ethical Board in Stockholm and the responsible health care authorities.

The Swedish Act for Ethics in research allows research to be conducted without informed consent in some cases. Paragraph §§ 20–22 state:

Research may be carried out without the consent, if mental illness, deteriorating health or any other similar condition of the subject prevent his or her opinion from being obtained, if:

- the research can be expected to provide knowledge that is not possible to obtain through research with consent, and
- the research can be expected to lead to direct benefit for the subject.

Even if the latter is not met, the research may be carried out if:

- the purpose is to contribute to a result that may be of benefit to the subject or someone else suffering from the same or similar disease or disorder, and
- the research entails an insignificant risk of injury or an insignificant discomfort for the subject.

### **Consent for publication**

Not applicable.

### **Competing interests**

The authors declare that they have no competing interests.

### **Availability of data and materials**

Data is not publicly available, but available upon request. Requests for access to the data can be put to our Research Data Office (rdo@ki.se) at Karolinska Institutet and will be handled according to the relevant legislation. This will require a data processing agreement or similar with the recipient of the data.

### **Funding**

This work was supported by the Stockholm Region research funds (LS 2016–1377; 2017;1342; 2018–1158). Open Access funding provided by Karolinska Institute.

### **Authors' contributions**

ER and GN contributed equally to the lead of the study. LC and ER contributed to the study conception. ER and CW collected the data, LC performed the ACG work, made most analyses of the data, and drafted the article. All authors interpreted the results, revised, and approved the final manuscript.

### **Acknowledgements**

Great thanks to Med. Cand. Kiarash Bashiri who assisted with conducting the analysis with the statistical program “R”.

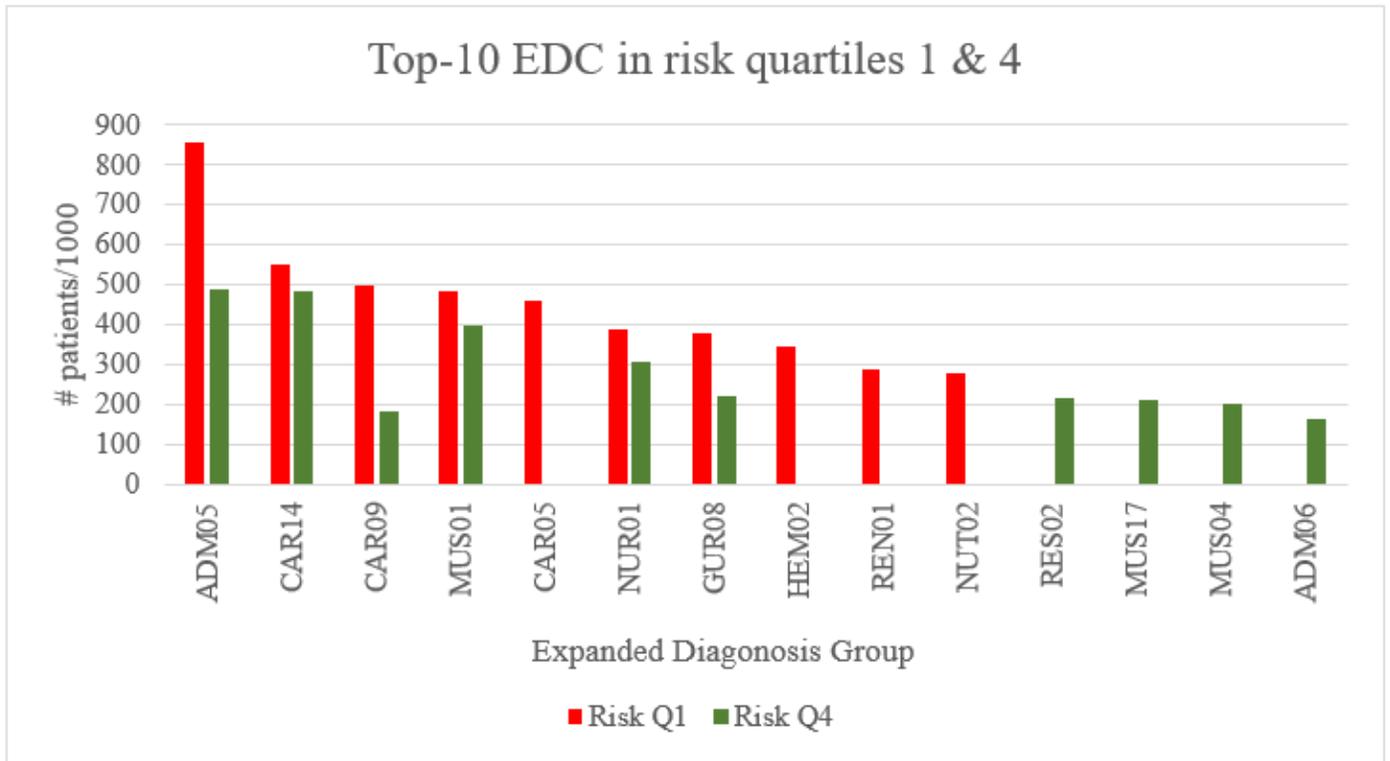
## **References**

1. van den Akker M, Buntinx F, Metsemakers JF, Roos S, Knottnerus JA. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. *J Clin Epidemiol.* 1998;51(5):367–75
2. Valderas JM, Starfield B, Sibbald B, Salisbury C, Roland M. Defining comorbidity: implications for understanding health and health services. *Ann Fam Med.* 2009 Jul-Aug;7(4):357-63.
3. Violan C, Foguet-Boreu Q, Flores-Mateo G, Salisbury C, Blom J, Freitag M, et al. Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies. *Plos One.* 2014;9(7): e102149.
4. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet.* 2012 Jul 7;380(9836):37-43.
5. Chris Salisbury, Leigh Johnson, Sarah Purdy, Jose M Valderas, Alan A Montgomery. Epidemiology and impact of multimorbidity in primary care: a retrospective cohort study. *British Journal of General Practice* 2011; 61 (582): e12-e21.
6. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, et al. (2011) Aging with multimorbidity: a systematic review of the literature. *Ageing Res Rev* 10: 430–9.

7. Jackson CA, Jones M, Tooth L, Mishra GD, Byles J, Dobson A. Multimorbidity patterns are differentially associated with functional ability and decline in a longitudinal cohort of older women. *Age Ageing*. 2015 Sep;44(5):810-6.
8. Vetrano DL, Palmer K, Marengoni A, Marzetti E, Lattanzio F, Roller-Wirnsberger R, et al. Frailty and multimorbidity: a systematic review and meta-analysis. *The Journals of Gerontology: Series A*. 2019;74(5):659–66.
9. Abad-Díez, J.M., Calderón-Larrañaga, A., Poncel-Falcó, A. et al. Age and gender differences in the prevalence and patterns of multimorbidity in the older population. *BMC Geriatr* **14**, 75 (2014).
10. Guisado-Clavero, M., Roso-Llorach, A., López-Jimenez, T., Pons-Vigués, M., Foguet-Boreu, Q., Muñoz, M. A., & Violán, C. (2018). Multimorbidity patterns in the elderly: a prospective cohort study with cluster analysis. *BMC geriatrics*, 18(1), 16.
11. Schäfer I, von Leitner E-C, Schön G, Koller D, Hansen H, et al. (2010) Multimorbidity Patterns in the Elderly: A New Approach of Disease Clustering Identifies Complex Interrelations between Chronic Conditions. *PLoS ONE* 5(12): e15941.
12. Tan XW, Xie Y, Lew JK, Lee PSS, Lee ES. Patterns of patients with multiple chronic conditions in primary care: A cross-sectional study. *PLoS One*. 2020 Aug 31;15(8)
13. Holden et al.: Patterns of multimorbidity in working Australians. *Population Health Metrics* 2011 9:15.
14. Schäfer et al.: Reducing complexity: a visualisation of multimorbidity by combining disease clusters and triads. *BMC Public Health* 2014 14:1285.
15. International Research Community on Multimorbidity (CIRMo/IRCMo). <http://www.crmcspl-blog.recherche.usherbrooke.ca> Accessed Sept 2, 2021.
16. Moffat K, Mercer SW. Challenges of managing people with multimorbidity in today's healthcare systems. *BMC Family Practice*. 2015;16:129.
17. Hafezparast, N., Turner, E.B., Dunbar-Rees, R. et al. Adapting the definition of multimorbidity – development of a locality-based consensus for selecting included Long Term Conditions. *BMC Fam Pract* 22, 124 (2021)
18. Vetrano, D.L., Roso-Llorach, A., Fernández, S., Guisado-Clavero, M., Violán, C., Onder, G., Fratiglioni, L., Calderón-Larrañaga, A., & Marengona, A. (2020). Twelve-year clinical trajectories of multimorbidity in a population of older adults. *Nature Communications* 11, 3223.
19. Muth C, van den Akker M, Blom JW, Mallen CD, Rochon J, Schellevis FG, et al. The Ariadne principles: how to handle multimorbidity in primary care consultations. *BMC Med*. 2014;12:223
20. Porter T, Ong BN. Health (United Kingdom). 2020 Nov 1;24(6):701-718.. [https://researchportal.northumbria.ac.uk/en/researchers/tom-sanders\(a43fa5b2-3763-4023-87ae-720c01616695\).html](https://researchportal.northumbria.ac.uk/en/researchers/tom-sanders(a43fa5b2-3763-4023-87ae-720c01616695).html) Accessed Apr 22, 2021.
21. Boehmer KR, Dabrh AMA, Gionfriddo MR, Erwin P, Montori VM. Does the chronic care model meet the emerging needs of people living with multimorbidity? A systematic review and thematic synthesis. *PloS one*. 2018 Feb;13(2). e0190852.

22. May C, Montori VM, Mair FS. We need minimally disruptive medicine. *BMJ*. 2009 Aug 11;339
23. Rydwick, E., Lindqvist, R., Willers, C. et al. Health status and health care utilization after discharge from geriatric in-hospital stay – description of a register-based study. *BMC Health Serv Res* 21, 760 (2021). <https://doi.org/10.1186/s12913-021-06751-3>
24. Willers C, Boström AM, Carlsson L, Lager A, Lindqvist R, Rydwick E. Readmission within three months after inpatient geriatric care. Incidence, diagnosis and associated factors in a Swedish cohort. *PLoS One*. 2021 Mar 22;16(3):e0248972.
25. Johns Hopkins HealthCare Solutions. [www.hopkinsacg.org](http://www.hopkinsacg.org) Accessed Febr 24, 2021.
26. Weiner, Jonathan P; Starfield, Barbara H.; Steinwachs, Donald M.; Mumford, Laura M. Development and Application of a Population-Oriented Measure of Ambulatory Care Case-Mix. *Medical Care*. 29(5):452-472, May 1991.
27. Carlsson L, Börjesson U, Edgren L. Patient based 'burden-of-illness' in Swedish primary health care. Applying the Johns Hopkins ACG case-mix system in a retrospective study of electronic patient records. *Int J Health Plann Manage*. 2002 Jul-Sep;17(3):269-82
28. Carlsson L, Strender LE, Fridh G, Nilsson GH. Clinical categories of patients and encounter rates in primary health care - a three-year study in defined populations. *BMC Public Health*. 2006 Feb 16;6:35.
29. The Johns Hopkins ACG system Version 12.0, User Documentation [Manual]. 2019.
30. RStudio, version 4.0.5 (2021-03-31) – "Shake and Throw". Copyright (C) 2021 The R Foundation for Statistical Computing.
31. Bastian M., Heymann S., Jacomy M. Gephi: an open source software for exploring and manipulating networks. *International AAAI Conference on Weblogs and Social Media*. (2009).
32. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci*. 2004 Mar;59(3):255-63.
33. Calderón-Larrañaga A, Vetrano DL, Ferrucci L, Mercer SW, Marengoni A, Onder G, Eriksdotter M, Fratiglioni L. Multimorbidity and functional impairment-bidirectional interplay, synergistic effects and common pathways. *J Intern Med*. 2019 Mar;285(3):255-271.
34. Jindai, K, Nielson, CM, Vorderstrasse, BA, et al. Multimorbidity and functional limitations among adults 65 or older, NHANES 2005-2012. *Prev Chronic Dis* 2016; 13: E151
35. Singer L, Green M, Rowe F, Ben-Shlomo Y, Kulu H, Morrissey K. Trends in multimorbidity, complex multimorbidity and multiple functional limitations in the ageing population of England, 2002-2015. *J Comorb*. 2019 Sep 4;9:2235042X19872030.
36. Forslund T, Carlsson AC, Ljunggren G, Ärnlov J, Wachtler C. Patterns of multimorbidity and pharmacotherapy: A total population cross-sectional study. *Fam Pract*. 2020
37. Kalgotra, P, Sharda, R. & Croff, J.M. Examining multimorbidity differences across racial groups: a network analysis of electronic medical records. *Sci Rep* 10, 13538 (2020).

## Figures



**Figure 1**

Top ten Expanded Diagnosis Clusters in highest (Q1) and lowest (Q4) risk quartile.

*Legend:*

**EDC**

**Expanded Diagnosis Cluster**

ADM05 Administrative concerns and non-specific laboratory abnormalities

CAR14 Hypertension, w/o major complications

CAR09 Cardiac arrhythmia

MUS01 Musculoskeletal signs and symptoms

CAR05 Congestive heart failure

NUR01 Neurologic signs and symptoms

GUR08 Urinary tract infections

HEM02 Deficiency anemias

REN01 Chronic renal failure

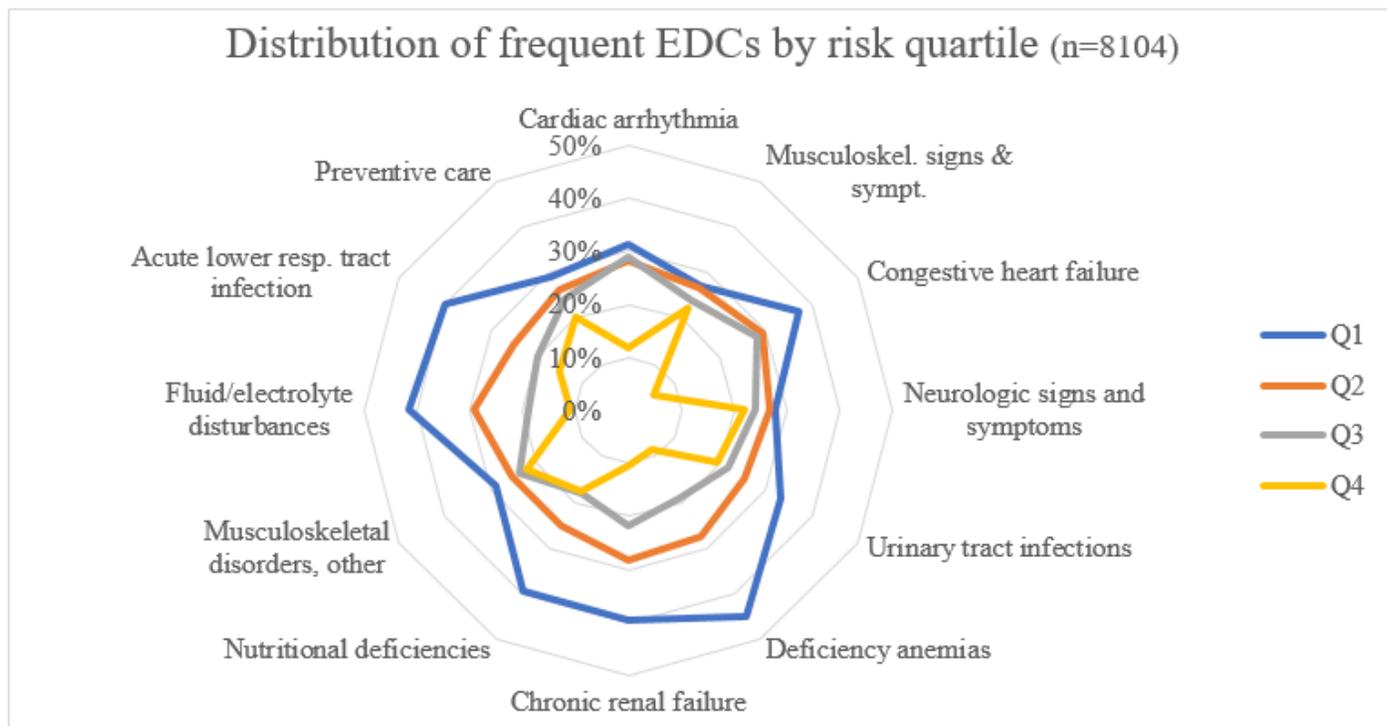
NUT02 Nutritional deficiencies

RES02 Acute lower respiratory tract infection

MUS17 Musculoskeletal disorders, other

MUS04 Fractures (excluding digits)

ADM06 Preventive care



**Figure 2**

Multimorbidity patterns by combinations of Expanded Diagnosis Clusters distributed by 'Rescaled Concurrent Risk' quartiles. (Q1=highest and Q4=lowest risk.)

## Supplementary Files

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