A comparative study demonstrated that prevalence figures on multimorbidity require cautious interpretation when drawn from a single database

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Abstract

Objective: We investigated the degree of comparability of the prevalence of chronic diseases and disease combinations in the elderly in two databases comparable with regard to diseases included, sex and age of the patients (65–85 years), and cutoff score for case definition.

Study Design and Setting: One study is based on chart-supported interviews with the primary care physicians within a cohort study of 3,189 multimorbid elderly patients. The second study analyzed claims data from ambulatory care delivered to the multimorbid members of one German Health Insurance (n = 70,031). Multimorbidity was defined by the presence of three or more chronic conditions from an identical list of 46 diseases.

Results: The difference of the median number of chronic conditions was 1 (mean 6.7 vs. 5.7). The prevalences of individual conditions were approximately one-third lower in the claims data, but the relative rank order corresponded well between the two databases. These relatively small prevalence differences cumulate when combinations of chronic conditions are investigated, for example, the prevalence differences between the two databases increased to nearly 100% for triadic combinations and nearly 170% for quartets.

Conclusion: The study shows that conclusions regarding the prevalence of combinations of diseases should be drawn with caution when based on a single database.

Keywords: Multimorbidity; Comorbidity; Chronic disease; Elderly; Prevalence; Epidemiology; Germany

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What is new?

Key findings

- The difference between the prevalence estimates in both databases was statistically significant. The number of chronic conditions was higher in the cohort study (average, 7.0) than that in the claims data study (average, 5.7). Also, the comparability of the rank order for individual chronic conditions (rho, 0.9) and combinations (rho, 0.7) was high. In both studies, the prevalence differences were small for age and sex. Observed-to-expected (O/E) ratios for triads and quartets of disease combinations exceeding a 1.5 cutoff score were very rare.

What this adds to what was known?

- We demonstrated that the relatively small prevalence differences detected when comparing individual chronic conditions cumulate when combinations of chronic conditions are investigated, and this problem grows with the number of chronic conditions under study. In our study, the prevalence differences between the two databases increased to nearly 100% for triadic combinations and nearly 170% for quartets.

What is the implication and what should change now?

- Caution is appropriate when presenting prevalence figures and/or O/E ratios for disease combinations from a single database. When investigating combinations of diseases, which are the essential quality of multimorbidity, small differences in the prevalence for individual diseases increase rapidly toward noncomparability. This study shows that differences in the study design and data source have an important influence on results concerning the prevalence of multimorbidity, even when the population under study and diseases under investigation correspond largely. This is especially the case when several chronic conditions (“multimorbidity patterns”) are investigated.

1. Background

Estimates of the prevalence of multimorbidity in epidemiological studies depend substantially on the following:

1. Case definition: for example, categories of medical nosology vs. inclusion of symptoms, complaints, and/or subjective burden, respectively [1]; their operationalizations, for example, single or grouped

International Classification of Diseases (ICD) codes, multimorbidity indexes [2], or causes for contact based on the International Classification of Primary Care (ICPC) categories [3]; the number of syndromes included, for example, using open or closed lists, list size, and the cutoff score for multimorbidity (e.g., at least two vs. three [chronic] conditions [4–8]).

2. Methods of case identification [8]: for example, standardized clinical examinations [9], chart review, patient self-reports [10], claims data analysis [11], parallel interviews with physicians and patients [12], or clinical registers [13].

3. Sampling and recruitment strategies: for example, general population vs. general practice population [5] or clinical populations in different medical care settings [4].

As a result, prevalences vary widely across studies, and therefore, reviews come to very general conclusions [8]. In general, prevalence estimates are highest when using a low cutoff point, a long or an open list of syndromes, and data from medical care settings. Little is known, especially, about the relationship between the method of case identification and detected prevalence rates in primary care. One way to increase the evidence on prevalence is to compare different methods of case identification in comparable populations and/or care settings. Only two studies in primary care comparing methods of case identification in the context of multimorbidity are known to the authors. Schram et al. [4] compared the prevalence of the five most frequent chronic conditions in diverse care settings in the Netherlands and reported large frequency and morbidity pattern differences. Fortin et al. compared two Canadian studies on adults older than 25 years of age, a telephone survey of the general population and a chart review based on a sample of patients from general practice. They found higher prevalence rates in the general practice population, especially when using an open list compared with a closed list [5]. Because of great differences between the databases examined in both important studies, conclusions on prevalence remained limited. As our study group has access to two large databases on the prevalence of chronic diseases in the elderly comparable with regard to their (extensive) disease list, country, sex and age of the patients, and cutoff score for case definition, we investigated the degree of comparability of the prevalence of the number of chronic diseases and disease combinations in these two databases and intended to identify explanations for eventual differences in prevalence. The differences in the study population and study design are described in the Methods section and Table 1.

2. Methods

The first study (“MultiCare Cohort Study” [MC-Cohort]) is based on chart-supported interviews with the
In both studies, multimorbidity was defined by the presence of three or more chronic conditions. The criterion of three conditions was considered to be a more valid cutoff score for multimorbidity in elderly patients treated in the ambulatory care setting than that for the criterion of two chronic conditions as the latter frequently leads to very high rates of multimorbidity in the age group older than 65 years. Recent research supports using the criterion of three or more chronic conditions. The criterion of at least three conditions was considered to be a more valid cutoff score for multimorbidity in elderly patients treated in the ambulatory care setting [4,5].

Both studies used an identical closed list of 46 chronic conditions. In the baseline data collection for MC-Cohort, however, dementia was excluded because severe cognitive impairment was a criterion for the exclusion. Also, patients living in a nursing home, suffering from a terminal illness with a prognosis of lethality within 3 months according to the PCP, or with insufficient capacity to consent were excluded in MC-Cohort but were included in MC-Claims. Individual ICD-10 codes were grouped together if diseases and syndromes had a close pathophysiological connection and/or if ICD-10 codes of related disorders were used ambiguously by physicians in daily coding, respectively. For example, codes I44–I45, I46.0, I46.9, I47–I48, and I49.1–I49.9 were grouped together under the heading “cardiac arrhythmias.” The diagnosis groups and corresponding ICD-10 codes in this list are found in Appendix at www.jclinepi.com. Because this list contains diseases, symptoms, and risk factors, we used the term “chronic condition” instead of chronic disease.

The patients for the MC-Cohort study were recruited in 158 PCP practices in eight study centers distributed throughout Germany (Bonn, Düsseldorf, Frankfurt/Main, Hamburg, Jena, Leipzig, Mannheim, and Munich). The design of the study, process of elaboration of the disease list, procedure for the recruitment of the patients, and process of data collection have been described in the study protocol [12] and a recent cohort description article [14]. The recruitment and baseline data collection for MC-Cohort took place from July 2008 to October 2009. The interviews were performed by trained interviewers (physicians, psychologists, or study nurses). They explicitly asked for every single condition for the presence, ICD code, duration in years, and degree of severity on a five-point scale. To increase the comparability of the period prevalence under study, we included only chronic conditions existing at least since 1 year according to the information of the PCP. The physicians were entitled to consult their charts during the interview in the practice.

The MC-Claims study is based on the claims data of the Gmünder ErsatzKasse (GEK), a statutory health insurance company with 1.7 million insurers in Germany (in 2008), which corresponded to 2.4% of the statutory insured population [15]. The study population of the policyholders aged 65 years and older consisted of 123,224 persons. The data were provided by GEK in a pseudonym form. A person was defined as multimorbid by the presence of at least three of the 20 chronic conditions in at least three quarters within the 1-year observation period, a criterion applying to 62% of the policyholders in this age group. The three-quarters criterion was chosen to avoid transitory or erroneous diagnoses and acute or subacute forms of...
certain conditions. This procedure is common when using health insurance claims data for research in Germany. To improve comparability, the MC-Claims sample was limited to the same age group as that of the MC-Cohort sample (65–85 years). As a result, 6,509 very old persons were excluded from the analysis, and therefore, the prevalences in the MC-Claims population presented in this article differ slightly from those in the original publication [11]. The sample in this study consists of n = 70,031 persons, of which 60% are females. Adjustment was performed for age and sex in the MC-Claims sample to the general German population according to data from the German Federal Bureau of Statistics as of December 31, 2004. The adjustment procedure and its results are shown in additional file 1 of [11]. The claims data stem from physicians in the ambulatory care setting, both PCPs and specialists. Claims were forwarded on a quarterly basis by the individual physician to the association of statutory health insurance physicians, in which they were checked for comprehensiveness and plausibility. Thereafter, the data were transmitted to the statutory insurance companies. According to German law, physicians in the ambulatory care setting must note all ICD-10 codes relevant to the current treatment of the individual patient in the electronic claim document. PCPs are obliged to take over all diagnoses made by specialists working in ambulatory care on referral and hospital diagnoses as well in their own patient records. More details on the German health care system were given in ref. [11]. Because the elderly multimorbid patients visited their PCP with an average frequency of 24 contacts/year [16], we are confident that the registration of morbidity by physicians in this study was not impeded by a detection bias in the sense of a small number of contacts. The comparability of the two studies is summarized in Table 1.

Descriptive data for both studies are presented as means, standard deviation, and median values in the case of continuous variables and percentages in the case of categorical variables. Diagnosis groups are ranked by prevalence. Observed-to-expected (O/E) ratios were calculated to estimate conditional probabilities of combinations of chronic conditions. All analyses were performed using the statistics software package SAS (SAS Institute Inc., Cary, NC, USA) (version 9.2) and R (version 2.14.0). Both studies were approved by the Ethics Committee of the Medical Association of Hamburg (MC-Cohort approval no. 2881 and MC-Claims approval no. PV3057).

3. Results

3.1. Number of chronic conditions

The sociodemographic characteristics and basic data on the number of chronic conditions in both populations are presented in Table 2. The average difference between MC-Cohort and MC-Claims with regard to the number of chronic conditions was 1 condition for the total population and for both sexes and age groups under study.

Because of the exclusion criteria for MC-Cohort (Table 1), the percentage of patients with long-term care dependency identified by the receipt of disability-related services and/or financial support from the national Statutory Long-Term Care Insurance scheme was much higher in the MC-Claims sample. Differences were also small for age groups within both databases; the difference in the number of chronic conditions between the younger (65–74 years) and older age groups (75–85 years) was 0.5 chronic condition in MC-Cohort and 0.6 in MC-Claims, although the mean difference in age between the two age groups was 9 years in MC-Cohort and 10 years in MC-Claims. Fig. 1 shows some sex-related differences for ages 65–72 years in MC-Cohort that disappeared in the higher ages.

3.2. Comparison of single chronic condition

Fig. 2 shows the prevalences of the most frequent chronic conditions in both study populations. The chronic conditions were ranked according to their prevalence in MC-Cohort. The figure shows all conditions with a prevalence of 15% and more in the MC-Cohort sample. The prevalences for all 46 conditions in both databases are shown in Appendix at www.jclinepi.com.

Prevalence figures were higher for all presented conditions in MC-Cohort compared with those in MC-Claims, except for severe vision reduction. The differences between the two databases were greater than average (more than one-third) for osteoarthrosis, thyroid diseases, cardiac

| Table 2. The sociodemographic characteristics and basic data in MC-Cohort and MC-Claims |
|-----------------------------------------------|---------------|---------------|
| **MC-Cohort** | **MC-Claims** |
| Mean age | 74.4 ± 5.2 | 73.8 ± 5.9 |
| Men | 74.0 ± 5.1 | 72.9 ± 5.6 |
| Women | 74.7 ± 5.3 | 74.3 ± 6.0 |
| Gender (% female) | 59.3 | 60.0 |
| Long-term care dependency (%) | All | 4.5 | 18.3 |
| | Men | 4.4 | 15.4 |
| | Women | 4.5 | 20.2 |
| Chronic conditions (Fig. 1) | Number (mean ± SD (MD)) | All | 6.7 ± 2.6 [6] |
| | | Men | 6.7 ± 2.6 [6] |
| | | Women | 6.7 ± 2.5 [6] |
| Age group, yr | 65–74 | 6.5 ± 2.5 [6] |
| | 75–85 | 7.0 ± 2.6 [7] |

*Standardized for age and sex to the German population as of December 31, 2004.
arrhythmias, asthma/chronic obstructive pulmonary disease (COPD), and osteoporosis. On the other hand, a striking correspondence of the rank order was observable, as expressed by a Spearman correlation coefficient of 0.90. Major divergences of the overall picture for sex or age group were not found (Appendix at www.jclinepi.com).

Although the average number of chronic conditions associated with every individual index condition differed between both databases, a high degree of correspondence between the two data sets was found for the mean number of associated conditions as expressed by a Spearman correlation coefficient of 0.91.

3.3. Comparison of combinations of chronic conditions (triads and quartets)

Of the 45 chronic conditions (not including dementia) in MC-Cohort, 14,190 triadic combinations were theoretically possible, of which 10,426 (73.5%) were found in the database. As for MC-Claims, we found 99% of the possible triadic combinations based on the 46er list (15,022 of 15,180). These figures demonstrate the overwhelming diversity of combinations under the heading of multimorbidity. On the other hand, the cumulative percentages for the 20 possible triadic combinations of the six most prevalent individual chronic conditions (hypertension, lipid metabolism disorders, chronic low back pain, diabetes mellitus, osteoarthritis, and chronic ischemic heart disease) were found in the multimorbidity pattern of 64% of the population in MC-Cohort and 42% of the multimorbidity sample in MC-Claims.

Fig. 3 shows the prevalence differences for the 10 most prevalent triadic combinations in MC-Cohort and MC-Claims ranked according to their prevalence in MC-Cohort. The figure shows that the relatively smaller differences for the single condition (Table 2) cumulated in the triads. For example, the prevalence of the most
frequent combination in both databases, hypertension + hyperlipidemia + chronic low back pain, was 100% higher in MC-Cohort than that in MC-Claims, and this difference size was found in almost all of these 10 combinations.

A comparison of the most 100 frequent triadic combinations in both studies resulted in 126 individual triadic combinations, of which 74 (59%) were found in both data sets. The Spearman correlation coefficient for these 74 triads was 0.70. When examining quartets, the prevalence differences between MC-Cohort and MC-Claims increased correspondingly. For example, the prevalence of the most prevalent quartet in both databases (hypertension + lipid metabolism disorders + chronic low back pain + osteoarthrosis) was 12.8% in MC-Cohort and 4.8% in MC-Claims, reflecting a difference of 167%. Most other highly prevalent quartets showed similar percentage differences.

3.4. O/E ratios

O/E ratios for combinations of chronic conditions also differed between MC-Cohort and MC-Claims, both for triads and quartets. We calculated the O/E ratios exceeding a predetermined cutoff score of O/E of 1.5 among the 100 most frequent triads and quartets. In none of the 10 most frequent triads in both MC-Cohort and MC-Claims, a combination with an O/E of ≥1.5 was found. Only one such a combination was found within the 20 quartets (O/E = 1.5 for hypertension + chronic low back pain + joint arthrosis + diabetes mellitus). Among the less prevalent triads, we found seven triads in MC-Cohort and 10 in MC-Claims with an elevated O/E ratio, but only four of those were found in both databases (Table 3). As for quartets, we found 14 combinations with an elevated O/E ratio in MC-Cohort and 40 in MC-Claims, but only two of those quartets were found in both databases.

Table 3. The combinations of triads and quartets in MC-Cohort and MC-Claims

<table>
<thead>
<tr>
<th>Triads</th>
<th>MC-Cohort</th>
<th>MC-Claims</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rank number, O/E</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension + diabetes mellitus + hyperuricemia/gout</td>
<td>47 1.6</td>
<td>20 1.6</td>
</tr>
<tr>
<td>Hypertension + chronic ischemic heart disease + atherosclerosis/PAOD</td>
<td>69 1.7</td>
<td>57 1.7</td>
</tr>
<tr>
<td>Hyperlipidemia + chronic ischemic heart disease + atherosclerosis/PAOD</td>
<td>88 1.9</td>
<td>89 2.0</td>
</tr>
<tr>
<td>Hyperlipidemia + diabetes mellitus + hyperuricemia/gout</td>
<td>83 1.6</td>
<td>50 2.0</td>
</tr>
<tr>
<td>Quartets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension (1) + hyperlipidemia (2) + chronic ischemic heart disease (7) + cardiac arrhythmias (9)</td>
<td>14 1.6</td>
<td>19 1.8</td>
</tr>
<tr>
<td>Hypertension (1) + hyperlipidemia (2) + chronic ischemic heart disease (9) + atherosclerosis/PAOD (18)</td>
<td>28 2.2</td>
<td>25 2.2</td>
</tr>
</tbody>
</table>

Abbreviations: MC-Cohort, MultiCare Cohort Study; MC-Claims, MultiCare Claims Study; O/E, observed-to-expected; PAOD, peripheral arterial occlusive disease.

Rank number: Position according to prevalence within the 100 most prevalent combinations.
databases (Table 3). Interestingly, all combinations with such an elevated O/E ratio in both data sets were related to the cardiovascular and metabolic systems.

4. Discussion

To our knowledge, this is the first study that investigates the prevalences of chronic conditions in two samples of multimorbid elderly patients, each assembled in the ambulatory medical care setting on the basis of an identical list of 46 ICD-10—coded chronic conditions. We found a high degree of correspondence between MC-Cohort and MC-Claims with regard to the number of chronic conditions for the total study population and for both sexes and age groups.

We also found almost no influence of age and gender on the prevalence of multimorbidity in either database. This is contrary to many studies, which found that multimorbidity increases with age also among the elderly [8] and more common in older females than in older males [8]. However, the methods of data collection and disease patterns under investigation may influence these differences. For example, investigating only a small number of diseases leads to a greater chance of selecting diseases with sex-specific prevalences and/or a greater chance of coincidence. Also, patient interviews might suffer from patients having greater recall problems and/or from male patients being less willing to communicate diseases than female patients. Furthermore, controls must be undertaken to examine a possible age-related bias.

Our data instead suggest that patients defined as multimorbid by the age of 65 years already possess most of the chronic diseases they will suffer from later and that this number shows almost no growth with increasing age. This perspective does not take into account, of course, increases in severity and/or complications of single diseases over time. Also, the small size of the age-related difference might be influenced by a survival bias in cross-sectional analyses as a higher number of chronic conditions is likely to be associated with increased mortality.

In both databases, we found that multimorbidity is characterized by two contrasting phenomena. On the one hand, the number of theoretically possible disease combinations is immense, and a large number of these combinations was found in actuality, albeit at a low prevalence. On the other hand, the combinations of few chronic conditions are associated with most chronic conditions found in the multimorbid elderly population. For example, the 20 possible triadic combinations of the six conditions with the highest prevalence (hypertension, lipid metabolism disorders, diabetes mellitus, chronic low back pain, osteoarthritis, and chronic ischemic heart disease) are found in the multimorbidity pattern of 64% of the MC-Cohort and of 42% in MC-Claims. This finding corresponds to the results of the German CONTENT Study, in which morbidity was continuously recorded in general practices in 2006 on the basis of contact episodes using the ICPC [3]. An adjustment and alignment of the clinical guidelines for this limited number of chronic conditions could constitute a big step toward an adaptation of guidelines for multimorbid patients.

In spite of the correspondence of age, sex, and list of chronic conditions between the two studies, differences in prevalence were statistically significant. The prevalences of individual chronic conditions were approximately one-third lower in the claims data for almost all conditions. The only exception was severe vision reduction, which may be due to the exclusion criteria in MC-Cohort. On the other hand, the relative rank order of conditions corresponded very well between the two databases. This was also the case for the average number of conditions associated with each individual chronic condition. Thus, the databases corresponded well with regard to the relative prevalence but not to the absolute prevalence of individual chronic conditions. We demonstrated that the relatively small prevalence differences detected when comparing individual chronic conditions cumulate when combinations of chronic conditions are investigated, and this problem grows with the number of chronic conditions per person under study. In our study, the prevalence differences between the two databases increased to nearly 100% for triadic combinations and nearly 170% for quartets. Therefore, caution is appropriate when presenting prevalence figures of disease combinations from a single database.

The lower prevalences of the individual chronic conditions in the MC-Claims database may be because of an underreporting of morbidity in claims data. This argument has been forwarded for clinical registers [17], Medicare data in the United States [18], and insurance data in Germany. In an exploratory study comparing claims data of German PCPs with their charts in 2003, Erler et al. [19] found an underreporting in the claims data in 30% of cases. However, underreporting was related mainly to minor medical problems, whereas the degree of correspondence for the “classical” chronic conditions requiring treatment (e.g., diabetes and ischemic heart disease) was high. In our study, however, the largest prevalence differences were found for osteoarthritis, thyroid diseases, cardiac arrhythmias, asthma/COPD, and osteoporosis. None of these conditions correspond well to the criteria of Erler et al., and this will need further investigation.

In contrast to MC-Cohort, the MC-Claims study population includes all nursing home residents treated by a physician, and this subsample shows a higher prevalence for some diseases (e.g., dementia and chronic stroke) but a smaller (recorded) morbidity spectrum than community dwelling elderly [4]. On the other hand, preliminary comparisons of baseline and follow-up data in the MC-Cohort study show that PCPs underreported an average of 0.7 chronic conditions in both interviews, suggesting that the actual prevalence in the MC-Cohort population is even higher. Also, PCPs may overlook complaints not presented...
by the patient or complaints that the PCPs do not consider to be severe or precise enough, for example, mental health complaints [20] or cognitive impairment [21,22]. As a result, caution is indicated when estimating multimorbidity prevalence as small differences in study design may have great consequences on figures.

O/E ratio differences in studies on multimorbidity allow the detection of excess prevalence not explicable by the mere addition of individual prevalences. Therefore, higher combinations with O/E differences are considered to indicate diseases interacting and bolstering each other within a cluster [23]. The cutoff score of 1.5 chosen in this study means that the prevalence of a combination is 50% higher than expected according to the prevalence of the individual conditions. We found a longer list of triads or quartets with an elevated O/E ratio, but only very few such combinations in both databases and none belonged to the high prevalence combinations. Furthermore, none of these was surprising from a medical standpoint as they all correspond to well-known pathophysiologic and clinical patterns. Thus, we have not found evidence in the triads and quartets for the postulation of a mutual bolstering of diseases in cases of multimorbidity (“cluster multimorbidity”). Again, prudence is necessary with regard to the validity of O/E ratio figures calculated from a single database.

4.1. Strengths and weaknesses

The strengths and weaknesses of both databases and their analyses have been extensively discussed in previous publications [11,14,16]. The MC Cohort is based on a response rate of 46%. A nonresponder analysis showed that there was no difference between participants and nonparticipants with regard to gender and only small differences in morbidity [14].

5. Conclusion

The comparative study shows that conclusions regarding the prevalence and/or excess prevalence of combinations of diseases should be drawn with caution when based on a single database.

Acknowledgments

References


Appendix

Supplementary material

Supplementary data related to this article can be found online at doi:10.1016/j.jclinepi.2012.07.019.

References