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A Call for Caution When Using Network Methods to Study Multimorbidity: An Illustration Using Data from the Canadian Longitudinal Study on Aging (CLSA)

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Abstract

Objective: To examine the impact of two key choices when conducting a network analysis (clustering methods and measure of association) on the number and type of multimorbidity clusters.

Study Design and Setting: Using cross-sectional self-reported data on 24 diseases from 30,097 community-living adults aged 45-85 from the Canadian Longitudinal Study on Aging, we conducted network analyses using 5 clustering methods and 11 association measures commonly used in multimorbidity studies. We compared the similarity among clusters using the adjusted Rand index (ARI); an ARI of 0 is equivalent to the diseases being randomly assigned to clusters and 1 indicates perfect agreement. We compared the network analysis results to disease clusters independently identified by two clinicians.

Results: Results differed greatly across combinations of association measures and cluster algorithms. The number of clusters identified ranged from 1 to 24, with low similarity of conditions within clusters. Compared to clinician-derived clusters, ARIs ranged from -0.02 to 0.24 indicating little similarity.

Conclusion: These analyses demonstrate the need for a systematic evaluation of the performance of network analysis methods on binary clustered data like diseases. Moreover, in individual older adults, diseases may not cluster predictably, highlighting the need for a personalized approach to their care.

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Keywords: multimorbidity, network analysis, chronic conditions, disease clusters, CLSA

Running title: Multimorbidity Network Analysis

What is new?**Key findings**

- There is no consistency in the clustering methods and measures of association currently used by researchers conducting multimorbidity network analyses.
- Using different clustering methods and measures of association results in important variation in the number and type of multimorbidity clusters identified.

What this adds to what is known

- There is little similarity in the clusters identified using different clustering algorithms/measures of association or with clinician-derived clusters.
- The epidemiological association measures seem to produce more clusters than the correlation and (dis)similarity measures.
- The patterns of clusters previously found in the literature using network methods may reflect clustering methods and association measures used as well as clinically relevant multimorbidity clusters.

What is the implication and what should change

- There are limitations to applying network analysis methods to a relatively small number of binary outcomes such as the existence of chronic conditions.
- Reporting of methods and choices in multimorbidity clustering research need to be fully transparent.

Introduction

Multimorbidity, the coexistence of multiple health conditions in an individual,¹ is associated with decreased quality of life, increased disability and healthcare utilization, and mortality^{2;3} and has been identified as a public health and clinical priority.⁴ Most research to date has focused on the number of health conditions from a prespecified list, with ≥ 2 or ≥ 3 conditions being the most common definitions of multimorbidity.⁵ While counts are important, it has been shown that the type of conditions (diseases, risk factors, and symptoms) included in multimorbidity frameworks impact associations with healthcare utilization and physical and social functioning.⁶⁻⁸

The identification of common combinations of health conditions is relevant to understanding overall healthcare burden. Conditions can also be associated non-randomly and co-occur because of shared genetic or environmental determinants, or because one condition (or its treatment) increases the risk of another. Understanding which conditions are non-randomly associated, and why, could inform preventive and therapeutic interventions that target several co-existing conditions rather than a single condition.⁹ However, systematic reviews of studies examining multimorbidity patterns report substantial heterogeneity, in part attributed to differences among analytical methods.¹⁰⁻¹² Because of this, further research has been suggested to guide the choice of methods to improve the validity and generalizability of findings.¹²

Network analysis has been increasingly used to identify clusters of chronic conditions that co-occur.¹³ Network analysis is a method of studying the relationships between nodes in a network (e.g., chronic conditions). It involves analyzing the connections, or links, between the nodes, as well as the characteristics of the nodes themselves. When conducting network analyses, researchers must choose the measure of effect to quantify the associations among conditions, and the clustering method. To better understand how these choices impact the number and types of clusters identified, we aimed to

apply the different combinations of association measure and clustering method choices identified from 11 multimorbidity network analysis studies published between 2010 and 2022¹⁴⁻²⁴ to population-based data from the Canadian Longitudinal Study on Aging (CLSA). We further asked two clinicians to independently identify potential chronic condition clusters *a priori* and compared their consensus clusters to those identified in the network analyses.

Methods

Study Design and Setting:

The CLSA is one of the most comprehensive research platforms used to study health and aging.²⁵ Of the 51,338 participants, 21,241 comprise a stratified random sample selected from the 10 Canadian provinces who provide data through telephone interviews (referred to as CLSA tracking). The other 30,097 (CLSA comprehensive) were randomly selected from the area 25-50 km around one of 11 Data Collection Sites (DCSs) located in 7 provinces. Comprehensive participants provide data through in-home interviews and underwent physical assessments at one of the CLSA DCSs. We used cross-sectional baseline data collected between 2011-2015 from 30,097 comprehensive participants. This study was approved by the Hamilton Integrated Research Ethics Board (Ethics certificate #: 7424). CLSA participants provided written informed consent to participate in the cohort study.

Participants:

At recruitment CLSA participants were community-dwelling adults aged 45 to 85 years. Exclusion criteria included: living on federal First Nations reserves, full-time members of the Canadian Armed Forces, residing in institutions (e.g., long-term care), inability to participate in English or French, and cognitive impairment precluding them from participating on their own..

Chronic Conditions:

Study physicians with expertise in multimorbidity research (PSJ, LS) chose 24 chronic conditions from those collected in the CLSA based on their importance in older adults' health and their use in the literature (listed below and in appendix eTable3). For each condition participants were asked "Has a physician ever told you that you have ___?". Excluded conditions included those that were thought to be ill-defined or represent symptoms rather than a diagnosis (memory problems, back problems, allergies) and acute conditions (pneumonia, influenza, urinary tract infection, and other infections). Before seeing the results of the network analysis, the study physicians independently identified clusters of chronic conditions that they expected to occur based on their clinical experience. The consensus clusters included: 1) stroke/transient ischemic attack, diabetes, heart disease (including angina and myocardial infarction), peripheral vascular disease, and kidney disease; 2) anxiety and depression; 3) osteoarthritis (hand, knee or hip) and rheumatoid arthritis; 4) urinary incontinence and bowel incontinence; 5) Alzheimer's disease and Parkinsonism; 6) asthma and chronic obstructive pulmonary disease. The other nine chronic conditions (osteoporosis, thyroid disease, cancer, eye disease (glaucoma or macular degeneration), migraine, irritable bowel disease, stomach ulcer, epilepsy, and multiple sclerosis) were hypothesized not to cluster predictably.

Literature Search:

To identify measures of association and clustering methods we conducted a titles and abstracts search describing patterns of multimorbidity using Google Scholar and PubMed, published from January 2010-January 2022 (later updated to January 2023). Publications that did not perform community detection using network analysis were excluded. Because our analysis was conducted using the iGraph R package, we further excluded clustering methods that were not in iGraph (see clustering methods below). A total of 11 articles were included in our review.

Measures of Association:

Eleven unique measures of association were identified in the 11 multimorbidity network analysis studies¹⁴⁻²⁴ (appendix eTable 1). We categorized association measures used in the multimorbidity network analysis literature into three groups: epidemiological, correlational, and (dis)similarity measures. The epidemiological measures include the odds ratio, the relative risk, and the joint prevalence. The correlational measures include the tetrachoric correlation, Pearson's ϕ , and Yule's Q. The similarity/dissimilarity measures include the Jaccard, Salton cosine, Kulczynski's index, lift, and standardized lift.

Clustering Methods:

In network analysis one of the most relevant features of graphs representing systems is their cluster structure, which provides a coarse-grained view of the graph connectivity; graph clustering is particularly helpful for systems with a large number of nodes, where the global graph structure may be obscured by the local connectivity of specific nodes.²⁶ We used R igraph to conduct our analyses. The most commonly used methods to identify multimorbidity clusters, Louvain,²⁷ Fast & Greedy,²⁸ Walktrap,²⁹ Label Propagation,³⁰ and Edge Betweenness,²⁶ are described in detail in appendix eTable 2. Each of these methods was used in more than one paper. Not included in igraph and thus our analyses are Partitioning Around Medoid (PAM) method²⁰ and BGLL¹⁸, each used by one researcher. Modularity measures the strength of division of a network into modules. The Louvain, Fast & Greedy, and Walktrap maximize modularity to determine the optimal number of clusters. In contrast, Label Propagation and Edge Betweenness use a stopping criterion (a condition) and not a measure that is being maximized. We categorized methods based on whether or not they used modularity to identify clusters.

Statistical Methods:

We calculated the 11 measures of association for each pair of chronic conditions as input for the five clustering methods. The network graphs consist of nodes (chronic conditions) connected by edges, with

the thickness of the edge proportional to the strength of the association between the chronic conditions. For each combination of association measure and clustering method we constructed a network graph and recorded the number of clusters and their constituent chronic conditions. The similarity of resulting clusters was compared using the Adjusted Rand Index (ARI).³¹ The ARI is an adjusted-for-chance version of the Rand Index, which takes a value of 0 when two clusters differ in all their node-cluster pairs and a value of 1 when there is an exact match across all pairs. We used ARI values to compare the networks generated using different association measures within each clustering method and between different clustering methods within each association measure. To simplify our results, for each clustering method we chose to compare networks derived using the odds ratio as a reference category for each of the other ten association measures and for each association measure we compared the networks derived using the Louvain as a reference category for the other four clustering methods. The odds ratio was chosen because it represents one of the most frequently used epidemiological association measures and the Louvain method because it is the most used multimorbidity network analysis technique. We also used ARI values to compare the multimorbidity clusters derived from each combination of association measure and clustering method with the *a priori* clinically derived clusters. Finally, two-way analysis of variance was used to test if the ARI values compared to the clinically derived networks and Poisson regression was used to test if the number of clusters differed by association measure type (epidemiological, correlational, and (dis)similarity) and clustering method (modularity maximization and other). In judging the overlap in resulting clusters, an $ARI \geq 0.9$ was considered excellent, $[0.8-0.9)$ good, $[0.65-0.8)$ moderate, and < 0.65 poor.³² As missing data was minimal ($< 1.5\%$ for each chronic condition), complete case analyses were conducted. All analyses were conducted using the software R, and for network analysis the iGraph package version 1.3.5 and R version 4.4.2.1³³ was used. We used Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) writing guidelines for reporting our findings.³⁴

Results

Of the 30,097 CLSA participants, 28,546 (94.8%) had complete data on the 24 chronic conditions and were included in the network analyses. The most common condition was osteoarthritis (26.4%) and the least common was Alzheimer's disease (0.2%) (appendix eTable 3). The mean number of chronic conditions reported was 4.2 (SD 3.7), with 75.2% reporting ≥ 2 chronic conditions. Slightly over half the sample was female; 25.3% were aged 45-54, 32.7% were 55-64, 24.5% were 65-74, and 17.6% were 75-85 years.

Multimorbidity Networks

A total of 55 multimorbidity networks were constructed using the 11 association measures and five clustering methods. Figure 1a presents networks created using a consistent association measure (odds ratio) and the different clustering methods. For example, when applying the odds ratio as the association measure, using Louvain resulted in 4 clusters (1: PK, STR, ALZ, EPI; 2: U_INC, B_INC, IBD, MS; 3: MIG, ANX, DEP; and 4: All other chronic conditions) and using Label Propagation resulted in a single cluster including all chronic conditions. Figure 1b uses a consistent clustering method (Louvain) and the different association measures.

Table 1 presents the number of clusters generated using the 11 association measures and 5 clustering methods. The average number of clusters was 4.8 (range: 1 to 24). There was a significant difference in the number of clusters by association measures group ($P < 0.001$) but not between method groups ($P = 0.37$). The epidemiological associations had the highest mean number of clusters (10.0; 95% CI: 8.2, 12.1), followed by the correlational measures (4.0; 95% CI: 2.9, 5.3) and the (dis)similarity measures (2.6; 95% CI: 2.0, 3.5).

Table 2a and 2b presents the ARIs comparing the similarity of clusters identified using different association measures within each clustering method (2a) and using different clustering methods within

each association measure (2b). There was little similarity between the networks produced using the odds ratio compared to other association measures except for the lift using the Louvain (ARI=0.91) and Fast & Greedy (ARI=1.0) methods, and the tetrachoric correlation using the Fast & Greedy method (ARI=0.80). Although the network similarity for association measures was perfect for all Label Propagation and many of the Edge Betweenness methods, this was because only one cluster was detected in these cases. Similar results were found when comparing clusters generated using the Louvain method compared to other clustering methods (Table 2b). There was generally poor consistency except for the comparison with Fast & Greedy; the ARI was 1 for Pearson's ϕ , Salton cosine, Kulczynski's Index, and standardized lift.

Figure 2 displays physician-derived chronic condition clusters and those generated using different association measures with the Louvain clustering method. The most commonly identified clusters were cardiovascular, mental health, and incontinence clusters, but the clusters most often included other conditions not thought to be related. Similar results were found when using different clustering methods with the odds ratio as the association measure (see appendix eFigure 1).

Table 3 presents the ARI comparing the chronic condition clusters generated using the 11 association measures and 5 clustering methods with the physician-derived clusters. The average similarity with the physician-derived clusters was 0.08 (range: -0.02 to 0.24). The ARIs differed by association measure ($P=0.01$) and clustering method group ($P<0.001$). The correlational measures had the highest ARIs on average followed by the (dis)similarity measures, and the epidemiological measures, and the modularity-based methods had a higher ARI than the non-modularity-based methods, but all were considered poor. Of note, the clusters that were most similar in Tables 2a and 2b were not substantially more like the physician-derived clusters than those that were not.

Discussion

Our study shows important variation in the number and type of multimorbidity clusters identified using different network analysis approaches applied to a single large population-based cohort of middle-aged and older adults. We found little consistency in the resulting clusters when we varied the clustering method and the association measures to quantify the association between chronic conditions. The clustering methods generally provided a similar number of clusters, but the epidemiological associations provided markedly larger numbers of clusters on average. Furthermore, although correlational association measures and modularity-based clustering methods resulted in higher similarity measures with physician-derived clusters, all similarity measures were considered poor ($ARI < 0.65$). Our findings reflect some of the limitations of using network methods to determine clusters of binary outcomes such as the presence of chronic conditions and highlights the importance of reporting all steps taken when using network analysis.

To our knowledge only two other studies have applied multiple analytical methods to identify multimorbidity clusters using population-based data. Ng et al.¹² applied multiple methods including network and cluster analysis to 25 self-reported conditions using population-based survey data from Australia. They found differences in chronic condition groupings both between methods and within methods when different criteria were used to form clusters. Although there were differences, the most common groups identified were: 1) cardiovascular and metabolic conditions, 2) mental illnesses, and 3) allergies. We also found the most consistent clusters were the cardiovascular and mental health conditions, however these clusters most often included additional conditions not related to cardiovascular or mental health respectively. Monchka et al.²³ examined the impact of using different association measures on multimorbidity networks using 167 chronic conditions using Manitoban administrative health data. In all cases, community structure was determined using the Louvain method. The authors also found a substantial range in the number and type of multimorbidity clusters. The

median ARI was 0.08 with the highest ARIs between Pearson's ϕ and Salton cosine; and the relative risk and lift. Using the Louvain method, we found the ARI between the Pearson's ϕ and Salton cosine was 0.71 and the relative risk and lift was 0 (appendix eTable 4). Neither of the other studies compared the similarity with physician-derived clusters.

The strengths of our study include the use of a large, national, population-based cohort collecting information on many chronic conditions using standardized protocols. We used these data to examine and evaluate the most reported clustering methods and measures of association on the number and type of multimorbidity clusters. We also compared our results to those derived by clinicians. Our study also has some limitations. Although we followed STROBE reporting guidelines, we did not pre-register our study protocol which is becoming more common in secondary data analysis. We included a restricted list of 24 self-reported chronic conditions. While using *a priori* criteria based on importance in older adults' health³⁵ and use in multimorbidity research³⁶ is a strength, other researchers may prioritize different conditions. Like us, most cohort studies we identified used a smaller list of chronic conditions, and even those using administrative data included hundreds of diseases, and thus nodes. Network analyses, however, have been traditionally used to identify clusters in graphs with thousands to millions of nodes.³⁷ Self-report may also differ from clinical data, administrative data, and biomarker data. Comparison of these data sources is important in future research. Moreover, there may be biases in the measurement of multimorbidity. For instance, selection bias based upon the use of prevalent rather than incident cases may influence both the items on a multimorbidity index, as well as the extent to which these items cluster. Severe conditions, like end organ failure, may lead to the exclusion of certain participants from the sample, potentially altering observed associations, especially those related to the preceding risk factors and diseases that culminated in organ failure. While we did not conduct a systematic review, we identified noteworthy inconsistencies in the methodologies used to identify multimorbidity patterns. We also focussed on clustering methods available in the R statistical package

and did not include other non-network analysis methods, such as k-mean non-hierarchical analysis,³⁸ fuzzy c-means cluster analysis,³⁹ m-means,⁴⁰ and multiple correspondence analysis,⁴¹ which have previously been used to identify multimorbidity clusters; it is not clear if our results would apply to these methods. An up-to-date comprehensive systematic review and evaluation of network and non-network methods could help to inform future guidelines. Furthermore, we did not examine the impact of other factors that may affect the clustering results. For example, we have dealt with fully connected graphs, i.e., where all nodes are connected to every other node, but other approaches to graph clustering involve edge pruning as a pre-processing step and thus focus the analyses on the strong connections only. The current practice in the studies dealing with multimorbidity networks is to set a cut-off on the edge weight, i.e., the effect sizes. However, such cut-off values are typically chosen in an ad-hoc manner and, moreover, edge pruning can lead to disconnected nodes, even if they have many (potentially weak) connections.⁴²

Conclusions and Clinical Implications

Our results have implications for research, health policy, and clinical care. Many multimorbidity studies examine disease clustering, but our study's results highlight the need to avoid over-reliance on these methods. Some diseases may share common etiological pathways which would logically lead to associations between these diseases. Indeed, most of the clustering methods we considered seemed to support a loose association between vascular risk factors and diseases. However, other diseases may not share a common pathway, and so may not be associated. Methodological research is needed into disease measurement and the effect that this may have upon clustering. Furthermore, our results hold significant implications for healthcare policy. If diseases do not cluster together or exhibit only weak clustering tendencies, the development of preventive and therapeutic interventions that target multiple diseases becomes a formidable challenge. There may not be a one-size-fits-all solution for the care of individuals with multimorbidity, necessitating highly personalized approaches. Likewise, healthcare

providers may need to devise customized care plans that accommodate the diverse health statuses of their patients. This diversity extends beyond physical health, encompassing various cognitive, emotional, functional, and social factors. Additionally, patients' health goals may vary considerably, further complicating the landscape of care. Embracing the intricacies of disease interactions may prove more fruitful than attempting to devise and implement overly simplistic interventions. Finally, while we have focussed on cross-sectional data, there is also interest in examining trajectories of multimorbidity clusters, their dynamic changes over time, and patterns of accumulation. Our findings suggest that further methodological research and development is critical to move this complex area forward.

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Conflict of interest

The authors declare no financial conflicts of interest

Authors contributions

LG, EvdH, and GM designed the project with the input from all authors. AB conducted all analyses with statistical input from DO and EvdH. LG wrote the first draft of the manuscript. LG, EvdH, GM, PSJ, AM worked together to obtain funding for the project. All authors worked together decide the scope and structure of the study and contributed to and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Hamilton Integrated Research Ethics Board (certificate #: 7424). Participants of the Canadian Longitudinal Study on Aging provided written informed consent to participate.

Availability of data and materials

Data are available from the Canadian Longitudinal Study on Aging (www.clsa-elcv.ca) for researchers who meet the criteria for access to de-identified CLSA data.

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Figure Legends:

Figure 1a: Multimorbidity clusters of 24 chronic conditions identified using a consistent association measure (odds ratio) and different clustering methods. STR=Stroke/TIA; DIAB=Diabetes; HRT=Heart Disease; PVD=Peripheral Vascular Disease; KID=Kidney Disease; ANX=Anxiety; DEP=Depression; OA=Osteoarthritis; RA=Rheumatoid Arthritis; U_INC=Urinary Incontinence; B_INC=Bowel Incontinence; ALZ=Alzheimer's Disease; PK=Parkinsonism; ASTH=Asthma; COPD=Chronic Obstructive Pulmonary Disease; OST=Osteoporosis; THY=Thyroid Disease; CAN=Cancer; EYE=Eye Disease; MIG=Migraine; IBD=Inflammatory Bowel Disease; ULC=Stomach Ulcer; EPI=Epilepsy; MS=Multiple Sclerosis; n=Number of clusters

Figure 1b: Multimorbidity clusters of 24 chronic conditions identified using a consistent clustering method (Louvain) and different association measures. n=Number of clusters; STR=Stroke/TIA; DIAB=Diabetes; HRT=Heart Disease; PVD=Peripheral Vascular Disease; KID=Kidney Disease; ANX=Anxiety; DEP=Depression; OA=Osteoarthritis; RA=Rheumatoid Arthritis; U_INC=Urinary Incontinence; B_INC=Bowel Incontinence; ALZ=Alzheimer's Disease; PK=Parkinsonism; ASTH=Asthma; COPD=Chronic Obstructive Pulmonary Disease; OST=Osteoporosis; THY=Thyroid Disease; CAN=Cancer; EYE=Eye Disease; MIG=Migraine; IBD=Inflammatory Bowel Disease; ULC=Stomach Ulcer; EPI=Epilepsy; MS=Multiple Sclerosis; n=Number of clusters

*The relative risk produced 24 clusters, one for each chronic condition

Figure 2: Physician-derived multimorbidity clusters of 24 chronic conditions and clusters generated using a consistent clustering method (Louvain) and different association measures. The physician-derived clusters are: Cardiovascular (C1-orange), Mental Health (C2-yellow), Musculoskeletal (C3-blue), Incontinence (C4-green), Neurological (C5-grey), and Respiratory (C6-pink). All other chronic conditions (C7-C15) were not expected to cluster predictably. For each association measure, the color and number reflect the physician-derived cluster with which the chronic condition was attributed.

*RR has no associated colors or numbers because using this measure of association resulted in 24 clusters each with one chronic condition.

Table 1. The number of chronic condition clusters generated using each association measure and clustering method combination individually and by group

		Number of clusters					Least Square Mean* (95% CI) by Association Measure Group
		Clustering Method					
		Modularity-Based Methods			Non-Modularity-Based Methods		
Group	Association Measure	Louvain	Fast & Greedy	Walktrap	Label Prop	Edge Betweenness	
Epidemiological Measures	Odds Ratio	4	3	5	1	1	10.0 (8.2, 12.1)
	Relative Risk	24	24	24	1	24	
	Joint Prev	2	2	2	1	1	
Correlational Measures	Tet Corr	4	3	2	1	1	4.0 (2.9, 5.3)
	Pearson's ϕ	4	4	2	1	6	
	Yule's Q	3	2	2	1	12	
Similarity and Dissimilarity Measures	Jaccard	3	3	4	1	8	2.6 (2.0, 3.5)
	Salton Cosine	3	3	2	1	3	
	Kulczynski	2	2	2	1	1	
	Lift	3	3	2	1	1	
	Std Lift	2	2	1	1	1	
Least Square Mean* (95% CI) by Clustering Method Group		4.4 (3.7, 5.2)			5.0 (3.9, 6.6)		

Joint Prev=joint prevalence; Tet Corr=tetrachoric correlation; Kulczynski=Kulczynski's index; Std Lift=standardized lift; Label Prop=label propagation; CI=confidence interval

*Least Square Mean generated from Poisson Model

Table 2a and 2b. Adjusted Rand Index (ARI) comparing chronic disease clusters generated using an odds ratio with those generated using other association measures across each clustering method (2a) and comparing chronic disease clusters generated using Louvain with those generated using other clustering methods across each association measure (2b)

Table 2a.

Association Measure	Clustering Method				
	Louvain	Fast & Greedy	Walktrap	Label Prop	Edge Betweenness
Odds ratio	Reference association measure				
Relative Risk	0*	0*	0*	1	0*
Joint Prevalence	0.22	0.18	0.17	1	1
Tetrachoric Corr	0.14	0.80	0.21	1	1
Pearson's ϕ	0.14	0.59	0.21	1	0
Yule's Q	0.24	0.68	0.21	1	0
Jaccard	0.43	0.24	0.16	1	0
Salton Cosine	0.32	0.34	0.21	1	0
Kulczynski's Index	0.22	0.25	0.16	1	1
Lift	0.91	1	0.16	1	1
Standardized Lift	0.22	0.25	0	1	1

Table 2b.

Association Measure	Clustering Method				
	Louvain	Fast & Greedy	Walktrap	Label Prop	Edge Betweenness
Odds ratio	Reference clustering method	0.30	0.44	0	0
Relative Risk		0*	0*	0*	0*
Joint Prevalence		0.83	0.22	0	0
Tetrachoric Corr		0.68	0.51	0	0
Pearson's ϕ		1	0.51	0	0.13
Yule's Q		0.48	0.51	0	0.17
Jaccard		0.54	0.28	0	0.14
Salton Cosine		1	0.25	0	0.03
Kulczynski's Index		1	0.54	0	0
Lift		0.23	0.43	0	0
Standardized Lift		1	0	0	0

Tetrachoric Corr=tetrachoric correlation; Label Prop=label propagation; CI=confidence interval

*The ARI was assumed to be zero when the number of clusters was equal to the number of chronic conditions for any association measure/clustering method combination.

ARI interpretation	≥0.9 - Excellent	0.8-0.90 - Good	0.65 - 0.80 - Moderate	<0.65 Poor
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Table 3. Adjusted Rand Index comparing chronic condition clusters generated using each association measure and clustering method combination with physician-derived clusters

		Clustering Method					Mean (95% CI) by Association Measure Group
Group	Association Measure	Modularity-Based Methods			Non-Modularity-Based Methods		
		Louvain	Fast & Greedy	Walktrap	Label Prop	Edge Betweenness	
Epidemiological Measures	Odds Ratio	0.13	0.18	0.15	0	0	0.03 (-0.002, 0.06)
	Rel Risk	0*	0*	0*	0	0*	
	Joint Prev	0.09	0.08	0.04	0	0	
Correlational Measures	Tet Corr	0.21	0.18	0.10	0	0	0.09 (0.06, 0.13)
	Pearson's ϕ	0.21	0.21	0.10	0	0.003	
	Yule's Q	0.24	0.10	0.10	0	-0.02	
Similarity and Dissimilarity Measures	Jaccard	0.15	0.10	0.05	0	-0.01	0.05 (0.02, 0.07)
	Salton Cos	0.13	0.13	0.10	0	0.05	
	Kulczynski	0.09	0.09	0.08	0	0	
	Lift	0.10	0.18	0.02	0	0	
	Std Lift	0.09	0.09	0	0	0	
Mean (95% CI) by Clustering Method Group		0.11 (0.09, 0.13)			0.004 (-0.028, 0.036)		

*The ARI was assumed to be zero when the number of clusters was equal to the number of chronic conditions for any association measure/clustering method combination.

ARI interpretation

≥ 0.9	0.8-0.90	0.65-0.80	<0.65
Excellent	Good	Moderate	Poor

Rel Risk=relative risk; Joint Prev=joint prevalence; Tet Corr=tetrachoric correlation; Salton Cos=Salton cosine; Kulczynski=Kulczynski's index; Std Lift=standardized lift; Label Prop=label propagation; CI=confidence interval