Methods of analyzing patterns of multimorbidity using network analysis: a scoping review protocol

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ABSTRACT

Objective: The purpose of this review is to summarize the techniques used for network analysis of multimorbidity to inform development of a standard methodology.

Introduction: There is a growing trend of using network analysis to investigate relationships between chronic illnesses in people with multimorbidities. However, there is currently no recommended approach to calculating and displaying networks of chronic health conditions. This review intends to summarize the current literature to further the development of a standard methodology.

Inclusion criteria: Studies will be included if they investigated the relationships between multiple chronic health conditions without referring to an index condition, using network analysis techniques. Studies using both survey and administrative data will be included. Studies including biological or genomic data sets will not be included as they are out of scope.

Methods: Databases searched will include PubMed (MEDLINE), Science Direct, Scopus, and PsycINFO. All relevant publications will be included provided they were published before October 2020. Publications from all languages will be included where an appropriate translation in English can be obtained. Data extracted will include country of origin, type of data used, measure of association, software used, and notes on any specific points of methodological interest relevant to the review question.

Keywords: comorbidity; multimorbidity; network analysis

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Introduction

Multimorbidity is commonly known as the presence of multiple chronic health conditions concurrently occurring within a person.¹,² Multimorbidity is a significant public health issue within communities across the world.³

Studying multimorbidity allows a deeper understanding of the clinically important relationships between health conditions. By examining which conditions most frequently co-occur, and conditions which unexpectedly co-occur, health care providers can better target prevention and intervention strategies among persons living with multiple chronic health conditions, and, by extension:

- reduce the associated burden of disease (morbidity/quality of life and mortality);
- reduce direct (eg, treatment) and indirect (eg, lost productive time) costs; and
- improve quality of life and efficiency-of-care provision via streamlined health care services and reduced polypharmacy.

Multimorbidity is a complex phenomenon and there is a large list of possible combinations of chronic health conditions. This makes tracking prevalence and patterns of multimorbidity challenging. Analysis techniques have thus evolved from simple counts of prevalence within a population to more sophisticated mathematical techniques investigating clusters of combinations of conditions within a population. However, a recent systematic review on research using clustering techniques demonstrates limitations in the two most frequently employed...
methods: Exploratory Factor Analysis (EFA) and clustering analysis.4

Exploratory Factor Analysis dictates that the researcher must postulate a pattern of the relationship of interest before the analysis in order to test a hypothesis that a relationship exists between observed variables and latent constructs.5 This approach does not allow for an unbiased exploration of the data, rather an affirmation of a preconceived idea, and increased risk of false positives.5 In short, by pre-determining which conditions may be related to each other or what structure they may form, this approach neglects potentially unknown relationships.

Clustering analysis identifies associations between groups of conditions without the introduction of previous knowledge to the algorithm. While it is a useful tool in investigating overarching structure regarding which conditions are likely associated with one another, it does not provide detailed information on the relationship between those conditions. Conditions in clusters can also overlap, making it difficult to determine if there is a condition (or conditions) acting as a “bridge” between two conditions or clusters.

Network analysis is an increasingly popular approach used to investigate individual associations between chronic health conditions in a multimorbid population.6-10 While the techniques of network analysis, also termed “social network analysis,” have been around since the 1960s, researchers have only recently started to apply them to the study of multimorbidity. Network analysis finds the conditions that occur most frequently together within multimorbid participants and provides a visualization of the strength of these associations through network maps using one of various potential techniques. Published studies commonly use either some form of correlation coefficient (e.g., Pearson's r or Phi) or an observed/expected ratio to assess the strength of the relationship between conditions. Some correlation methods may not be appropriate for network analysis, as they are not designed for binary data. However, lack of transparent or sufficient reporting of methods precludes replicability and/or testability. If network analysis can be consistently applied, with some consensus on the techniques used, this approach could be important in reaching a standard methodology for multimorbidity research. For researchers to determine a recommended method of network analysis in this field, a review of current research must be undertaken.

A preliminary search of PROSPERO, MEDLINE, the Cochrane Database of Systematic Reviews, and JBI Evidence Synthesis was conducted and no current or in-progress scoping reviews or systematic reviews on the topic were identified.

Review objective

The purpose of this review is to collect and detail the current literature on network analysis methods used to analyze patterns of multimorbidity, including software used, statistical methods of association between conditions, and any other information deemed relevant by the authors after review of the literature.

Inclusion criteria

Participants

As the participants of any data included are not the focus of this work, there are no restrictions on participant types.

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Concept

This scoping review will summarize the current methods of network analysis being used to investigate the associations between chronic health conditions in a multimorbid population. Specifically, the focus will be the statistical methods by which the associations are estimated, as differing methodologies can produce different results. Transparency of the method employed in each study will be explored, as this is a key factor in determining the appropriateness and rigor of statistical measures of association in network analysis. A summary of statistical packages used to display networks within the discovered literature will also be provided.

Context

This scoping review will include studies using both administrative and self-reported survey data. Studies from any country will be included. There is no specific preference for studies to be published in English, however, given English is the first language of the reviewers, if a study is in another language, an English translation must be obtainable for the study to be included in the final list of publications for synthesis. References for non-English-language studies that are excluded at the full text stage and do not have an English translation, will be provided. There will be no restriction on software employed.
Exclusion criteria
Notably, there is another body of research on multiple chronic conditions using network analysis, focusing on genomic factors and symptoms. These studies attempt to uncover links between a person’s biological processes and/or genomic markers and symptoms and/or diagnoses of health conditions (ie, to link specific biological or genetic traits to symptoms). The findings of these studies are generally more applicable in clinical or gene research, rather than an epidemiological setting and are thus outside the scope of this review.

Types of sources
Studies will be included if they:
- investigated the relationship between multiple chronic health conditions using administrative or self-report survey data;
- used some form of correlation or regression analysis to assess the strength of relationships between chronic health conditions; and
- used network analysis techniques to present the data in a network form.

In the included studies, any type of software package will be permitted for the assessment of correlations and presentation. It is anticipated this focus will demonstrate the breadth of available software employed.

This search strategy aims to find peer-reviewed published literature, articles published as part of symposia/colloquia/conferences, and theses. Abstracts will be excluded, given concerns about sufficiency of the included information. This review will not include unpublished or gray literature as it can be difficult to retrieve and has not necessarily undergone a peer-review process.

Methods
The proposed scoping review will be conducted in accordance with the JBI methodology for scoping reviews.11

Search strategy
An initial limited search will first be undertaken in the databases MEDLINE (PubMed) and Science Direct, using keywords and phrases “multimorbidity”, “comorbidity”, paired with “network”, as outlined in Appendix I. These terms were chosen as the individual terms or their pairings were considered essential to identifying relevant research, and coincide with the recognized MeSH terms “multimorbidity” and “comorbidity.” An analysis of the text words contained in the title and abstract of retrieved papers will then be used to refine the index words. Following this, a second search using all identified keywords will be conducted across MEDLINE (PubMed), Science Direct, Scopus (Elsevier B.V.), Google Scholar, and PsycINFO (Ovid). The search will include articles published in or before October 2020. A subsequent search of reference lists of included articles for additional relevant articles will be conducted.

Study selection
Following the search, all identified records will be collated and uploaded into EndNote v.X9 (Clarivate Analytics, PA, USA) and duplicates removed. Titles and abstracts will then be screened by two independent reviewers for assessment against the inclusion criteria for the review. The full text of selected citations will be assessed in detail against the inclusion criteria by the two independent reviewers. Reasons for exclusion of full-text papers that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion or with a third reviewer. The results of the search will be reported in full in the final scoping review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses for Scoping Reviews (PRISMA-ScR) flow diagram.12

Data extraction
Data will be extracted from papers included in the scoping review by two independent reviewers using a data extraction tool (see Appendix II) developed by the reviewers in accordance with JBI guidelines. The data extracted will include specific details about the country of origin, type of data used, measure of association, software used, and notes on any specific points of methodological interest relevant to the review question. The draft data extraction tool will be modified and revised as necessary during the process of extracting data from each included paper. Modifications will be detailed in the full scoping review. Any disagreements that arise between the reviewers will be resolved through discussion or with a third reviewer. Authors of papers will be contacted.
to request missing or additional data, where required.

**Data analysis and presentation**

Studies will be summarized in table format. Tables will include the type of data used in each study and the statistical methodology of measures of association used for each study. The PRISMA-ScR checklist\(^\text{12}\) will be used as a guide in forming and presenting the scoping review.

**Acknowledgments**

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**References**

**Appendix I: Search strategy**

MEDLINE (PubMed)

Search conducted October 2020.

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Appendix II: Data extraction instrument

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