

Replicability of Co-occurring Comorbidities: Implications for Precision Medicine

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Abstract

A critical step in the design of targeted interventions in precision medicine is to identify which patient variables such as comorbidities co-occur across patients. However, while several studies have used networks to identify co-occurring comorbidities, few of them have replicated those associations across datasets. Here we describe a method for comparing the degree of similarity in the co-occurrence of comorbidities between two networks of hip-fracture (HFx) patients retrieved from the 2010 and 2009 Medicare Claims Database. We demonstrate a significance test for this similarity measure, designed for testing the replicability of variable co-occurrences across networks.

Introduction

While networks have been effective in identifying complex associations among subjects and variables¹, few of these studies have replicated their results in another dataset. Here we demonstrate a method for measuring the degree of similarity in comorbidity co-occurrence between two cohorts of 30-day hospital readmitted HFx patients from the Medicare Claims Database.

Method

We extracted all 30-day readmitted HFx patients without joint replacement from the 2010 and 2009 Medicare database, in addition to 69 of their comorbidities determined to be critical² in the elderly. Next, as the patients had a median of 2 comorbidities, we identified all comorbidities that were bivariately significant for 30-day readmission in both years, and used bipartite networks and co-cluster modularity¹ (representing degree of clusteredness) to analyze how those comorbidities co-occurred in 2010, and in 2009. Finally, we measured the similarity of comorbidity co-occurrence across the two years by (1) using the Rand index which measures the proportion of comorbidity pairs that co-occurred and did not co-occur in a cluster in both years (where 0=no inter-network cluster similarity, and 1=total inter-network cluster similarity), and (2) testing its significance by comparing it to a distribution of the same measure generated from 1000 random permutations of the 2010 and 2009 networks.

Results and Conclusion

Co-cluster modularity was similarly high (2010=0.440, 2009=0.444) and significant (2010: $p < .001$, 2009: $p < .001$) in both years, and the degree of inter-network cluster similarity measured by the Rand index between the two years was significant ($p < .05$, Medicare=0.93, random mean=0.87). An inspection of the two network layouts revealed that although the total number of clusters in both years (2010=7, 2009=7) was identical, two co-occurring comorbidities (renal failure and diabetes) separated into different clusters across the two years, whereas two (CHF and arrhythmia) merged into the same cluster (changed clusters are shown white in Fig. 1). The results pinpoint the similarities and differences in the prevalence and co-occurrence of comorbidities across the two years, which enabled domain experts to comprehend the nature of replication and therefore interventions to reduce readmission. The results also suggest that the approach of combining the Rand measure with the network visualization could be effective for testing the replicability of co-occurrences for a wide range of variables ranging from molecules to comorbidities.

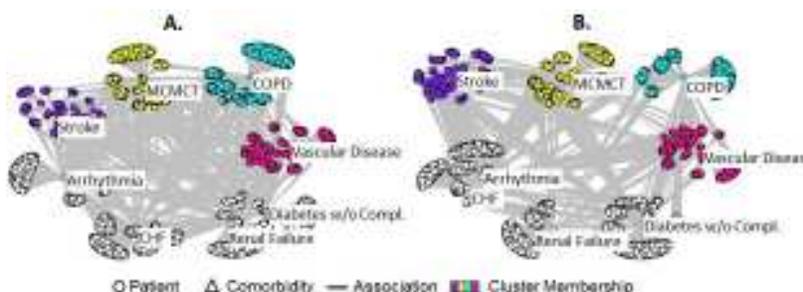


Figure 1. Bipartite networks showing patient-comorbidity clusters in 2010 (A), and in 2009 (B) using an exploded layout which pulls apart clusters identified through modularity, while preserving the size and spread of the nodes in each cluster.

Acknowledgements

Supported by the UTMB CTSA, #UL1TR001439.

References

1. Newman M. Networks: An Introduction. Oxford University Press; 2010.
2. Pope GC, Kautter J, Ellis RP, et al. Risk Adjustment of Medicare Capitation Payments Using the CMS-HCC Model. Health Care Financ Rev. 2004 Summer; 25(4):119-41.