Clustering Temporal Disease Networks to Assist Clinical Decision Support Systems in Visual Analytics of Comorbidity Progression

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Outline

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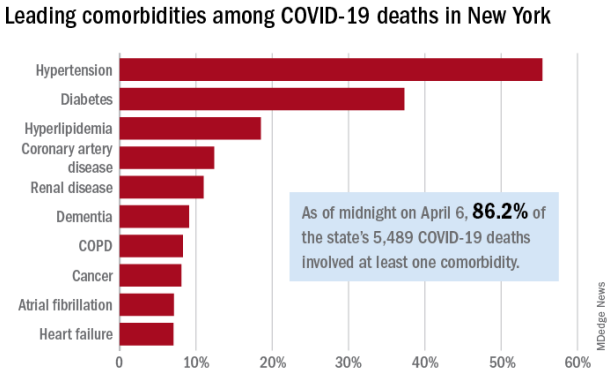
Comorbidity

Comorbidity refers to one or more other health conditions coexisting among patients with a particular index disease (Feinstein, 1970; Gijsen et al., 2001).



Comorbidity Network

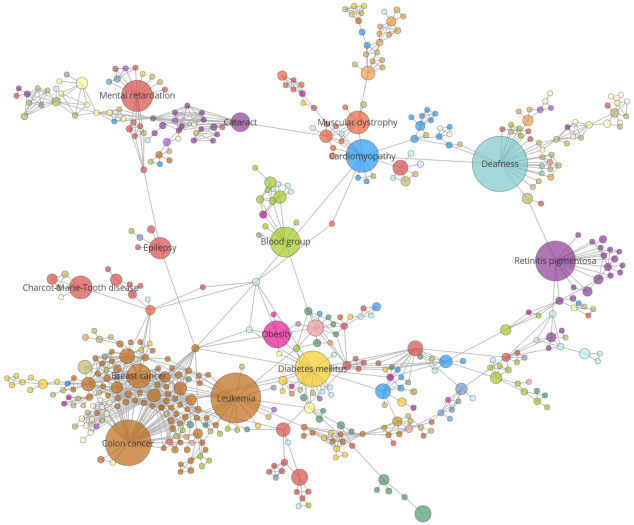
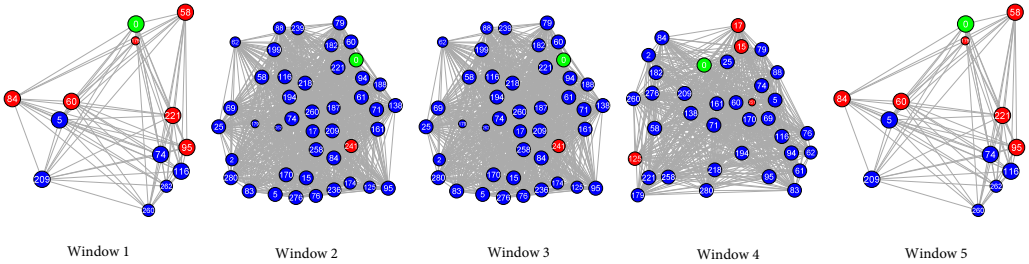


Image source: https://github.com/empet

- Better presentation of disease associations (Divo et al., 2015; Warner et al., 2015)
- Capability to incorporate additional biomarkers (Nam et al., 2019)
- Support for disease progression investigation (Chen et al., 2009; Chmiel et al., 2014)

Temporal Disease Network

By discretizing the entire time frame of the index disease into different windows, modeling comorbidity within each window as a disease network is referred to as temporal disease network (TDN).



A sequence of TDNs across five time windows

Research Gaps

In the area of TDN modeling and analysis, there has been limited capability to:

- Detect the progression timing.
  - Most TDN-related studies (Chen et al., 2009; Martel et al., 2016; McElroy et al., 2018) predefined a granularity parameter m
  - Then discretized the entire time frame of the study cohort into m windows of even length or even sample size, without providing algorithms that can detect at which window(s) notable changes of TDNs had occurred.

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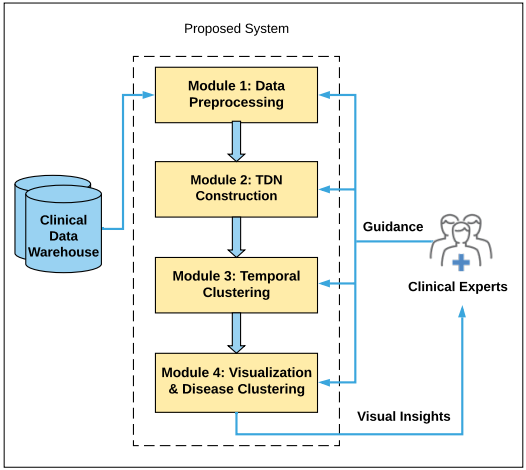
- Streamline the visualization.
  - TDNs are often large, dense networks that can result in disordered display in visualization.

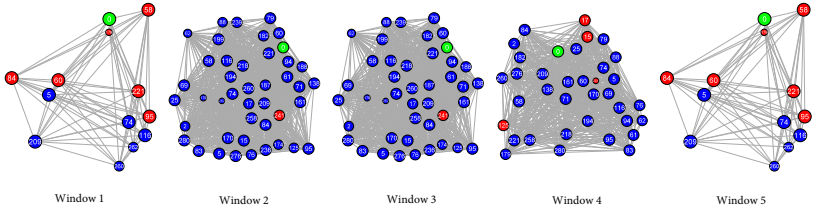
Research Goal



The proposed TDN-based clinical decision support system for pattern detection and visualization of comorbidity progression.

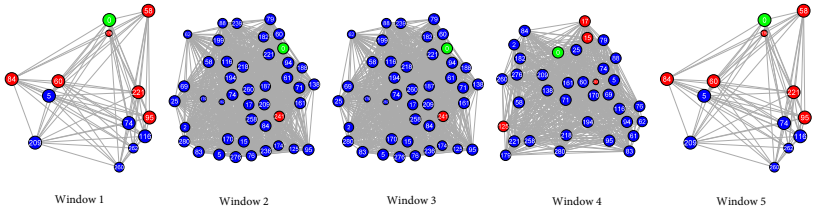
Outline

Consecutive *p*-Median Clustering (CPMP)



A sequence of TDNs across five time windows, of which the ones on Window 1 and Window 5 are identical and the ones through Window 2 to Window 4 are highly similar.

Consecutive p-Median Clustering (CPMP)



A sequence of TDNs across five time windows, of which the ones on Window 1 and Window 5 are identical and the ones through Window 2 to Window 4 are highly similar.

Problem: Consecutive p-median problem.
Input: A positive integer p, a collection of m objects $\mathscr{O} := \{O_1, O_2 \ldots, O_m\}$, and the distance between any two objects.
Output: From $\mathscr{O}$, find p objects with indices $\{j_1, j_2, \ldots, j_p\}$ as medians and assign the remaining $m-p$ objects to the medians such that

- The total summation of distances from each O_i to its assigned median is minimized, and
- When O_i is assigned to median O_{j_q}, if $i \geq j_q$ then O_k for all $j_q \leq k < i$ must be assigned to O_{j_q}, otherwise O_k for all $i < k \leq j_q$ must be assigned to O_{j_q}.

An Integer Programing (IP) Formulation for the CPMP

$$\min \sum_{i=1}^{m}\sum_{j=1}^{m} d(G_i, G_j)x_{ij} \tag{1}$$

$$\text{subject to: } \sum_{j=1}^{m} x_{jj} \leq p \tag{2}$$

$$\sum_{j=1}^{m} x_{ij} = 1 \qquad \forall i \in \{1,2,\cdots,m\} \tag{3}$$

$$x_{ij} \leq x_{jj} \qquad \forall i,j \in \{1,2,\cdots,m\} \mid i \neq j \tag{4}$$

$$x_{ij} \leq x_{kj} \qquad \forall i \in \{1,2,\cdots,m-2\}, j \in \{i+2, i+3,\cdots,m\}, k \in \{i+1, i+2,\cdots,j-1\} \tag{5}$$

$$x_{ij} \leq x_{kj} \qquad \forall i \in \{3,4,\cdots,m\}, j \in \{1,2,\cdots,i-2\}, k \in \{j+1, j+2,\cdots,i-1\} \tag{6}$$

$$x_{ij} + x_{i+1,j} \leq 1 \qquad \forall j \in \{1,2,\cdots,m\}, i \in \{1,2,\cdots,m-1\} \mid d(G_i, G_{i+1}) \geq \tau \tag{7}$$

$$x_{ij} \in \{0,1\} \qquad \forall i,j \in \{1,2,\cdots,m\}. \tag{8}$$

- $x_{ij} = 1$ if and only if TDN G_i is assigned to median G_j, for any $i,j \in \{1,2,\ldots,m\}$ such that $i \neq j$, otherwise $x_{ij} = 0$.
- $x_{jj} = 1$ indicates that G_j is served as a median for any $j \in \{1,2,\cdots,m\}$.

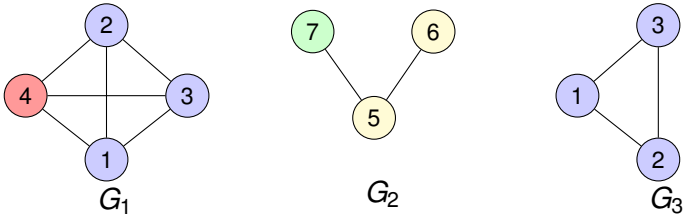
Outline

Atomic Clique

Given a network, a clique is a subset of nodes connecting with each other.

Definition 1 (Atomic Clique)

Given a collection of networks, $\mathscr{G} = \{G_1, G_2, \cdots, G_m\}$, a subset $S \subseteq \bigcup_{i=1}^{m} V(G_i)$ is called an atomic clique if S is a clique in $G_j, \forall j \in M$, but $S \cap V(G_k) = \emptyset, \forall k \notin M$, where $M = \{i \in \{1,2,\cdots,m\} \mid S \subseteq V(G_i)\}$.



Four atomic cliques $\{1,2,3\}$, $\{4\}$, $\{5,6\}$, and $\{7\}$ across three networks $\{G_1, G_2, G_3\}$.

Algorithm 1: Atomic clique partition algorithm

Input: A collection of networks $\mathscr{G} = \{G_1, G_2, \cdots, G_m\}$.
Output: An atomic clique partition $\mathscr{K}$.

$\mathscr{K} \longleftarrow \emptyset$
while $\mathscr{G} \neq \emptyset$ **do**
  $M \longleftarrow \emptyset$
  $D \longleftarrow V(G_k)$, where $k = \min\{i \mid G_i \in \mathscr{G}\}$
  for $G_i \in \mathscr{G}$ **do**
    if $D \cap V(G_i) \neq \emptyset$ **then**
      $D \longleftarrow D \cap V(G_i)$
      $M \longleftarrow M \cup \{i\}$
  while $D \neq \emptyset$ **do**
    find a subset $K \subseteq D$ such that K is a clique in $G_i[D], \forall i \in M$ and $|K|$ is maximized
    $\mathscr{K} \longleftarrow \mathscr{K} \cup K$
    for $i \in M$ **do**
      $G_i \longleftarrow G_i[V(G_i) \setminus K]$
      if $V(G_i) = \emptyset$ **then**
        $\mathscr{G} \longleftarrow \mathscr{G} \setminus G_i$
    $D \longleftarrow D \setminus K$
return $\mathscr{K}$

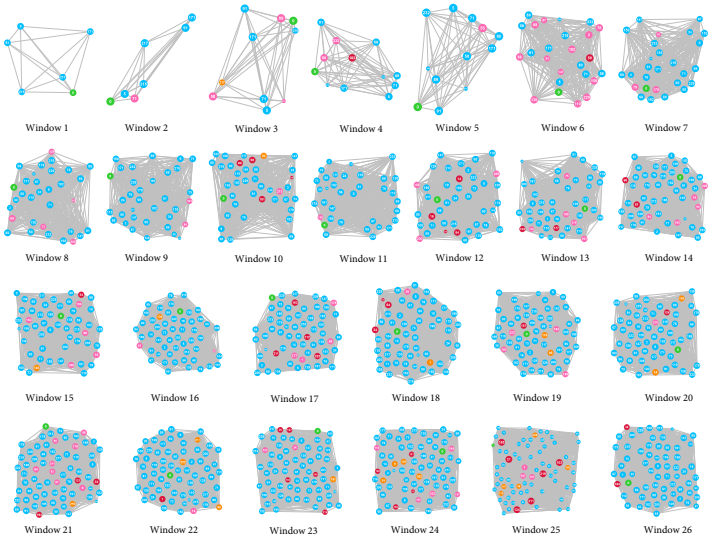
Outline

C. Diff & Stroke Background, Data Source, and Preparation

- C. Diff is a bacterial infection that can cause life-threatening diarrhea and colitis (Centers for Disease Control and Prevention, 2019).
- Stroke is one of the leading chronic conditions for death/disability in the U.S. (Members et al., 2016).
- Integrated Cerner Health Facts® EHR data warehouse as the data source into our system.
- Extracted all inpatient hospital encounters of female patients aged 65 or older with the onset of C. Diff/Stroke between November 1999 and August 2017.

C.Diff		Stroke	
Enct #	Diag #	Enct #	Diag #
2,229,051	20,677,407	117,262	571,186

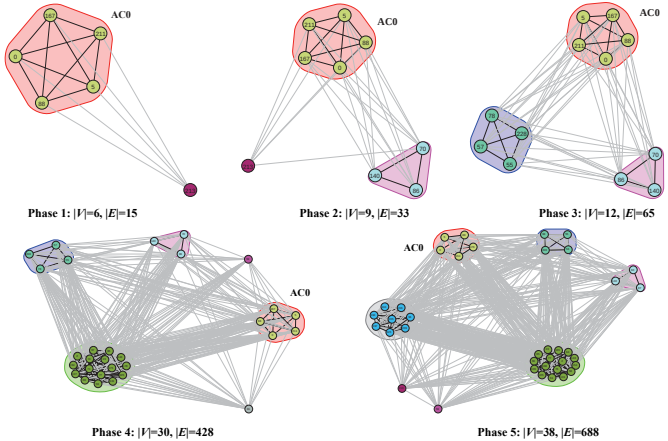
TDNs constructed for the senior female cohort (C.Diff)



Phases and corresponding windows and days

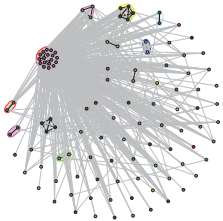
Cohorts	Time Unit	Phase 1	Phase 2	Phase 3	Phase 4	Phase 5
C. Diff	Window	1 – 3	4 – 5	6 – 11	12 – 20	21 – 26
	Day	2 – 3	3 – 4	4 – 7	7 – 11	12 – 14
Stroke	Window	1 – 8	9 – 15	16 – 26	–	–
	Day	2 – 5	6 – 9	9 – 14	–	–

Visualization of TDNs in Phases for C.Diff Cohort

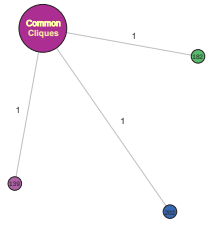


TDNs constructed on clustered phases of the senior female cohort.

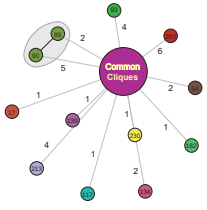
Visualization of TDNs in Phases for Stoke Cohort



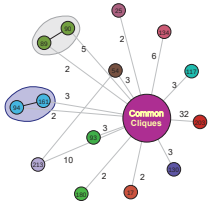
Common Cliques: $|V|$=109, $|E|$=696



Phase 1: $|V|$=112, $|E|$=699



Phase 2: $|V|$=121, $|E|$=882



Phase 3: $|V|$=123, $|E|$=1060

The common cliques are visualized in detail at the upper left part of the figure and simplified as a large node in the TDNs across the phases. The edge weight in the TDNs indicates how many nodes inside the set of common cliques are connected to a node outside the common cliques.

Outline

Concluding remarks

- Comorbidity is a prominent challenge in healthcare practice and research
- We modeled comorbidity progression as a sequence of TDNs, and designed a clinical decision support system
- The temporal and disease clustering technologies were developed to mine and visualize progression patterns from the TDN sequence
- Case studies of applying the system to C. Diff and Stroke demonstrates the effectiveness of the system

THANK YOU

Q & A

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