Visualizing Clinical Trial Design Trends by Mapping the Alzheimer’s Disease Trial Space

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BACKGROUND

• Ultimate goal is optimization of clinical trial design and evaluation in light of rising cost and failure rate [1]
• Lack of historical understanding of therapeutic space, what has been done, what has worked, and what has failed
• Research aims to provide a novel approach to identify promising clinical trial design patterns across time by qualifying and quantifying the evolution of clinical trials within a therapeutic space

PURPOSE AND RATIONALE

• Past work has focused on clustering similar clinical trials [2]
• Latent topical structures are contained within plain-text documents such as clinical trial protocols, which are pervasive throughout time
• Plain-text protocol repositories (e.g. ClinicalTrials.gov) can be extended from a simple document repository by providing analytical capabilities and insights
• Enhance ability to recognize and exploit dependency of key clinical trial design variables based on past experience
• Ultimate goal is to provide insights into the temporal dynamics of research being conducted within therapeutic spaces

METHODOLOGY (cont.)

• Utilize a graph-based nonnegative Matrix Factorization (NMF) approach for identifying latent themes based on annotated graph [3]
• Calculate trial similarities based on projected lower dimensional space
• Sort similarities temporally to establish direction of influence between similar clinical trials, resulting in a weighted directed graph
• Calculate graph metrics over sub-graphs obtained by expanding time window (yearly), such as betweenness centrality and PageRank
• Utilize Kleinberg’s Burst Detection algorithm (Fig.2) against graph metrics within each window to identify emergence of pivotal clinical trials

CURRENT PROGRESS (cont.)

• Utilizing numerous visual tools to qualitify dynamics of therapeutic area:
  • Sankey diagrams to visualize change in graph dynamics over time windows [4]
  • Swim-lane timeline visualizations to visualize emergence of pivotal clinical trials
  • Interactive graphs for exploration of conceptual graph space
  • Ability to export to other applications, such as CiteSpace [5] (Fig. 4)

FUTURE DIRECTION

• Anticipate ability to map underlying ontological concepts to biomedical endpoints found within publicly-available observational datasets (i.e. Alzheimer’s Disease Neuroimaging Initiative)
• Quantify within and between cluster variance of endpoints to further visualize influence key clinical trial design considerations have on prospective patient populations over time

REFERENCES


Figure 2. Kleinberg’s Burst Algorithm reveals influential drivers of change within the network across periods of time.

Figure 3. Querying and exploring the connections which exist between similar clinical trial protocols.

Figure 4. Identifying key themes at varying levels of granularity. Shift in treatment from targeting moderate AD (early 2000’s) to more recently early AD (2012) is apparent.