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Leveraging Semantic Clinical Similarity to Improve Early Signal Detection

Ontology-Informed Bayesian Borrowing for Pharmacovigilance Signal Detection

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Why Early Signal Detection Is Challenging

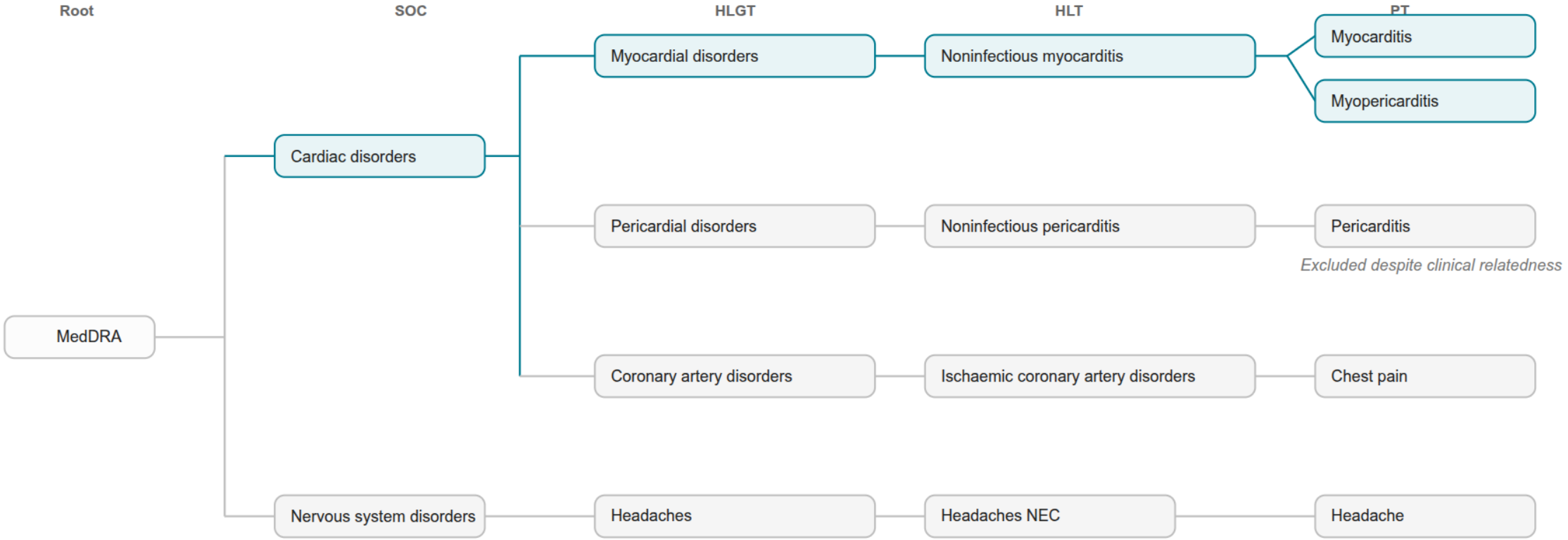
The problem:

- Early signs of signals will often be fragmented across related MedDRA preferred terms (PTs)
- Traditional quantitative approaches evaluate PTs independently
- Clinically related outcomes may contain shared safety information
- Borrowing information across clinically related outcomes may improve sensitivity

Traditional MedDRA Hierarchy vs Semantic Similarity

Rigid hierarchy-based inclusion

- Concepts are either fully included or fully excluded based on hierarchy membership.
- Included concepts contribute equally regardless of degree of clinical similarity



Hierarchy-based grouping applies fixed inclusion without similarity weighting

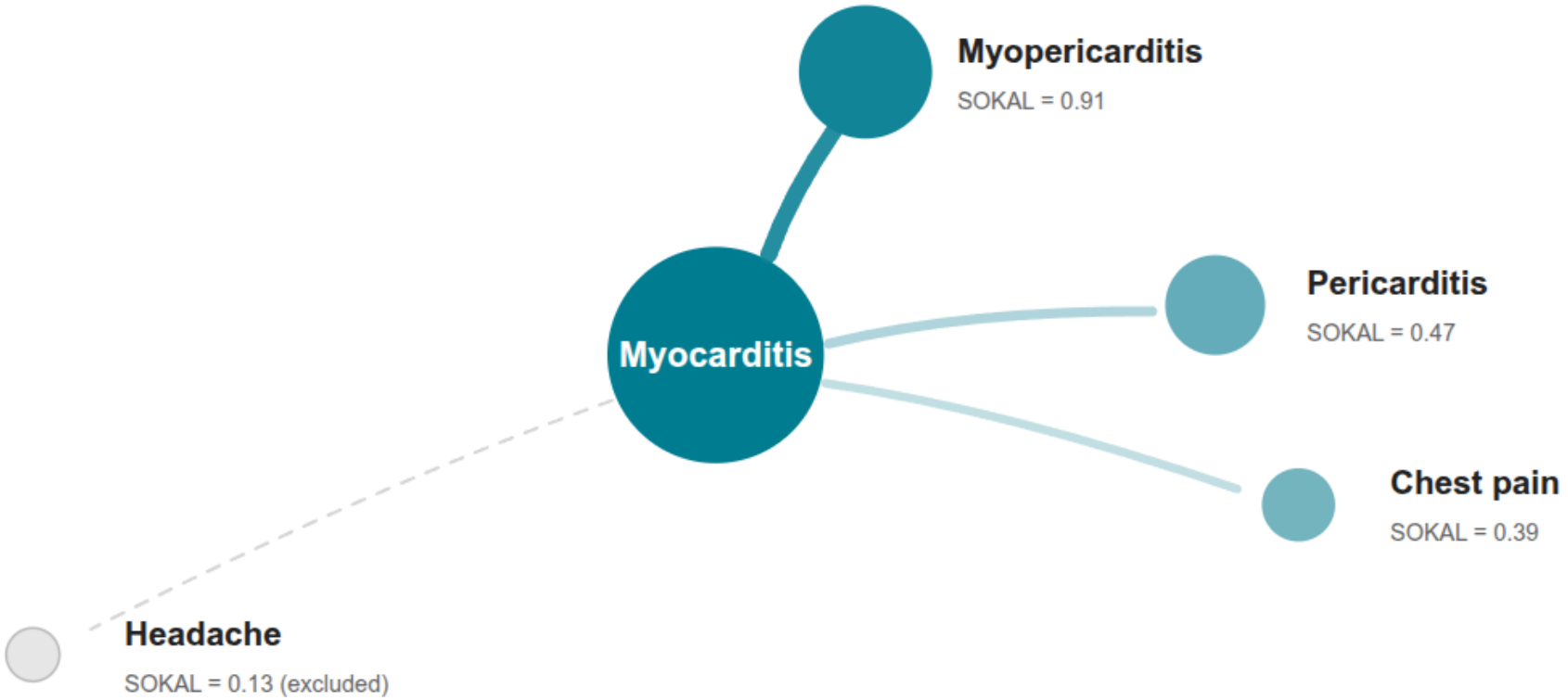
Clinically related Pts outside the selected branch are excluded despite potential clinical similarity.

SOC (System/Organ Class), HLGT (High-Level Group Term), HLT (High-Level Term), PT (Preferred Term)

Traditional MedDRA Hierarchy vs Semantic Similarity

Semantic Similarity Relationships

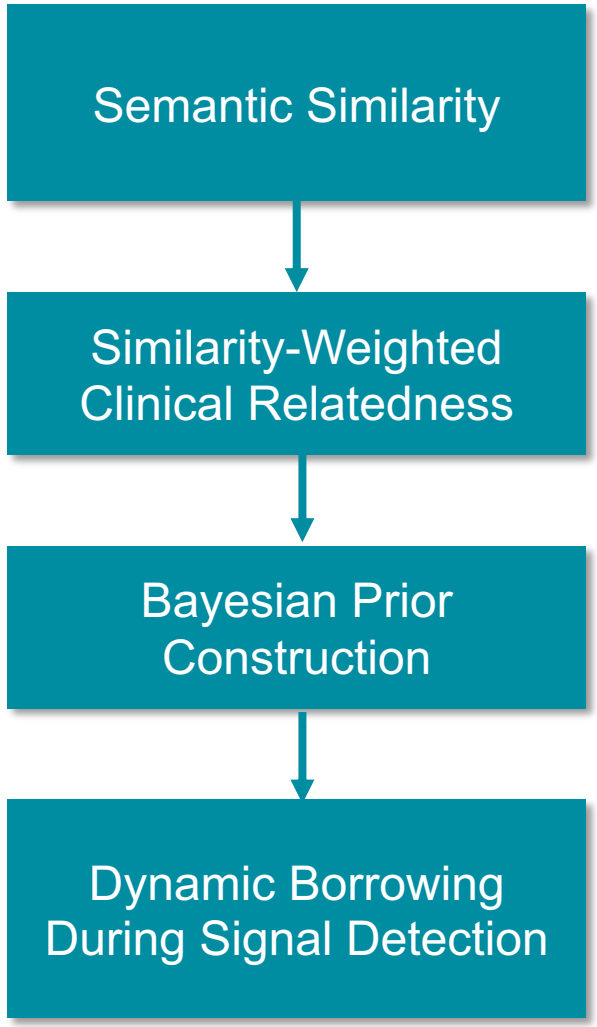
Continuous similarity-based borrowing (threshold >= 0.30)
Dashed gray links indicate measurable similarity below the inclusion threshold



Borrowing strength varies continuously above threshold
Similarity determines inclusion and weight

From Clinical Similarity to Bayesian Borrowing

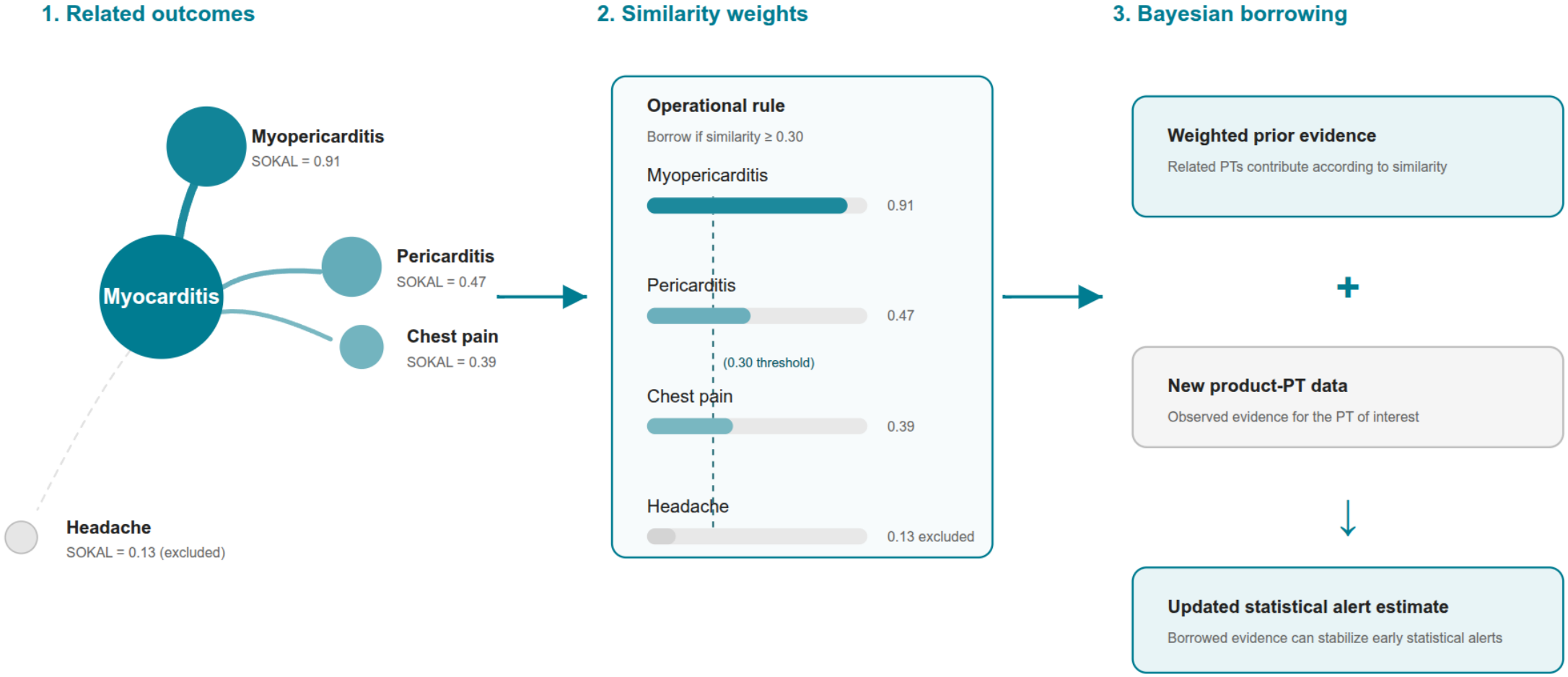
Bridging Concept to Methods



Related outcomes contribute proportionally rather than equally. Ontology-based similarity is one approach; data-driven similarity methods may capture additional latent clinical relationships.

How Semantic Similarity Guides Bayesian Borrowing

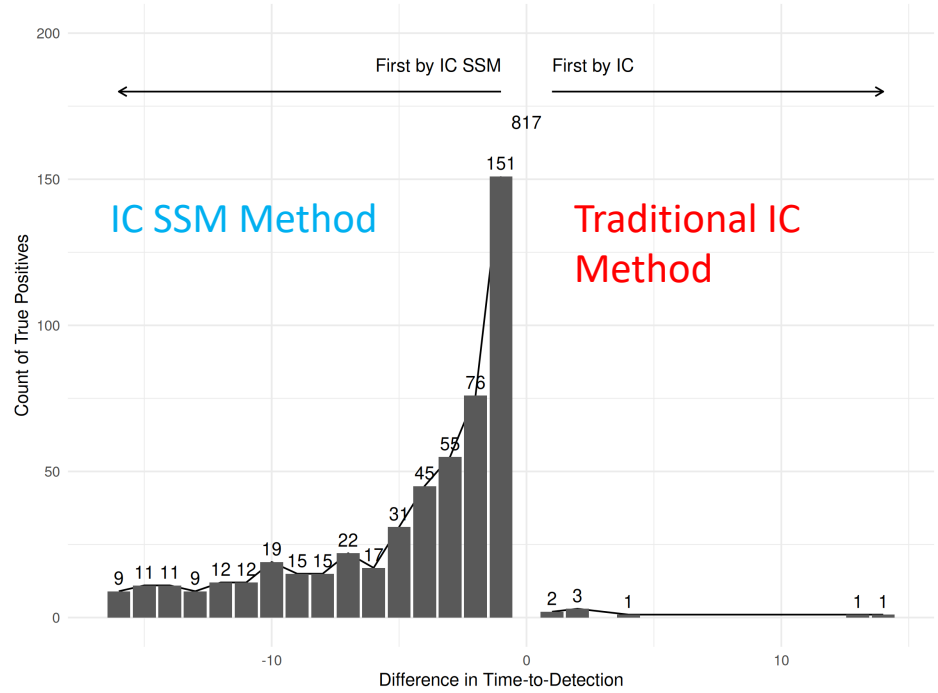
Related outcomes contribute evidence in proportion to clinical similarity



Key idea: Similarity determines how much information is borrowed, not whether outcomes are treated as identical.

Overall Performance

- New method delivers higher sensitivity and improved quantitative signal detection performance compared to existing methods
  - Identified more true positives, and detects them on average over 5 months earlier than the traditional methods.



- IC SSM = Semantic similarity-informed Bayesian borrowing method
- IC = Traditional Information Component signal detection method

Earlier quantitative signal detection, while only one element of PV systems, may improve the timeliness of pharmacovigilance processes and, ultimately, safety decision-making.

Limitations & Future Directions

Limitations

- **Sparse-data false positives**
  - Low-count PTs may occasionally trigger excessive borrowing.
- **Dependence on ontology structure**
  - Performance depends on the quality and granularity of semantic relationships.
- **Parameter sensitivity**
  - Performance varies with similarity thresholds and prior weighting.
- **Computational complexity**
  - Large-scale similarity informed borrowing increases computation burden compared to traditional methods.
- **Limited evaluation dataset**
  - Experiments were conducted using public FAERS data only.

Future Directions

- **Alternative similarity metrics**
  - Evaluate additional ontology-based and hybrid semantic similarity approaches.
- **External validation**
  - Assess performance across additional spontaneous reporting systems and real-world datasets.
- **Adaptive borrowing strategies**
  - Explore dynamic weighting schemes and more advanced Bayesian borrowing formulations.

Thank You

For more information, please find links to many of our papers, pre-prints and code made available here:

https://github.com/GSK-Global-Safety/DIA2026

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