

Real-World Evidence of Association between Autoimmune Diseases

Shah Lab

Observational Health Data Science
Weekly Meeting



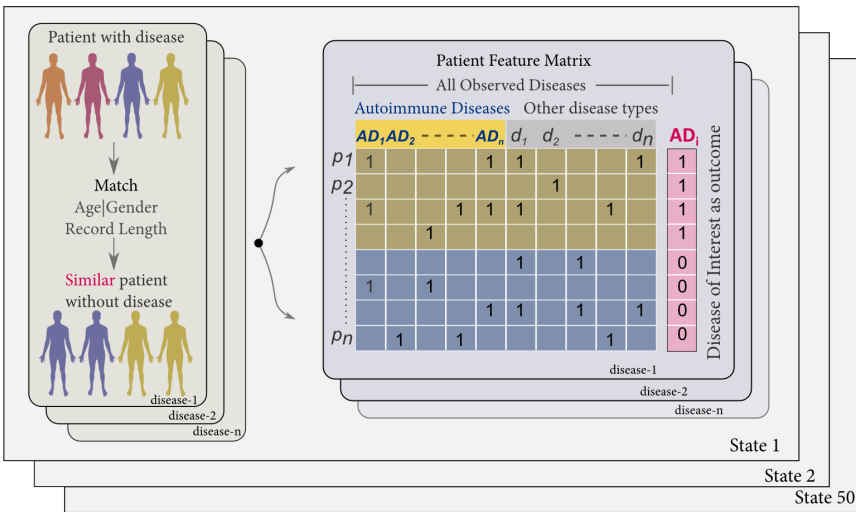
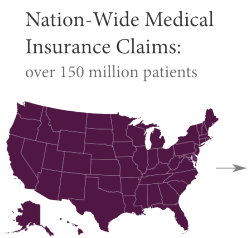
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Hypothesis

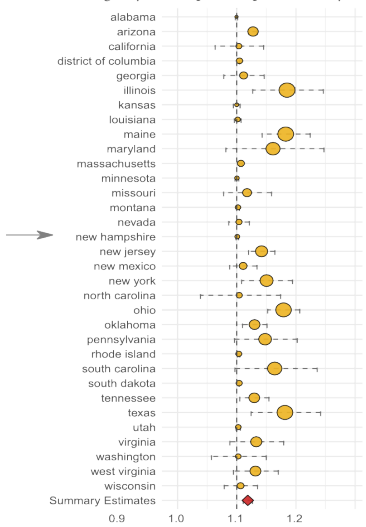
Association amongst diseases seen in medical claims data can guide molecular understanding of diseases

Summary of Analysis

Build Clinical Profiles: each disease, each State across the United States



Meta Analysis: each disease across the United States
account for heterogeneity and improve reproducibility

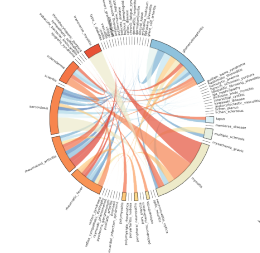


Understudied: Connected if there is less than 50% chance of association inferred from PubMed

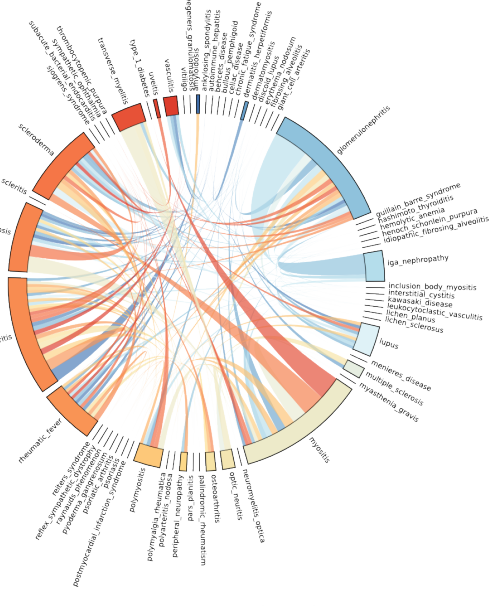
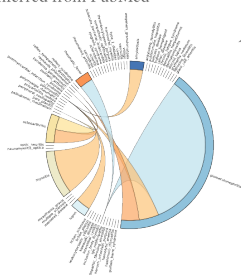
Association: between autoimmune diseases representing medical practice

Systems Immunology: understanding shared genetic signature for informed medical decision making

- BioPlex: analysis of biophysical interactions at genome scale
- ImmunoState: analysis of blood gene expression across GEO
- UKBiobank: genetic correlation and polygenicity



Not studied: Connected if there is no association inferred from PubMed



Nigam Shah Lab

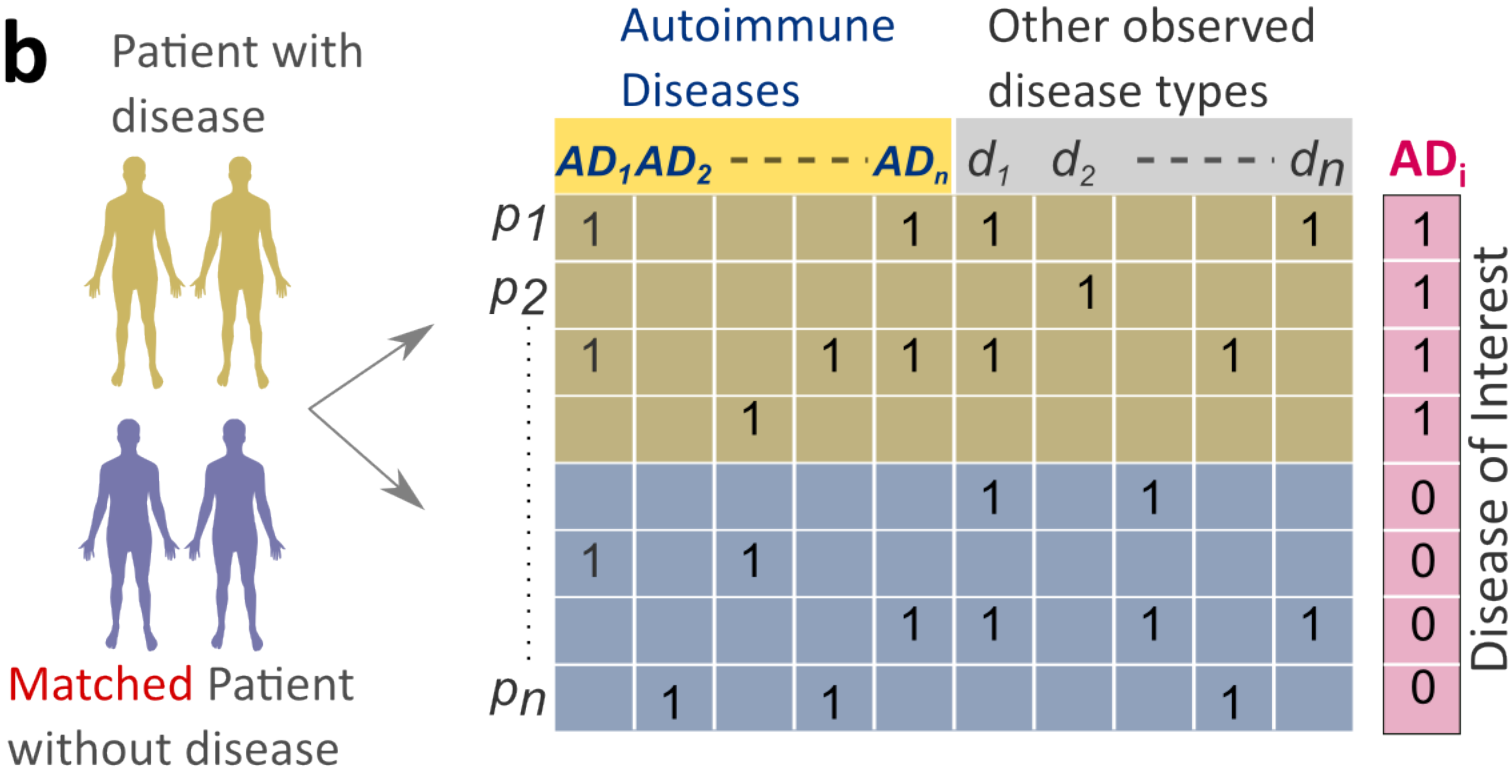
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evidence from Science of Medicine

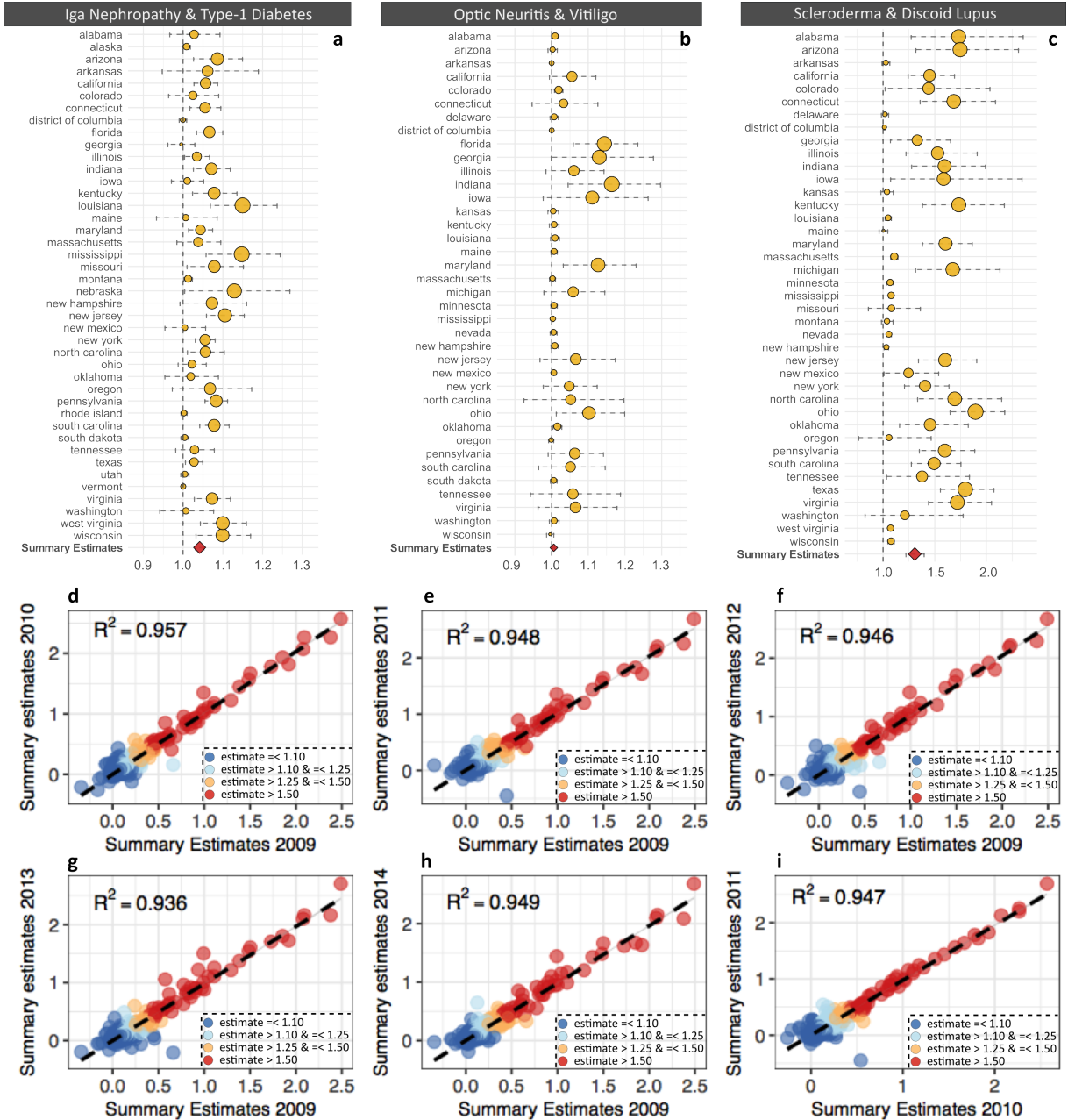
evidence from Practice of Medicine

Creating a Clinical Profile



Clinical profile of a disease D is a vector of length i, where each feature is another disease Di and the values are the strength of association between D and Di obtained from a matched cohort of patient with and without disease D.

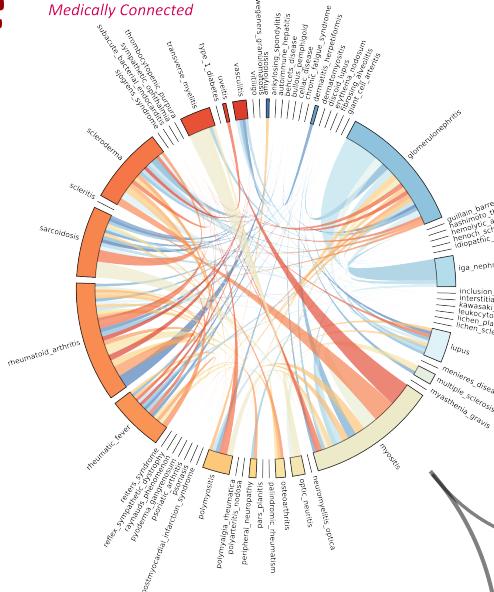
Meta analysis of associations among diseases



Associations seen in practice, but not in literature

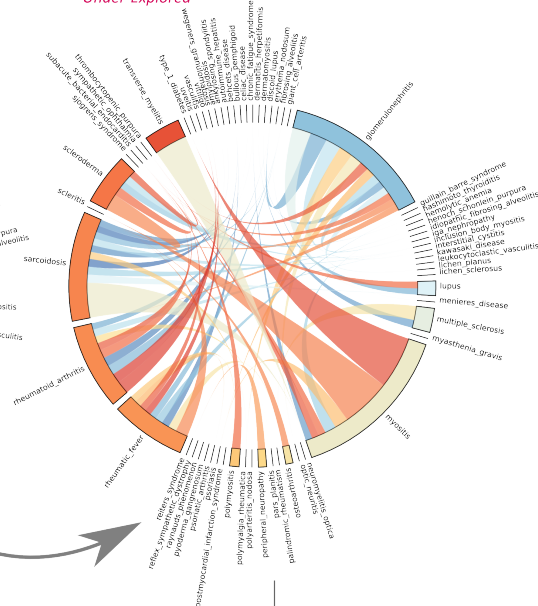
a Evidence from Nation-Wide Medical Claims
Connected if evidence is strong
Medically Connected

140 Disease Pairs with **strong real-world evidence**.



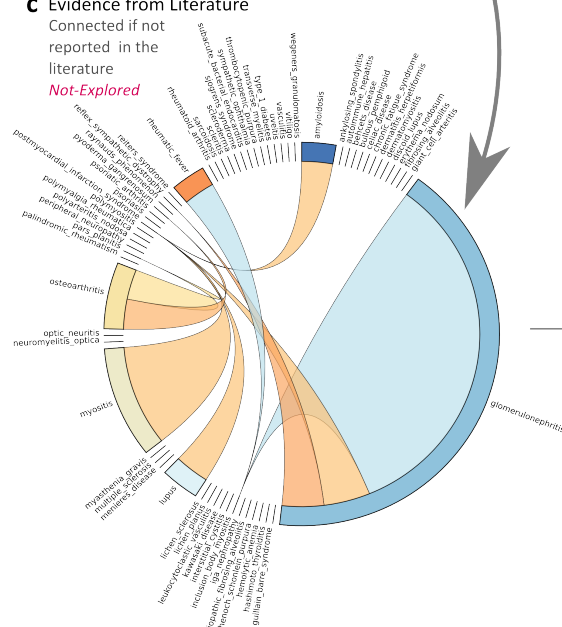
b Evidence from Literature
Connected if under reported in the literature
Under-Explored

52 Understudied Disease Pairs



c Evidence from Literature
Connected if not reported in the literature
Not-Explored

9 Novel Disease Pairs



d Systems Immunology Analysis

- Shared Genetic Signature
Biophysical interactions
- Blood Gene Signatures
MultiCohort blood gene expression analysis
- Genetic correlation & Polygenicity
UkBiobank analysis of genome wide associations

Preliminary results

- We identified 140 pairs of autoimmune diseases that have a strong relation based on nationwide medical claims of over 150 million patients.
- Of the 140 pairs, **52** had **very poor** evidence of being associated in the literature and **9** pairs have **never been studied** together based on PubMed.
- For each of the **61** pairs we performed a systematic genome-wide analysis using the UK BioBank and gene expression data from GEO to uncover **genetic correlation**, **polygenicity** and **co expressed genes** underlying a disease pair to understand shared genetic signatures.

Related Work

- *A Non-degenerate code of deleterious variants in Mendelian loci contribute to complex disease risk* **Blair et al.** Cell 2013 Sep26;155(1):70-80
- *A dynamic network approach for the study of human phenotypes* **Hidalgo et al.** PLoS Comput Biol. 2009 Apr; 5(4):e1000353

Thank You

lets see a demo before we get to questions

<http://autoimmunedb.stanford.edu>