

Real-World Evidence of Association between Autoimmune Diseases

Shah Lab

Observational Health Data Science
Weekly Meeting



STANFORD
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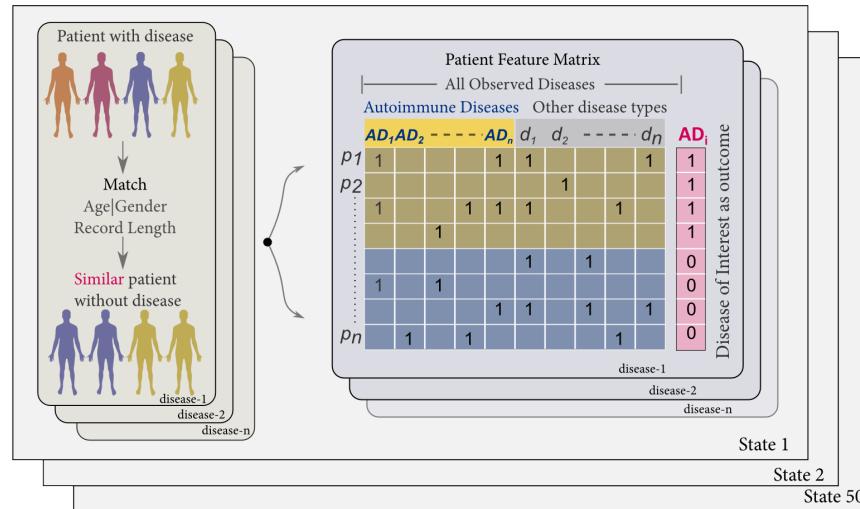
Hypothesis

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

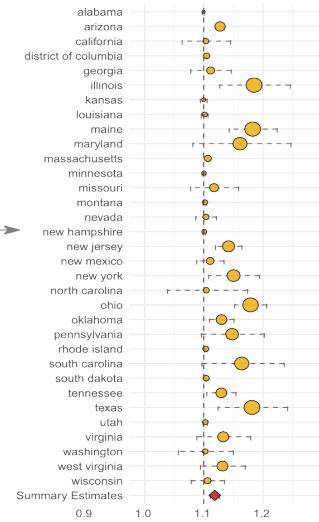
Summary of Analysis

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

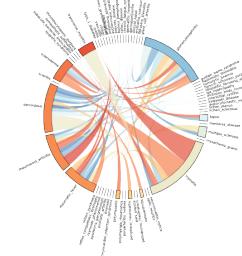
Nation-Wide Medical Insurance Claims:
over 150 million patients



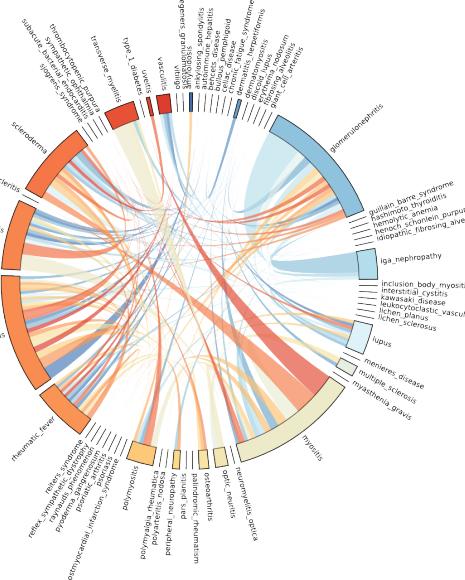
Meta Analysis: each disease across the United States account for heterogeneity and improve reproducibility



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

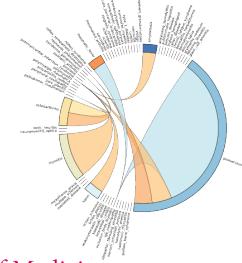


Association: between autoimmune diseases representing medical practice



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

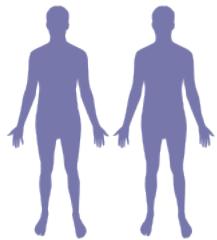
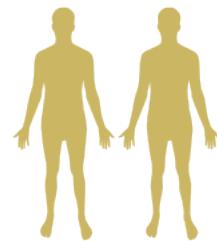


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Creating a Clinical Profile

b Patient with disease

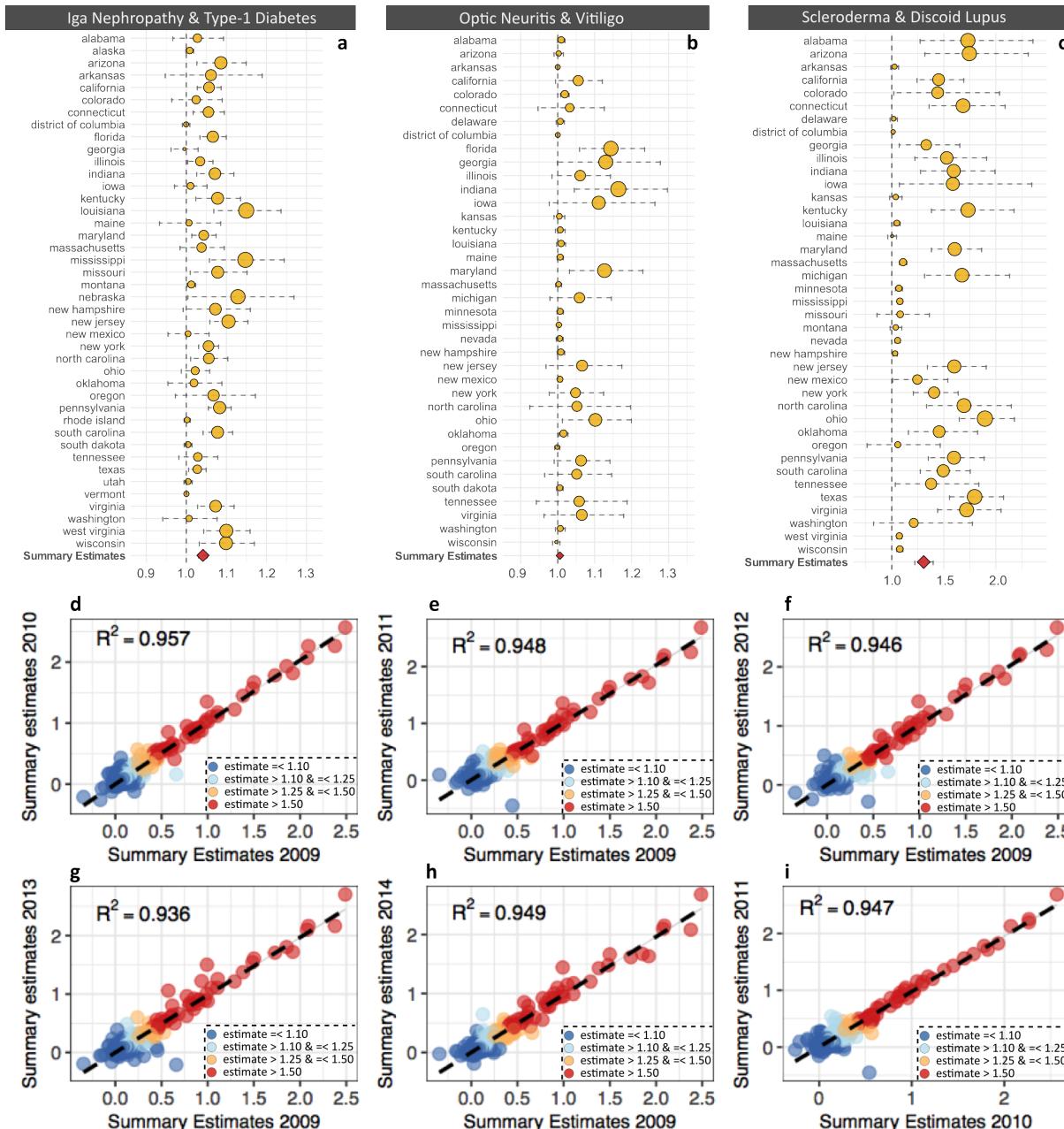


Matched Patient without disease

	Autoimmune Diseases									AD _i
	AD_1	AD_2	\dots	AD_n	d_1	d_2	\dots	d_n		
p_1	1				1	1			1	1
p_2		1			1	1	1		1	1
			1							1
p_n	1	1			1	1	1	1	1	0
			1							0
				1						0
					1					0

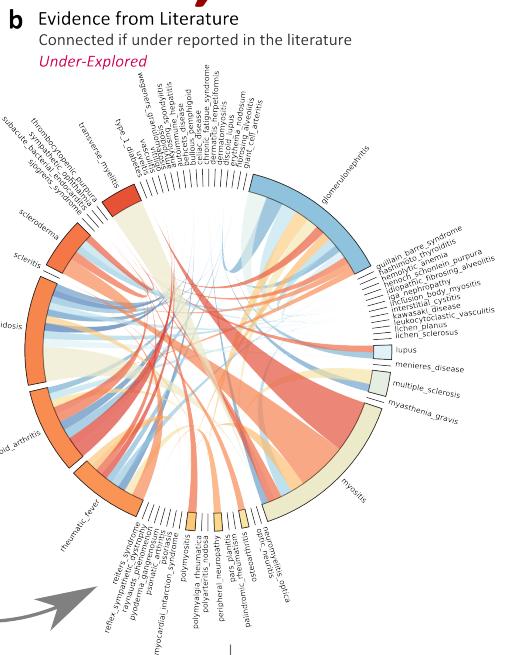
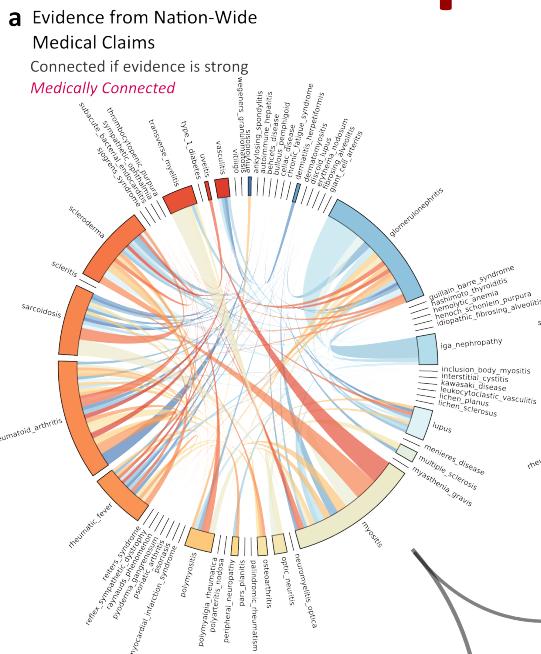
Clinical profile of a disease D is a vector of length i, where each feature is another disease Di and the values are the strength of association between D and Di obtained from a matched cohort of patient with and without disease D.

Meta analysis of associations among diseases

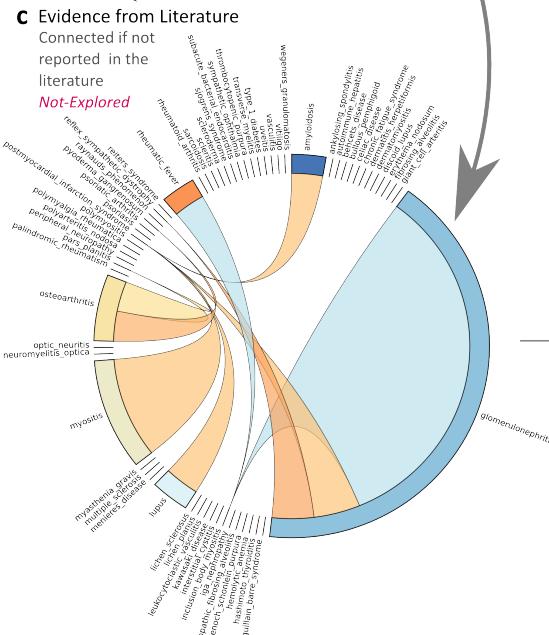


Associations seen in practice, but not in literature

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



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>