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12:00-1:00 pm

via Zoom Link

<https://uwmadison.zoom.us/j/91593359262?pwd=5XA5YmtPZWdDYmJwZXdHaVJFbm1WQT09>

Modelling hidden genetic risk from family history for improving polygenic risk prediction and increasing yield of diagnostic sequencing

Abstract: Polygenic risk scores based on common genetic variants have demonstrated significant potential in both research and clinical settings. However, it is important to consider whether family history, a traditional genetic predictor, still provides valuable information. Family history of complex traits and diseases can be influenced by various factors, including the transmission of rare pathogenic variants, shared environmental exposures within families, and a common genetic predisposition.

In this presentation, I will introduce a latent factor model that aims to quantify disease risk beyond what is captured by a common genetic variant-based polygenic risk score but inferable from family history. I will discuss how this model can enhance population-level risk stratification for complex diseases such as cardiovascular diseases, Alzheimer's disease, and idiopathic short stature. Additionally, I will discuss its potential in prioritizing individuals who are more likely to carry clinically actionable rare pathogenic variants for diagnostic sequencing.

At the end of the presentation, I will provide an overview of other ongoing and future research directions, focusing on the development and implementation of statistical genetics methods for improving the prevention, diagnosis, and treatment of complex diseases.

Relevant publications:

Lu et al. Capturing additional genetic risk from family history for improved polygenic risk prediction. *Commun Biol* 2022. PMID: 35710731

Lu et al. Polygenic risk score as a possible tool for identifying familial monogenic causes of complex diseases. *Genet Med* 2022. PMID: 35460399

Lu et al. Individuals with common diseases but with a low polygenic risk score could be prioritized for rare variant screening. *Genet Med* 2021. PMID: 33110269



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