

Submitter Name: Laura Jean Bierut
Submitted email: laura@wustl.edu

When will we be ready to bring polygenic risk scores into clinical medicine?

Laura Jean Bierut, Alex Ramsey, Li-Shiun Chen

Department of Psychiatry, Washington University School of Medicine

Precision health is built on the premise that an individual's genomic data and environmental exposures will allow more targeted disease prevention and guide clinical care. Polygenic risk scores, which synthesize genomic risk over an individual's entire genome, can predict who is at greatest risk of developing a disease, including substance use disorders. For genomic applications such as polygenic risk scores to enter clinical medicine, key components need to be evaluated: analytic validity, clinical validity, clinical utility, as well as ethical and legal implications. The treatment of cigarette smoking and tobacco use disorder represents a prime area for the implementation of precision health given the strong foundation in genomic discovery to date. The genes *CHRNA5* and *CYP2A6* are strongest genomic contributors that alter the risk of heaviness of smoking, tobacco use disorder, and smoking-related diseases in humans. These biomarkers have proven analytic and clinical validity, and evidence for their clinical utility continues to grow. We propose that these genomic biomarkers improve the identification of elevated disease risk in people who smoke, aid in the personalization smoking cessation treatments, and promote positive behavioral changes. In addition, individuals who smoke report a desire for receiving their own genomic information. The ethical implications of returning genomic information needs further study to understand if potential positive effects of providing genomic information to individuals outweighs concerns about potential stigma and discrimination.