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Transforming the understanding of human health and disease

Researchers identify 76 environmental exposures associated with type 2 diabetes using innovative precision environmental health framework.

BY MARLA BROADFOOT

NIEHS efforts have demonstrated how knowledge of the [exposome](https://www.niehs.nih.gov/health/topics/science/exposure/index.cfm) (<https://www.niehs.nih.gov/health/topics/science/exposure/index.cfm>), or the totality of our environmental exposures can be harnessed to transform research on human health and disease. Now, the publication of a high-impact, clinically relevant paper from a [decades-long study](https://www.niehs.nih.gov/research/clinical/studies/pegs/index.cfm) (<https://www.niehs.nih.gov/research/clinical/studies/pegs/index.cfm>) of environmental exposures demonstrates that a framework known as precision environmental health is coming of age.

Creating the evidence base

The [Personalized Environment and Genes Study](https://joinastudy.niehs.nih.gov/studies/pegs/index.htm) (<https://joinastudy.niehs.nih.gov/studies/pegs/index.htm>) (PEGS) has collected health, family history, environmental exposures, and lifestyle data on more than 20,000 North Carolinians since its inception 20 years ago. The PEGS research team has compiled genetics data on a subset of that cohort by sequencing the whole genomes of 4,700 participants.

In a study published in November in the journal [Diabetes Care](https://pubmed.ncbi.nlm.nih.gov/36383734/) (<https://pubmed.ncbi.nlm.nih.gov/36383734/>), NIEHS researchers examined how this data can be tapped to predict a person's risk of developing type 2 diabetes. Using statistical methods and machine learning, they identified 76 environmental exposures associated with the disease.

"We were able to recapitulate known risk factors, as well as identify previously unknown associations with asbestos and coal dust exposure, which was really interesting," said lead study author [Alison Motsinger-Reif, Ph.D.](https://www.niehs.nih.gov/research/atniehs/labs/bb/staff/motsinger-reif/index.cfm) (<https://www.niehs.nih.gov/research/atniehs/labs/bb/staff/motsinger-reif/index.cfm>), chief of the Biostatistics and Computational Biology Branch.

The team combined 13 of these environmental exposures to create a predictive value known as a polyexposure score (PXS). They compared the predictive performance of this score with a polygenic risk score (PGS) based on genomic variants associated with diabetes and an overall clinical score (OCS) built using established risk factors such as BMI and prediabetes.



Motsinger-Reif and [Janet Hall, M.D.](https://www.niehs.nih.gov/research/atniehs/labs/crb/pi/rpp/index.cfm) (<https://www.niehs.nih.gov/research/atniehs/labs/crb/pi/rpp/index.cfm>), lead the PEGS initiative, which has enrolled more than 20,000 participants. To learn more, [visit the PEGS website](https://joinastudy.niehs.nih.gov/studies/pegs) (<https://joinastudy.niehs.nih.gov/studies/pegs>). (Photo courtesy of Steve McCaw / NIEHS)

One of the key outcomes from the workshop series was to collect data to help formulate an operational model on how to conduct experiments in exposomics. There was a consensus to establish a community of practice to guide best practices and enable coordination among various exposome efforts.

According to Cui, more than 200 pages of meeting reports emerged from the discussions, which will be helpful to define next steps for operationalizing exposomics. A lot of work remains to be done.

“Those notes contain many great ideas proposed and research gaps identified that can inform individual researchers and programs as well as exposome initiatives supported by NIH or other institutions,” she said. Currently, she and others at NIEHS are working to prioritize those ideas in order to develop an operational model that will help investigators know and understand how to collect exposomic data that can be shared across the biomedical research community.

*Citation: Akhtari FS, Lloyd D, Burkholder A, Tong X, House JS, Lee EY, Buse J, Schurman SH, Fargo DC, Schmitt CP, Hall J, Motsinger-Reif AA. (<https://diabetesjournals.org/care/article/doi/10.2337/dc22-0295/147936/Questionnaire-Based-Polyexposure-Assessment>) Questionnaire-based polyexposure assessment outperforms polygenic scores for classification of type 2 Diabetes in a multiancestry cohort. *Diabetes Care*; doi:10.2337/dc22-0295 [Online 16 November 2022].*

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