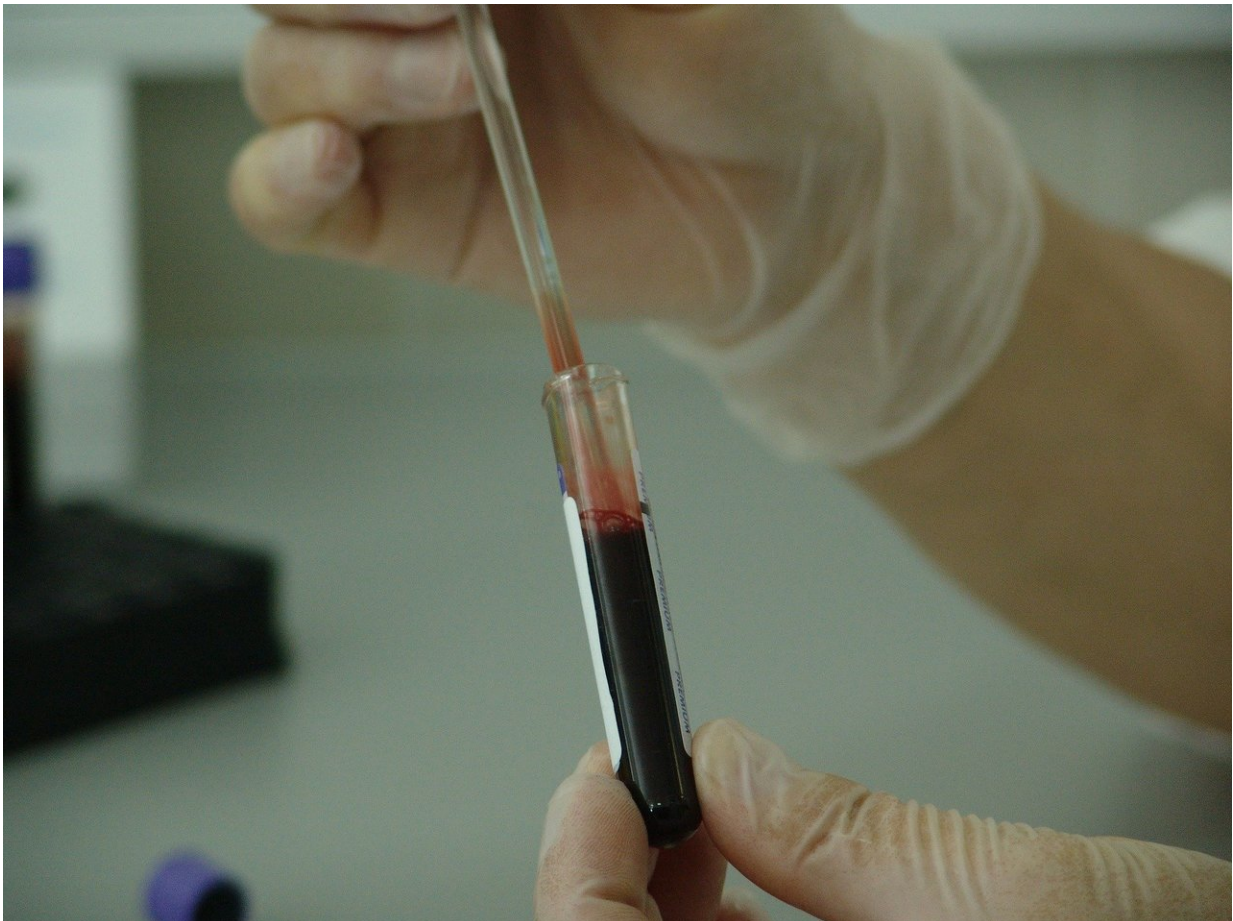


# Team's study reveals hidden lives of medical biomarkers

October 12 2018, by Paul Govern

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What do medical biomarkers do on evenings and weekends, when they

might be considered off the clock?

The hidden lives of medical biomarkers are the focus of a recent study in *Nature Communications* by Jonathan Mosley, MD, Ph.D., assistant professor of Medicine and Biomedical Informatics, and colleagues from Vanderbilt University Medical Center and 11 other institutions.

Any reliable measure of a physiological state might qualify as a biomarker. Some of the biomarkers used in disease risk assessment and diagnosis are themselves mediators of disease, LDL-cholesterol and blood pressure being two well-known examples.

The study introduces a method to define biomarker-outcomes spectrums. The authors write that, "Defining the complete spectrum of disease outcomes associated with a biomarker not only provides insights into disease mechanisms, but may also reveal potential beneficial and adverse effects of modulating biomarker levels."

Employing genome-wide trait analysis, the team scans for correlations between 53 commonly used medical biomarkers, as measured in an epidemiological study cohort, and 1,139 well recognized disease outcomes, as reflected in de-identified [electronic medical records](#) of a separate genotyped research cohort. In all, the demo involves 44,893 genotyped research subjects.

"If you were to try tackling this question with conventional epidemiological methods, you'd break the bank," Mosley said.

"Repurposing available genetic data is not only comparatively affordable, it also provides results immediately. With our method, we're circumventing the decades-long wait for nature to take its course and produce measurable outcomes."

If you measure a group of strangers for both similarity of traits and chance genetic similarity, you can estimate the cumulative genetic influence of genes on each of the measured traits. For each trait, you can also measure correlation with each of the genetic variants you've tested, and calculate a cumulative genetic score for the trait.

"You can use this score to predict the trait in any individual who's undergone genotyping for common genetic variants," Mosley said.

To derive genetic scores for 53 atherosclerosis biomarkers, the team used data from 7,740 genotyped individuals in the Atherosclerosis Risk in Communities study.

Using those scores, they predicted values for the 53 biomarkers in 37,153 genotyped patients seen at VUMC and other centers in the eMERGE Network (Electronic Medical Records and Genomics Network). In this latter group, the team measured associations between the predicted biomarker values and 1,139 diagnoses.

"Along with replicating many known biomarker-outcome associations, we turned up a number of undescribed associations. However, some seemingly obvious associations were the most surprising to me. For instance, a [biomarker](#) predicting smoking was associated with diagnoses of tobacco use, alcohol use and obesity, indicating that these behaviors have common genetic drivers and that some individuals have a strong genetic predisposition toward them.

"I didn't expect that genetics would predict behaviors. This observation has made me a more compassionate physician when approaching patients struggling with these issues," Mosley said.

The team also found an inverse association between high LDL-cholesterol and septicemia, an association they replicated (without

recourse to genotype data) in a separate cohort.

**More information:** Jonathan D. Mosley et al. A study paradigm integrating prospective epidemiologic cohorts and electronic health records to identify disease biomarkers, *Nature Communications* (2018). [DOI: 10.1038/s41467-018-05624-4](https://doi.org/10.1038/s41467-018-05624-4)

Provided by Vanderbilt University

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