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DISEASE GENETICS

Phenome-wide association studies go large

There is great interest in making use of the large amounts of phenotypic data that are stored in electronic medical records (EMRs) in the quest to understand the genetic basis of disease. One way to do this is to carry out phenome-wide association studies (PheWASs), in which genetic variants are tested for association with a wide range of medically relevant phenotypes. A new study reports the first large-scale PheWAS using data from EMRs and demonstrates the use of this approach — for replicating associations, finding new ones and providing insights into pleiotropy.

Denny and colleagues used phenotypic data from the EMRs of

13,835 individuals, and they looked for associations between 1,358 phenotypes and 3,144 single-nucleotide polymorphisms (SNPs) that had previously been found to show association with one or more traits in genome-wide association studies (GWASs). In cases for which the PheWAS was sufficiently powered, 66% of associations from GWASs were replicated.

Apart from these replications, the study also uncovered 63 cases of previously unknown, potentially pleiotropic effects. EMR-based PheWASs provide an approach to detecting pleiotropy that is much simpler than current methods that are based on findings from GWASs,

which require complex integration of data from multiple studies.

Importantly, the size of the study that was reported in this paper was not sufficient to assess pleiotropy for all SNPs, and the authors speculate that larger EMR-based studies might reveal more pleiotropy than has been estimated from GWASs. Such studies have the potential to increase our understanding of the shared molecular etiologies of diseases.

Louisa Flintoft

ORIGINAL RESEARCH PAPER Denny, J. C. et al. Systematic comparison of phenome-wide association study of electronic medical record data and genome-wide association study data. *Nature Biotech.* <http://dx.doi.org/10.1038/nbt.2749> (2013)

FURTHER READING Kohane, I. S. Using electronic health records to drive discovery in disease genomics. *Nature Rev. Genet.* **12**, 417–428 (2011) | Jensen, P. B., Jensen, L. J. & Brunak, S. Mining electronic health records: towards better research applications and clinical care. *Nature Rev. Genet.* **13**, 395–405 (2012)