bitive, however, if scientists are systematically doomed to drown in a sea of false-positive results before reaching the shore of genuine effects. Many causative genetic variants of moderate effect will inevitably have to be discarded by GWAS due to insufficient sample sizes. This has already become evident by the strength of successfully replicated disease associations which, for most published GWAS, were at the limit of what these studies were powered to detect. The need for qualified hypothesis generation does not vanish with a growing wealth of data! With realistic sample sizes, it will be hampered instead by the multiple-testing problem. In other words, most GWAS will not substantially reduce ignorance; they will make it recur faster.

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Thank you for your comments most of which are quite well understood in the GWAS community. I would gladly confess that I understated Poppers' conceptual framework of hypothesis-driven research for the sake of being a bit provocative. Indeed, several readers have pointed out that the idea of 'always finding what you are looking for, by studying all data and discarding data only after assessing their relevance … ' is a hypothesis *per se*. That is probably true, and then, after all, we are all doing hypothesis-based research.

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