Supplemental Figure 1

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Figure S1 - The GWAS "inflection point": discoveries in relation to sample size

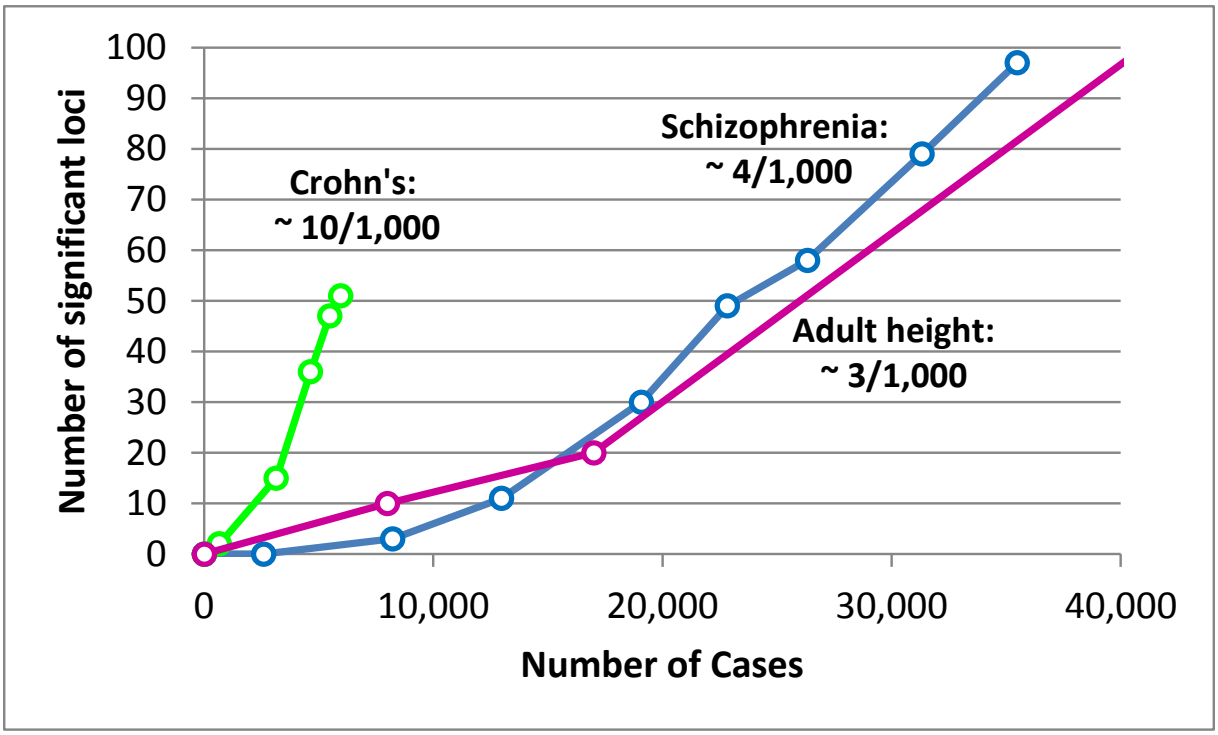

Figure S1: The GWAS "inflection point": discoveries in relation to sample size. Each point represents the number of independent chromosomal regions (loci) containing SNPs associated with the disease or trait at a genome-wide level of significance in a GWAS analysis with a given number of cases (and a control group of similar or greater size). The curve for adult height is truncated but the next datapoint is 180 loci with the equivalent of ~65,000 cases. These data points are results of unpublished meta-analyses carried out by S.R. on roughly chronological subsets of each dataset in order to demonstrate the linear relationship between sample size and discoveries once a minimum N ("inflection point") has been achieved. The ratios for each trait are the approximate number of discoveries per 1,000 additional cases (plus controls). Each ratio results from a combination of the number of susceptibility loci for the trait and the size of their genetic effects. Large Ns would discover additional loci for each trait.

Supplemental references: The data for the schizophrenia curve are drawn from the PGC dataset as described in reference S1 (below). Data for Crohn's disease are drawn from the dataset reported in reference S2. Data from human height are drawn from the GIANT consortium dataset reported in reference S3 (and a larger meta-analysis, currently under review, yields similar conclusions. As noted above, the datapoints on each curve do not

correspond specifically to separate published analyses; rather, they represent meta-analyses carried out by S.R. using increasingly larger proportions of each multisite dataset, in roughly chronological order, to illustrate the relationship between N(cases) and N("hits"). Similar analyses of additional traits have been described in reference S4, concluding similarly that after an initial inflection point, the number of hits increases linearly with sample size or more rapidly.

S1. Schizophrenia Working Group of the Psychiatric Genomics Consortium (In press): Biological insights from 108 schizophrenia-associated genetic loci. Nature.

S2. Jostins L, Ripke S, Weersma RK, Duerr RH, McGovern DP, Hui KY, et al. (2012): Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. Nature. 491:119-124.

S3. Lango Allen H, Estrada K, Lettre G, Berndt SI, Weedon MN, Rivadeneira F, et al. (2010): Hundreds of variants clustered in genomic loci and biological pathways affect human height. Nature. 467:832-838.

S4. Panagiotou OA, Willer CJ, Hirschhorn JN, Ioannidis JP (2013): The power of meta-analysis in genome-wide association studies. Annu Rev Genomics Hum Genet. 14:441-465.