

Supplemental Information

The Benefits of Using Genetic Information to Design Prevention Trials

Youna Hu, Li Li, Margaret G. Ehm, Nan Bing, Kijoung Song, Matthew R. Nelson, Philippa J. Talmud, Aroon D. Hingorani, Meena Kumari, Mika Kivimäki, Chun-Fang Xu, Dawn M. Waterworth, John C. Whittaker, Gonçalo R. Abecasis, Cathie Spino, and Hyun Min Kang

Supplemental Inventory

Figure S1

Figure S2

Table S1

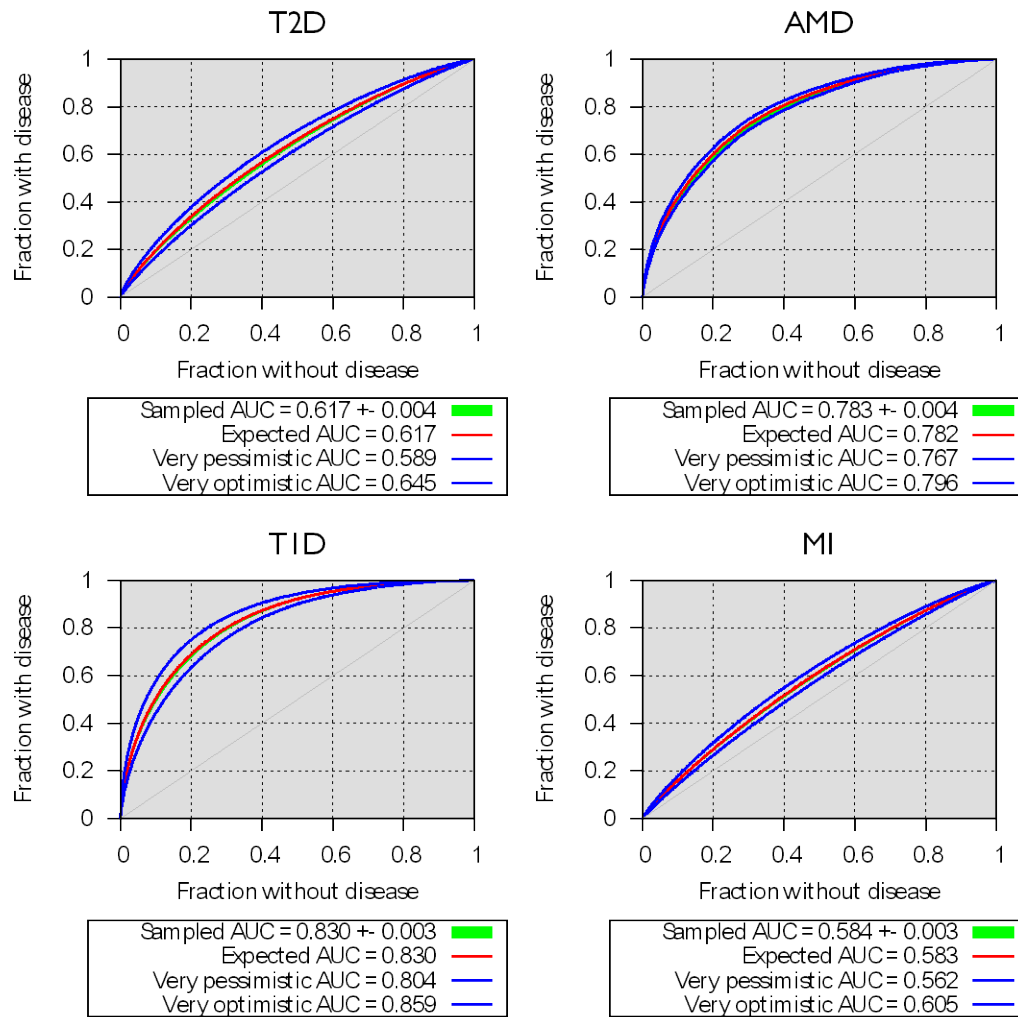


Figure S1. Receiver Operating Characteristics curve of the genetic risk score from known risk variants. Expected AUC represent area under the ROC curve using expected odds ratio. The sampled AUC is calculated from 100 sets of sampled odds ratios from lognormal distribution from reported odds ratios and confidence intervals. Very pessimistic and optimistic AUC is computed from lower and upper bound of 95% CI of odds ratio from each SNP, respectively.

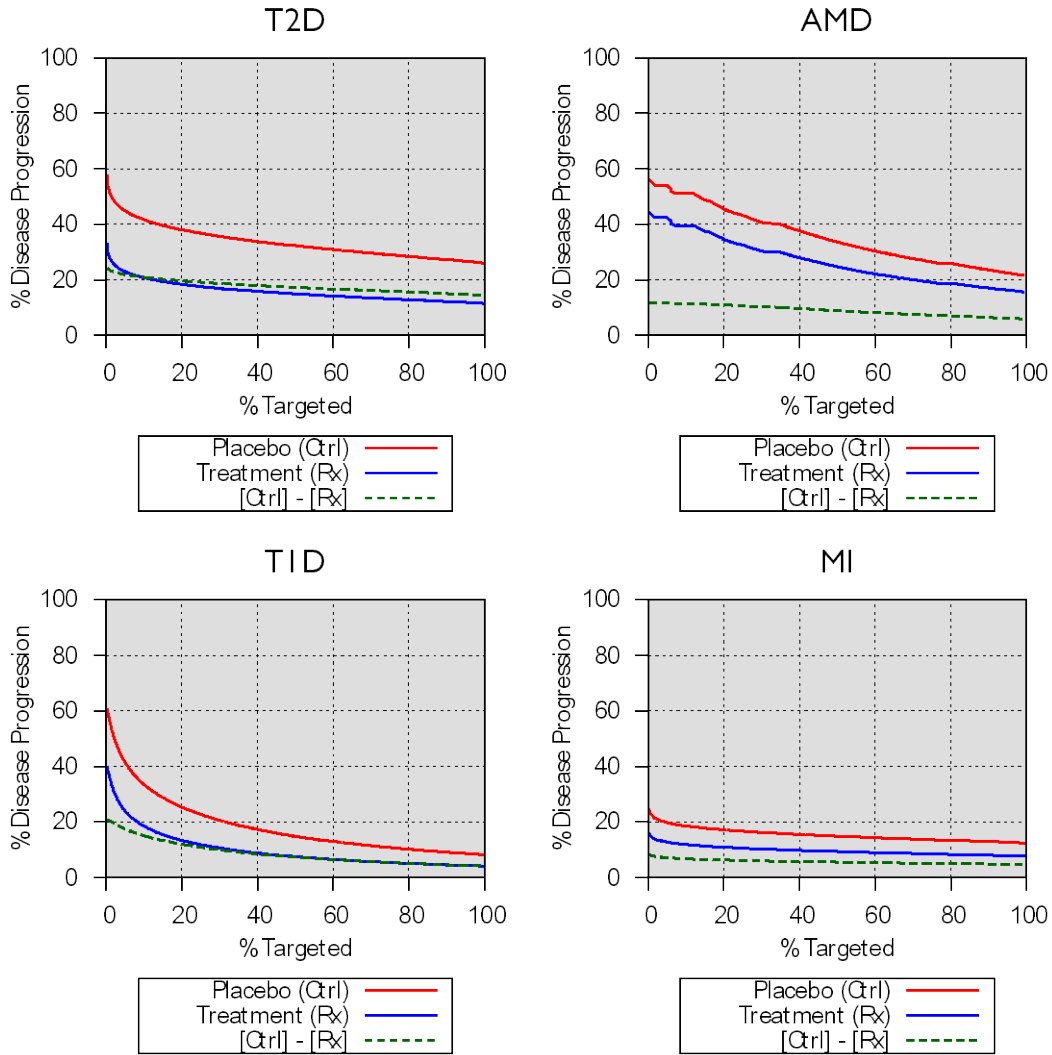


Figure S2. Changes in disease progression rate by the threshold of genetic risk score. The x-axis represents the targeted proportion of individuals at high genetic risk, and the y-axis represents the proportion of individuals with disease onset within 3 years of trial period in placebo (Ctrl) and Treatment (Rx) group. Dashed lines represent treatment effect as the differences between two progression rates.

Disease Trait	Trial Design	Optimized Trial Cost (Fixed trial duration)				Reduced trial duration (Fixed # subjectamples)			
		%Targeted Subjects*	Trial # Subjects	Trial Duration	Total Cost (\$)	%Targeted Subjects*	Trial #Subjects	Trial Duration	Total Cost (\$)
T2D	Genetic Enrichment – 25% heritability	30%	131	3.0 yrs.	3.05M	20%	231	1.9 yrs.	4.51M
T2D	Genetic Enrichment - 50% heritability	25%	98	3.0 yrs.	2.40M	20%	231	1.6 yrs.	4.09M
AMD	Genetic Enrichment - 25% heritability	33%	828	5.0 yrs.	18.5M	20%	1,342	3.1 yrs.	26.6M
AMD	Genetic Enrichment - 50% heritability	27%	629	5.0 yrs.	11.9M	20%	1,342	2.5 yrs.	24.2M
T1D	Genetic Enrichment - 25% heritability	8%	242	4.0 yrs.	16.5M	20%	1,061	1.5 yrs.	27.3M
T1D	Genetic Enrichment - 50% heritability	7%	771	4.0 yrs.	10.7M	20%	1,061	1.1 yrs.	22.7M
MI	Genetic Enrichment - 25% heritability	16%	560	5.0 yrs.	22.4M	20%	1,309	2.6 yrs.	30.9M
MI	Genetic Enrichment - 50% heritability	14%	405	5.0 yrs.	16.8M	20%	1,309	2.1 yrs.	27.2M

Table S1. Sample size, cost, and trial duration of enrichment trials, simulated from hypothetical risk variants explaining 25% and 50% of heritability.

* Cost-optimizing fraction of targeted subjects is selected for determining reduced trial cost, and 20% of targeted subjects is selected for determining reduced trial duration