

Supplementary Note: Fast and accurate imputation of summary statistics enhances evidence of functional enrichment

Correlation between statistics due to Linkage Disequilibrium

We consider two SNPs i and j tested for association in a genome-wide association study over a quantitative trait (similar derivations for case-control traits can be found here^{2,1,3}). Let y_k denote the phenotypic value for individual k and let $g_{i,k}$ denote the genotype (i.e. reference allele count 0,1,2) at SNP i and individual k . Let \vec{y} denote the $(n \times 1)$ vector of phenotypes across the k individuals and let \vec{x}_i denote the $(n \times 1)$ vector of normalized genotypes at SNP i such that $\sum_k \vec{x}_i[k] = 0$ and $\frac{1}{n} \vec{x}_i' \vec{x}_i = 1$. We assume that

$$\vec{y} = \mu + \vec{e}$$

where μ is the mean phenotype value and $\vec{e} \sim \mathcal{N}(0, \sigma^2 I)$, where I is the identity matrix and σ is a scalar.

A standard test for association at SNP i (z-score) is

$$Z_i = \frac{\vec{x}_i' \vec{y}}{\sqrt{n\sigma}}$$

Under null model of no association of SNP i and the phenotype y , Z_i is well approximated at large sample sizes by a normal distribution $\mathcal{N}(0, 1)$. Similarly we can write a test of association at SNP j as

$$Z_j = \frac{\vec{x}_j' \vec{y}}{\sqrt{n\sigma}}$$

Therefore the covariance between Z_i and Z_j is:

$$Cov(Z_i, Z_j) = E[Z_i, Z_j] = E[E[Z_i, Z_j | \vec{x}_i, \vec{x}_j]]$$

with

$$E[Z_i, Z_j | \vec{x}_i, \vec{x}_j] = \frac{\vec{x}_i' \vec{x}_j}{n}$$

and

$$E\left[\frac{\vec{x}_i' \vec{x}_j}{n}\right] = r_{ij}$$

where r_{ij} is the sample correlation coefficient between SNPs i and j .

References

1. Han, B., Kang, H. M., and Eskin, E. (2009). Rapid and accurate multiple testing correction and power estimation for millions of correlated markers. *PLoS genetics*, 5(4), e1000456.

2. Pritchard, J. K. and Przeworski, M. (2001). Linkage disequilibrium in humans: models and data. *The American Journal of Human Genetics*, **69**(1), 1–14.
3. Wen, X. and Stephens, M. (2010). Using linear predictors to impute allele frequencies from summary or pooled genotype data. *Ann. Appl. Stat.*, **4**(3), 1158–1182.

1 Supplementary Tables

Supplementary Table 1: Ratio of observed versus expected number of associations at different thresholds in null data simulations. 2.3M null GWAS were simulated by randomly selecting 1000 cases and 1000 controls from the random panel followed by imputation using the rest of the European haplotypes. Results displayed at various thresholds on confidence of imputed SNPs (r^2_{pred}). Standard Error denoted in parenthesis.

Method	1E-01	1E-02	1E-03	1E-04	1E-5
$r^2_{pred} > 0.3$, 1.9M simulations					
Typed	1.00(0.00)	0.98(0.01)	0.95(0.02)	0.97(0.07)	0.98(0.23)
Beagle	1.00(0.00)	0.98(0.01)	0.97(0.02)	1.05(0.07)	0.88(0.21)
ImpG-Summary ($\lambda=0.000$)	1.05(0.00)	1.26(0.01)	1.97(0.03)	4.61(0.15)	16.66(0.93)
ImpG-Summary ($\lambda=0.050$)	0.94(0.00)	0.93(0.01)	1.04(0.02)	1.37(0.09)	2.67(0.38)
ImpG-Summary ($\lambda=0.100$)	0.92(0.00)	0.86(0.01)	0.85(0.02)	0.94(0.07)	1.37(0.27)
ImpG-Summary ($\lambda=0.150$)	0.88(0.00)	0.80(0.01)	0.76(0.02)	0.74(0.06)	1.13(0.25)
ImpG-SummaryLD	1.00(0.00)	0.99(0.01)	0.97(0.02)	0.98(0.07)	0.98(0.23)
$r^2_{pred} > 0.6$, 1.8M simulations					
Typed	1.00(0.00)	0.98(0.01)	0.96(0.02)	0.95(0.07)	0.97(0.24)
Beagle	1.00(0.00)	0.98(0.01)	0.97(0.02)	1.04(0.08)	0.86(0.22)
ImpG-Summary ($\lambda=0.000$)	1.04(0.00)	1.19(0.01)	1.74(0.03)	3.81(0.15)	13.52(0.88)
ImpG-Summary ($\lambda=0.050$)	0.95(0.00)	0.92(0.01)	0.97(0.02)	1.18(0.08)	2.04(0.35)
ImpG-Summary ($\lambda=0.100$)	0.92(0.00)	0.85(0.01)	0.78(0.02)	0.72(0.07)	0.82(0.23)
ImpG-Summary ($\lambda=0.150$)	0.89(0.00)	0.80(0.01)	0.75(0.02)	0.70(0.07)	1.09(0.27)
ImpG-SummaryLD	1.00(0.00)	0.99(0.01)	0.98(0.02)	1.00(0.08)	0.97(0.24)
$r^2_{pred} > 0.9$, 1.4M simulations					
Typed	1.00(0.00)	0.98(0.01)	0.95(0.03)	0.96(0.08)	0.86(0.25)
Beagle	1.00(0.00)	0.98(0.01)	0.96(0.03)	0.98(0.08)	0.79(0.24)
ImpG-Summary ($\lambda=0.000$)	1.03(0.00)	1.13(0.01)	1.50(0.03)	2.95(0.15)	10.06(0.85)
ImpG-Summary ($\lambda=0.050$)	0.96(0.00)	0.89(0.01)	0.84(0.03)	0.68(0.09)	0.47(0.23)
ImpG-Summary ($\lambda=0.100$)	0.92(0.00)	0.85(0.01)	0.78(0.02)	0.72(0.07)	0.82(0.23)
ImpG-Summary ($\lambda=0.150$)	0.89(0.00)	0.80(0.01)	0.75(0.02)	0.70(0.07)	1.09(0.27)
ImpG-SummaryLD	1.00(0.00)	0.99(0.01)	0.97(0.03)	0.95(0.08)	0.86(0.25)

Supplementary Table 2: Ratio of observed versus expected number of associations at different thresholds in null data simulations. 2.3M null GWAS were simulated by randomly selecting 1000 cases and 1000 controls from the GBR panel followed by imputation using the rest of the European haplotypes. Results displayed at confidently imputed SNPs ($r^2_{pred} > 0.6$). Standard Error denoted in parenthesis.

Method	1E-01	1E-02	1E-03	1E-04	1E-05
<i>r</i> ² _{pred} > 0.3, 1.9M simulations					
Typed	1.00(0.00)	1.00(0.01)	0.97(0.02)	0.95(0.07)	0.57(0.17)
Beagle	1.01(0.00)	0.99(0.01)	0.97(0.02)	0.96(0.07)	0.52(0.16)
ImpG-Summary ($\lambda=0.000$)	1.08(0.00)	1.33(0.01)	2.16(0.03)	5.15(0.16)	17.31(0.95)
ImpG-Summary ($\lambda=0.050$)	0.95(0.00)	0.96(0.01)	1.08(0.02)	1.48(0.09)	3.38(0.43)
ImpG-Summary ($\lambda=0.100$)	0.91(0.00)	0.87(0.01)	0.94(0.02)	1.21(0.08)	1.88(0.32)
ImpG-SummaryLD	1.00(0.00)	0.99(0.01)	0.97(0.02)	0.95(0.07)	0.73(0.19)
<i>r</i> ² _{pred} > 0.6, 1.7M simulations					
Typed	1.00(0.00)	1.00(0.01)	0.97(0.02)	0.95(0.07)	0.57(0.18)
Beagle	1.01(0.00)	1.00(0.01)	0.97(0.02)	0.96(0.07)	0.57(0.18)
ImpG-Summary ($\lambda=0.000$)	1.06(0.00)	1.25(0.01)	1.92(0.03)	4.24(0.16)	12.73(0.85)
ImpG-Summary ($\lambda=0.050$)	0.95(0.00)	0.93(0.01)	1.00(0.02)	1.29(0.09)	2.71(0.40)
ImpG-Summary ($\lambda=0.100$)	0.92(0.00)	0.86(0.01)	0.90(0.02)	1.07(0.08)	1.60(0.32)
ImpG-SummaryLD	1.01(0.00)	0.99(0.01)	0.97(0.02)	0.94(0.07)	0.69(0.20)
<i>r</i> ² _{pred} > 0.9, 1.4M simulations					
Typed	1.01(0.00)	1.00(0.01)	0.97(0.03)	0.97(0.08)	0.64(0.21)
Beagle	1.01(0.00)	1.00(0.01)	0.97(0.03)	0.98(0.08)	0.64(0.21)
ImpG-Summary ($\lambda=0.000$)	1.04(0.00)	1.17(0.01)	1.67(0.03)	3.36(0.16)	9.95(0.84)
ImpG-Summary ($\lambda=0.050$)	0.95(0.00)	0.89(0.01)	0.87(0.03)	0.91(0.10)	1.05(0.35)
ImpG-Summary ($\lambda=0.100$)	0.92(0.00)	0.86(0.01)	0.90(0.02)	1.07(0.08)	1.60(0.32)
ImpG-SummaryLD	1.01(0.00)	0.99(0.01)	0.99(0.03)	0.99(0.08)	0.79(0.24)

Supplementary Table 3: Effective sample size decrease (ratio of imputed χ^2 to typed χ^2) in simulations at odds ratio 1.5. Results displayed at all imputed SNPs.

Method	All SNPs	> 5% SNPs	1 – 5% SNPs
ImpG-Summary ($\lambda=0.000$)	0.875	0.889	0.659
ImpG-Summary ($\lambda=0.050$)	0.842	0.859	0.572
ImpG-Summary ($\lambda=0.100$)	0.823	0.841	0.539
ImpG-Summary ($\lambda=0.150$)	0.808	0.826	0.518

Supplementary Table 4: WTCCC data set summary. After data merging, 459,446 SNPs were typed for each phenotype; 133,893 were removed in the QC step resulting in 325,553 SNPs used in imputation. For imputed data we applied the standard filtering based on imputation accuracy; for HMM we also removed SNPs that had more than 5% of imputed calls missing at a posterior confidence threshold of 0.9.

Phenotype	Sample Size	Imputed SNPs (HMM)	Imputed SNPs (MVN)	Intersection HMM+MVN
		$r^2_{hat} > 0.6$	$r^2_{pred} > 0.6$	
BD	4806	4,790,856	6,468,537	4,384,152
CAD	4864	4,790,049	6,468,961	4,384,110
CD	4686	4,791,672	6,470,920	4,385,247
HT	4890	4,790,303	6,468,101	4,383,711
RA	4798	4,791,130	6,469,116	4,384,220
T1D	4901	4,791,957	6,469,880	4,384,948
T2D	4862	4,792,723	6,470,571	4,385,825

Supplementary Table 5: Association statistics (z -scores) at imputed data using HMM or ImpG-Summary across the WTCCC and B58C data sets.

Phenotype	RsID	Chr	HMM-Imputation	ImpG-Summary	r^2_{hat}	r^2_{pred}
BD (WTCCC)	rs4650608	1	1.49	1.44	1.00	0.92
BD (WTCCC)	rs2271893	2	3.02	3.02	0.97	0.90
BD (WTCCC)	rs2727943	3	-0.53	-0.48	1.00	0.96
BD (WTCCC)	rs10994336	10	-2.89	-2.50	0.97	0.89
BD (WTCCC)	rs4948418	10	-2.85	-2.34	0.94	0.85
BD (WTCCC)	rs12576775	11	-3.31	-3.58	1.00	0.93
BD (WTCCC)	rs4765913	12	2.67	3.04	0.96	0.88
BD (WTCCC)	rs420259	16	3.65	3.40	1.00	0.92
BD (WTCCC)	rs1064395	19	-1.91	-1.79	1.00	0.93
CAD (WTCCC)	rs17114036	1	2.65	1.94	0.98	0.90
CAD (WTCCC)	rs599839	1	-4.29	-4.01	1.00	0.91
CAD (WTCCC)	rs17465637	1	-4.31	-4.30	1.00	0.97
CAD (WTCCC)	rs2123536	2	2.19	1.92	0.95	0.85
CAD (WTCCC)	rs6725887	2	-1.72	-1.67	1.00	0.97
CAD (WTCCC)	rs2306374	3	-2.37	-2.52	1.00	0.96
CAD (WTCCC)	rs9818870	3	-2.49	-2.48	1.00	0.97
CAD (WTCCC)	rs1842896	4	-0.30	-0.31	0.99	0.95
CAD (WTCCC)	rs12526453	6	1.66	1.79	1.00	0.95
CAD (WTCCC)	rs17609940	6	1.40	1.34	1.00	0.95
CAD (WTCCC)	rs6922269	6	-4.55	-3.98	1.00	0.96
CAD (WTCCC)	rs6601299	8	-0.12	0.48	1.00	0.88
CAD (WTCCC)	rs7865618	9	-6.03	-6.21	1.00	0.97
CAD (WTCCC)	rs10757274	9	-7.22	-7.38	1.00	0.97
CAD (WTCCC)	rs4977574	9	-7.23	-7.35	1.00	0.97
CAD (WTCCC)	rs944797	9	-7.09	-7.26	0.98	0.94
CAD (WTCCC)	rs1333049	9	-7.70	-7.49	1.00	0.95
CAD (WTCCC)	rs3739998	10	-2.73	-2.71	1.00	0.94
CAD (WTCCC)	rs1746048	10	3.06	2.98	1.00	0.98
CAD (WTCCC)	rs974819	11	0.43	0.70	0.98	0.89
CAD (WTCCC)	rs964184	11	2.41	2.27	0.99	0.93
CAD (WTCCC)	rs7136259	12	-0.48	-0.37	1.00	0.95
CAD (WTCCC)	rs4773144	13	-1.40	-1.49	0.98	0.84
CAD (WTCCC)	rs1994016	15	3.84	3.80	1.00	0.92
CAD (WTCCC)	rs4380028	15	3.47	3.32	0.98	0.92
CAD (WTCCC)	rs3729639	16	0.32	0.25	1.00	0.97
CAD (WTCCC)	rs1231206	17	-2.10	-2.19	0.99	0.95
CAD (WTCCC)	rs216172	17	-2.06	-2.14	0.99	0.96
CAD (WTCCC)	rs46522	17	-2.94	-2.91	1.00	0.97
CAD (WTCCC)	rs11669133	19	-0.55	-0.57	1.00	0.96
CAD (WTCCC)	rs1122608	19	3.07	2.94	1.00	0.96
CAD (WTCCC)	rs9982601	21	-3.18	-2.94	0.97	0.80
CD (WTCCC)	rs2797685	1	-2.86	-2.64	1.00	0.94
CD (WTCCC)	rs11805303	1	-7.04	-6.80	1.00	0.93

Phenotype	RsID	Chr	HMM-Imputation	ImpG-Summary	r^2_{hat}	r^2_{pred}
CD (WTCCC)	rs7517847	1	7.93	7.14	0.98	0.86
CD (WTCCC)	rs11465804	1	8.22	6.81	0.98	0.67
CD (WTCCC)	rs2476601	1	-3.33	-3.35	0.99	0.87
CD (WTCCC)	rs2274910	1	-3.59	-3.19	0.98	0.87
CD (WTCCC)	rs9286879	1	-3.88	-3.74	1.00	0.96
CD (WTCCC)	rs10801047	1	3.81	3.55	1.00	0.93
CD (WTCCC)	rs1998598	1	-2.15	-2.45	0.98	0.76
CD (WTCCC)	rs11584383	1	3.97	4.10	1.00	0.95
CD (WTCCC)	rs3024505	1	-0.74	-0.63	1.00	0.92
CD (WTCCC)	rs780093	2	4.32	4.17	1.00	0.89
CD (WTCCC)	rs10495903	2	-2.65	-2.53	1.00	0.97
CD (WTCCC)	rs10181042	2	-3.35	-3.31	1.00	0.93
CD (WTCCC)	rs2058660	2	3.33	3.23	1.00	0.98
CD (WTCCC)	rs6738825	2	1.07	0.92	1.00	0.98
CD (WTCCC)	rs7423615	2	-4.00	-4.03	0.99	0.96
CD (WTCCC)	rs10210302	2	-7.47	-6.92	1.00	0.93
CD (WTCCC)	rs2241880	2	-7.42	-6.86	1.00	0.93
CD (WTCCC)	rs3792109	2	-7.41	-6.96	0.98	0.90
CD (WTCCC)	rs13073817	3	-2.54	-2.64	0.98	0.91
CD (WTCCC)	rs9858542	3	-4.85	-4.75	1.00	0.96
CD (WTCCC)	rs4613763	5	-7.37	-7.63	1.00	0.95
CD (WTCCC)	rs17234657	5	-7.46	-7.63	1.00	0.95
CD (WTCCC)	rs11742570	5	-7.41	-7.17	1.00	0.97
CD (WTCCC)	rs1373692	5	-7.07	-7.09	1.00	0.96
CD (WTCCC)	rs9292777	5	-7.03	-7.10	1.00	0.97
CD (WTCCC)	rs7702331	5	1.77	1.34	0.99	0.87
CD (WTCCC)	rs2549794	5	2.86	2.73	1.00	0.97
CD (WTCCC)	rs7705924	5	0.59	0.22	0.97	0.88
CD (WTCCC)	rs3091338	5	-3.48	-4.04	0.99	0.91
CD (WTCCC)	rs2188962	5	-5.47	-5.64	0.99	0.92
CD (WTCCC)	rs12521868	5	-5.48	-5.67	0.99	0.93
CD (WTCCC)	rs11167764	5	-3.55	-3.35	0.98	0.92
CD (WTCCC)	rs7714584	5	-5.20	-5.19	1.00	0.98
CD (WTCCC)	rs10045431	5	-4.59	-4.57	0.97	0.79
CD (WTCCC)	rs359457	5	-2.60	-2.14	0.99	0.94
CD (WTCCC)	rs17309827	6	4.10	3.92	1.00	0.97
CD (WTCCC)	rs6908425	6	-4.53	-4.39	1.00	0.95
CD (WTCCC)	rs2301436	6	-3.05	-2.90	1.00	0.97
CD (WTCCC)	rs12677663	8	-1.43	-1.16	1.00	0.92
CD (WTCCC)	rs1551398	8	-3.93	-3.89	1.00	0.93
CD (WTCCC)	rs6651252	8	2.87	2.91	1.00	0.98
CD (WTCCC)	rs4263839	9	-3.93	-3.86	1.00	0.95
CD (WTCCC)	rs12722489	10	2.14	1.89	1.00	0.93
CD (WTCCC)	rs1819658	10	1.60	1.62	1.00	0.95
CD (WTCCC)	rs7076156	10	-2.55	-2.71	1.00	0.97
CD (WTCCC)	rs10761659	10	-5.17	-5.20	1.00	0.93
CD (WTCCC)	rs224136	10	4.05	4.08	1.00	0.95

Phenotype	RsID	Chr	HMM-Imputation	ImpG-Summary	r^2_{hat}	r^2_{pred}
CD (WTCCC)	rs4409764	10	5.68	5.66	0.99	0.98
CD (WTCCC)	rs10883365	10	5.64	5.62	1.00	0.98
CD (WTCCC)	rs11190140	10	5.68	5.60	1.00	0.98
CD (WTCCC)	rs102275	11	-2.20	-2.06	0.98	0.92
CD (WTCCC)	rs7927894	11	-3.29	-3.29	1.00	0.93
CD (WTCCC)	rs11175593	12	-1.98	-2.18	1.00	0.95
CD (WTCCC)	rs11564258	12	-2.04	-2.12	1.00	0.98
CD (WTCCC)	rs2062305	13	2.54	2.67	1.00	0.94
CD (WTCCC)	rs8005161	14	-3.94	-3.56	1.00	0.84
CD (WTCCC)	rs17221417	16	-6.82	-6.75	1.00	0.95
CD (WTCCC)	rs5743289	16	-7.88	-7.95	0.97	0.68
CD (WTCCC)	rs3091315	17	2.71	1.95	0.98	0.92
CD (WTCCC)	rs3091316	17	2.70	1.95	0.98	0.92
CD (WTCCC)	rs2872507	17	-2.87	-2.68	1.00	0.97
CD (WTCCC)	rs744166	17	4.36	4.42	1.00	0.94
CD (WTCCC)	rs2542151	18	5.39	5.64	1.00	0.94
CD (WTCCC)	rs4809330	20	-4.15	-4.21	1.00	0.77
CD (WTCCC)	rs1736135	21	2.96	2.78	1.00	0.98
CD (WTCCC)	rs762421	21	3.35	3.29	1.00	0.98
CD (WTCCC)	rs181359	22	-2.22	-2.03	1.00	0.97
CD (WTCCC)	rs713875	22	2.70	2.82	0.98	0.89
HT (WTCCC)	rs1173771	5	-2.09	-1.83	0.99	0.93
HT (WTCCC)	rs1799945	6	-2.57	-2.23	0.99	0.87
HT (WTCCC)	rs932764	10	-2.01	-2.11	0.99	0.94
HT (WTCCC)	rs633185	11	-2.60	-2.12	0.99	0.90
HT (WTCCC)	rs2681472	12	2.18	2.27	0.99	0.93
HT (WTCCC)	rs13333226	16	0.73	0.80	1.00	0.91
HT (WTCCC)	rs6015450	20	-2.06	-2.15	0.97	0.92
RA (WTCCC)	rs6679677	1	-10.59	-10.23	1.00	0.92
RA (WTCCC)	rs2476601	1	10.56	10.17	0.99	0.87
RA (WTCCC)	rs13017599	2	0.38	0.10	0.98	0.85
RA (WTCCC)	rs11900673	2	-0.75	-0.85	0.96	0.91
RA (WTCCC)	rs934734	2	1.58	1.64	1.00	0.97
RA (WTCCC)	rs11676922	2	3.53	3.55	0.98	0.93
RA (WTCCC)	rs231735	2	-0.96	-0.92	0.99	0.97
RA (WTCCC)	rs3087243	2	1.75	1.77	1.00	0.96
RA (WTCCC)	rs874040	4	-3.97	-3.97	0.99	0.90
RA (WTCCC)	rs657075	5	-0.93	-1.33	0.98	0.90
RA (WTCCC)	rs12529514	6	-1.38	-1.54	0.91	0.52
RA (WTCCC)	rs615672	6	10.69	10.19	1.00	0.91
RA (WTCCC)	rs10499194	6	2.28	2.44	0.98	0.93
RA (WTCCC)	rs6920220	6	-4.56	-4.37	1.00	0.92
RA (WTCCC)	rs10488631	7	-2.20	-1.96	0.99	0.76
RA (WTCCC)	rs2736340	8	-2.66	-2.43	1.00	0.96
RA (WTCCC)	rs2812378	9	3.37	3.20	1.00	0.92
RA (WTCCC)	rs881375	9	-0.17	-0.25	1.00	0.98
RA (WTCCC)	rs3761847	9	-0.44	-0.28	1.00	0.96

Phenotype	RsID	Chr	HMM-Imputation	ImpG-Summary	r^2_{hat}	r^2_{pred}
RA (WTCCC)	rs706778	10	-4.10	-4.02	0.99	0.89
RA (WTCCC)	rs2847297	18	-1.58	-1.51	1.00	0.94
RA (WTCCC)	rs4810485	20	-1.74	-1.61	1.00	0.95
T1D (WTCCC)	rs6679677	1	-10.46	-10.10	1.00	0.92
T1D (WTCCC)	rs2476601	1	10.66	10.09	0.99	0.87
T1D (WTCCC)	rs3024505	1	2.44	2.28	1.00	0.92
T1D (WTCCC)	rs478222	2	2.42	2.34	0.99	0.94
T1D (WTCCC)	rs3087243	2	4.13	4.20	1.00	0.96
T1D (WTCCC)	rs10517086	4	-2.98	-3.17	0.98	0.88
T1D (WTCCC)	rs9272346	6	-24.68	-24.36	1.00	0.91
T1D (WTCCC)	rs11755527	6	-2.72	-2.93	1.00	0.96
T1D (WTCCC)	rs9388489	6	-2.59	-2.60	1.00	0.96
T1D (WTCCC)	rs7804356	7	0.72	0.62	1.00	0.97
T1D (WTCCC)	rs4948088	7	-2.70	-2.61	1.00	0.91
T1D (WTCCC)	rs7020673	9	-3.12	-3.00	1.00	0.97
T1D (WTCCC)	rs61839660	10	5.43	5.58	0.97	0.75
T1D (WTCCC)	rs12251307	10	4.15	4.16	1.00	0.92
T1D (WTCCC)	rs947474	10	-3.50	-2.94	1.00	0.94
T1D (WTCCC)	rs10509540	10	1.85	2.33	0.98	0.89
T1D (WTCCC)	rs11171739	12	6.81	6.56	1.00	0.94
T1D (WTCCC)	rs2292239	12	6.26	6.16	1.00	0.94
T1D (WTCCC)	rs17696736	12	-7.92	-7.77	1.00	0.92
T1D (WTCCC)	rs539514	13	-2.23	-2.28	0.99	0.87
T1D (WTCCC)	rs1465788	14	-2.27	-2.00	1.00	0.95
T1D (WTCCC)	rs4900384	14	-2.20	-2.04	1.00	0.96
T1D (WTCCC)	rs3825932	15	-3.34	-3.11	1.00	0.92
T1D (WTCCC)	rs12708716	16	5.32	5.35	1.00	0.96
T1D (WTCCC)	rs2903692	16	5.17	5.03	0.97	0.91
T1D (WTCCC)	rs4788084	16	2.71	2.38	0.99	0.91
T1D (WTCCC)	rs2290400	17	-1.66	-1.60	0.99	0.94
T1D (WTCCC)	rs7221109	17	-4.22	-4.00	1.00	0.94
T1D (WTCCC)	rs2542151	18	4.63	4.72	1.00	0.94
T1D (WTCCC)	rs1893217	18	-4.74	-4.62	1.00	0.89
T1D (WTCCC)	rs425105	19	2.12	2.20	0.96	0.83
T1D (WTCCC)	rs2281808	20	-2.37	-2.22	1.00	0.96
T1D (WTCCC)	rs11203203	21	-3.07	-3.08	1.00	0.94
T1D (WTCCC)	rs9976767	21	-3.02	-3.04	1.00	0.94
T1D (WTCCC)	rs5753037	22	-2.18	-2.21	0.99	0.93
T1D (WTCCC)	rs229541	22	-3.40	-3.20	1.00	0.96
T2D (WTCCC)	rs7578597	2	2.23	2.12	1.00	0.98
T2D (WTCCC)	rs243021	2	-4.03	-3.80	0.99	0.93
T2D (WTCCC)	rs7593730	2	-4.46	-4.47	1.00	0.98
T2D (WTCCC)	rs4607103	3	2.59	2.51	1.00	0.95
T2D (WTCCC)	rs4402960	3	-3.11	-3.08	1.00	0.97
T2D (WTCCC)	rs1470579	3	-3.09	-3.08	1.00	0.97
T2D (WTCCC)	rs6769511	3	-3.03	-3.08	1.00	0.97
T2D (WTCCC)	rs7656416	4	1.58	2.23	0.97	0.67

Phenotype	RsID	Chr	HMM-Imputation	ImpG-Summary	r^2_{hat}	r^2_{pred}
T2D (WTCCC)	rs6815464	4	1.82	1.89	1.00	0.94
T2D (WTCCC)	rs1801214	4	-2.05	-1.88	0.99	0.96
T2D (WTCCC)	rs4712523	6	-4.23	-4.15	0.99	0.97
T2D (WTCCC)	rs4712524	6	-4.27	-4.05	0.99	0.98
T2D (WTCCC)	rs10946398	6	-4.13	-4.05	1.00	0.98
T2D (WTCCC)	rs7754840	6	-4.08	-4.05	1.00	0.98
T2D (WTCCC)	rs7756992	6	-5.39	-4.73	0.97	0.89
T2D (WTCCC)	rs7766070	6	-5.04	-4.64	0.97	0.89
T2D (WTCCC)	rs9470794	6	-0.01	0.12	0.99	0.94
T2D (WTCCC)	rs1535500	6	-1.16	-0.76	0.99	0.69
T2D (WTCCC)	rs1048886	6	0.46	0.39	1.00	0.96
T2D (WTCCC)	rs864745	7	3.79	3.73	1.00	0.95
T2D (WTCCC)	rs849134	7	3.91	3.73	0.99	0.94
T2D (WTCCC)	rs6467136	7	0.48	0.54	1.00	0.96
T2D (WTCCC)	rs972283	7	-2.47	-2.56	0.98	0.95
T2D (WTCCC)	rs515071	8	-2.46	-2.54	1.00	0.95
T2D (WTCCC)	rs896854	8	2.58	2.51	0.99	0.95
T2D (WTCCC)	rs7041847	9	1.39	1.32	0.99	0.96
T2D (WTCCC)	rs2383208	9	3.17	3.13	1.00	0.95
T2D (WTCCC)	rs10965250	9	3.40	3.21	0.99	0.95
T2D (WTCCC)	rs10811661	9	3.37	3.21	1.00	0.95
T2D (WTCCC)	rs1333051	9	3.29	3.28	1.00	0.94
T2D (WTCCC)	rs13292136	9	1.82	0.83	0.98	0.77
T2D (WTCCC)	rs10906115	10	1.51	1.36	1.00	0.94
T2D (WTCCC)	rs1802295	10	-1.93	-1.87	1.00	0.93
T2D (WTCCC)	rs1111875	10	4.62	3.90	0.98	0.83
T2D (WTCCC)	rs7901695	10	-7.22	-7.24	1.00	0.96
T2D (WTCCC)	rs4506565	10	-7.17	-7.18	1.00	0.97
T2D (WTCCC)	rs7903146	10	-7.25	-7.37	0.98	0.92
T2D (WTCCC)	rs2237892	11	1.88	1.95	0.94	0.64
T2D (WTCCC)	rs5215	11	3.19	3.18	1.00	0.94
T2D (WTCCC)	rs5219	11	3.27	3.18	0.99	0.94
T2D (WTCCC)	rs1552224	11	1.26	0.84	0.96	0.75
T2D (WTCCC)	rs7961581	12	4.67	4.65	1.00	0.93
T2D (WTCCC)	rs1359790	13	2.53	2.52	1.00	0.95
T2D (WTCCC)	rs7172432	15	0.47	0.59	0.99	0.87
T2D (WTCCC)	rs7178572	15	-1.72	-1.52	0.99	0.94
T2D (WTCCC)	rs2028299	15	0.74	0.98	0.99	0.93
T2D (WTCCC)	rs8042680	15	-1.67	-1.71	0.99	0.93
T2D (WTCCC)	rs8050136	16	-5.66	-5.36	1.00	0.98
T2D (WTCCC)	rs9939609	16	-5.44	-5.34	1.00	0.98
T2D (WTCCC)	rs3786897	19	0.39	0.18	0.98	0.78
T2D (WTCCC)	rs6017317	20	-0.72	-0.84	0.97	0.86
Height(B58C)	rs425277	1	-1.03	-0.92	0.73	0.96
Height(B58C)	rs2284746	1	-2.19	-2.30	0.67	0.91
Height(B58C)	rs1738475	1	0.14	0.04	0.82	0.97
Height(B58C)	rs4601530	1	1.52	1.76	0.85	0.95

Phenotype	RsID	Chr	HMM-Imputation	ImpG-Summary	r^2_{hat}	r^2_{pred}
Height(B58C)	rs7532866	1	2.09	2.02	0.81	0.93
Height(B58C)	rs2154319	1	-3.42	-3.67	0.76	0.91
Height(B58C)	rs17391694	1	-2.12	-1.93	0.87	0.92
Height(B58C)	rs6699417	1	-1.90	-2.01	0.88	0.98
Height(B58C)	rs10874746	1	-0.15	-0.26	0.70	0.88
Height(B58C)	rs9428104	1	-2.53	-2.03	0.66	0.94
Height(B58C)	rs11205277	1	-2.73	-2.71	0.93	0.91
Height(B58C)	rs17346452	1	-2.32	-2.32	0.75	0.95
Height(B58C)	rs1325598	1	-1.36	-0.90	0.83	0.96
Height(B58C)	rs1046934	1	-2.62	-2.63	0.87	0.97
Height(B58C)	rs10863936	1	2.07	2.09	0.86	0.97
Height(B58C)	rs6684205	1	-2.76	-2.88	0.80	0.98
Height(B58C)	rs11118346	1	0.84	0.81	0.78	0.96
Height(B58C)	rs10799445	1	-0.02	-0.30	0.90	0.96
Height(B58C)	rs4665736	2	-3.15	-2.89	0.66	0.94
Height(B58C)	rs6714546	2	-3.78	-3.19	0.74	0.92
Height(B58C)	rs17511102	2	-2.11	-1.32	0.26	0.53
Height(B58C)	rs2341459	2	2.31	2.37	0.92	0.97
Height(B58C)	rs12474201	2	-0.06	0.09	0.70	0.95
Height(B58C)	rs3791675	2	2.77	3.15	0.71	0.94
Height(B58C)	rs11684404	2	0.14	-0.25	0.68	0.93
Height(B58C)	rs7567288	2	-0.13	-0.91	0.57	0.91
Height(B58C)	rs7567851	2	-1.21	-1.14	0.79	0.95
Height(B58C)	rs1351164	2	2.73	2.78	0.63	0.94
Height(B58C)	rs12470505	2	-0.43	-0.68	0.66	0.94
Height(B58C)	rs2629046	2	-0.89	-1.38	0.78	0.94
Height(B58C)	rs2580816	2	1.60	1.66	0.86	0.95
Height(B58C)	rs12694997	2	0.61	0.61	0.94	0.96
Height(B58C)	rs2597513	3	1.07	1.33	0.89	0.94
Height(B58C)	rs13088462	3	-0.69	-1.39	0.23	0.91
Height(B58C)	rs2336725	3	1.63	1.35	0.86	0.98
Height(B58C)	rs9835332	3	1.37	1.49	0.79	0.96
Height(B58C)	rs17806888	3	1.10	1.48	0.63	0.88
Height(B58C)	rs9863706	3	3.23	3.20	0.59	0.90
Height(B58C)	rs6439167	3	-1.13	-1.09	0.83	0.96
Height(B58C)	rs9844666	3	2.12	1.92	0.95	0.95
Height(B58C)	rs724016	3	-3.40	-3.59	0.83	0.94
Height(B58C)	rs572169	3	-2.62	-3.35	0.86	0.96
Height(B58C)	rs720390	3	0.09	0.29	0.70	0.91
Height(B58C)	rs2247341	4	-1.27	-1.14	0.76	0.93
Height(B58C)	rs6449353	4	4.48	4.48	0.73	0.95
Height(B58C)	rs17081935	4	-1.39	-0.78	0.58	0.93
Height(B58C)	rs7697556	4	1.10	1.37	0.73	0.93
Height(B58C)	rs788867	4	-5.13	-5.39	0.77	0.95
Height(B58C)	rs10010325	4	-2.80	-2.74	0.62	0.96
Height(B58C)	rs7689420	4	-1.46	-1.78	0.74	0.94
Height(B58C)	rs955748	4	-0.81	-0.92	0.96	0.96

Phenotype	RsID	Chr	HMM-Imputation	ImpG-Summary	r^2_{hat}	r^2_{pred}
Height(B58C)	rs1173727	5	3.41	3.43	0.82	0.95
Height(B58C)	rs11958779	5	2.37	2.52	0.77	0.94
Height(B58C)	rs10037512	5	2.29	2.73	0.75	0.94
Height(B58C)	rs13177718	5	-0.09	0.36	0.94	0.94
Height(B58C)	rs1582931	5	1.58	2.35	0.57	0.90
Height(B58C)	rs274546	5	-2.08	-2.18	0.69	0.98
Height(B58C)	rs526896	5	0.59	-0.45	0.56	0.87
Height(B58C)	rs4282339	5	1.70	1.93	0.85	0.96
Height(B58C)	rs12153391	5	2.76	2.63	0.59	0.83
Height(B58C)	rs889014	5	2.96	3.44	0.72	0.95
Height(B58C)	rs422421	5	-1.53	-0.66	0.80	0.86
Height(B58C)	rs6879260	5	-2.46	-2.60	0.63	0.89
Height(B58C)	rs3812163	6	-2.77	-2.47	0.74	0.94
Height(B58C)	rs1047014	6	-1.96	-1.75	0.94	0.93
Height(B58C)	rs806794	6	1.53	1.90	0.69	0.91
Height(B58C)	rs3129109	6	-1.20	-1.28	0.00	0.07
Height(B58C)	rs2256183	6	3.33	3.71	0.00	0.44
Height(B58C)	rs2780226	6	2.74	2.29	0.76	0.63
Height(B58C)	rs9472414	6	1.38	1.74	0.80	0.97
Height(B58C)	rs9360921	6	-0.98	-1.16	0.83	0.95
Height(B58C)	rs310405	6	-1.23	-1.50	0.85	0.94
Height(B58C)	rs7759938	6	2.14	2.12	0.69	0.97
Height(B58C)	rs1046943	6	-0.15	-0.21	0.79	0.96
Height(B58C)	rs961764	6	-2.52	-2.11	0.75	0.97
Height(B58C)	rs1490384	6	-4.23	-4.39	0.72	0.94
Height(B58C)	rs6569648	6	1.89	2.15	0.92	0.96
Height(B58C)	rs7763064	6	2.43	2.75	0.69	0.96
Height(B58C)	rs543650	6	-3.42	-3.53	0.88	0.94
Height(B58C)	rs9456307	6	1.75	2.20	0.28	0.80
Height(B58C)	rs798489	7	2.58	2.91	0.55	0.96
Height(B58C)	rs4470914	7	-0.89	-0.63	0.78	0.96
Height(B58C)	rs12534093	7	0.60	0.69	0.71	0.93
Height(B58C)	rs1708299	7	3.32	3.05	0.78	0.95
Height(B58C)	rs6959212	7	-1.63	-1.40	0.73	0.98
Height(B58C)	rs42235	7	-2.55	-2.47	0.74	0.91
Height(B58C)	rs822552	7	-0.14	-0.19	0.43	0.83
Height(B58C)	rs2110001	7	-0.32	-0.38	0.68	0.94
Height(B58C)	rs1013209	8	0.68	0.01	0.77	0.93
Height(B58C)	rs7460090	8	3.67	3.50	0.64	0.90
Height(B58C)	rs6473015	8	-3.20	-3.04	0.97	0.96
Height(B58C)	rs6470764	8	4.57	4.49	0.80	0.97
Height(B58C)	rs12680655	8	4.03	3.52	0.74	0.98
Height(B58C)	rs7864648	9	-0.93	-0.71	0.88	0.94
Height(B58C)	rs11144688	9	2.11	2.67	0.34	0.63
Height(B58C)	rs7853377	9	-1.24	-1.84	0.54	0.90
Height(B58C)	rs8181166	9	-2.88	-2.63	0.71	0.92
Height(B58C)	rs2778031	9	1.08	1.81	0.78	0.95

Phenotype	RsID	Chr	HMM-Imputation	ImpG-Summary	r^2_{hat}	r^2_{pred}
Height(B58C)	rs9969804	9	2.19	2.32	0.87	0.97
Height(B58C)	rs1257763	9	1.83	2.29	0.29	0.63
Height(B58C)	rs473902	9	2.51	0.44	0.15	0.41
Height(B58C)	rs7027110	9	-3.03	-2.92	0.87	0.97
Height(B58C)	rs1468758	9	2.36	2.00	0.53	0.92
Height(B58C)	rs751543	9	-2.19	-1.94	0.49	0.72
Height(B58C)	rs7466269	9	1.16	1.13	0.88	0.96
Height(B58C)	rs7849585	9	-1.00	-0.91	0.70	0.89
Height(B58C)	rs7909670	10	1.29	1.93	0.72	0.96
Height(B58C)	rs2145998	10	1.56	1.55	0.76	0.96
Height(B58C)	rs11599750	10	1.10	1.38	0.85	0.95
Height(B58C)	rs2237886	11	-1.26	-1.40	0.96	0.92
Height(B58C)	rs7926971	11	-1.38	-1.09	0.76	0.96
Height(B58C)	rs1330	11	-1.99	-1.95	0.86	0.95
Height(B58C)	rs10838801	11	1.11	1.50	0.70	0.93
Height(B58C)	rs1814175	11	1.04	0.69	0.61	0.94
Height(B58C)	rs3782089	11	0.17	0.51	0.52	0.79
Height(B58C)	rs7112925	11	0.91	0.97	0.98	0.92
Height(B58C)	rs634552	11	2.08	2.01	0.75	0.94
Height(B58C)	rs494459	11	-0.19	-0.45	0.82	0.96
Height(B58C)	rs654723	11	-0.57	-0.01	0.69	0.90
Height(B58C)	rs2856321	12	1.99	2.09	0.85	0.97
Height(B58C)	rs10770705	12	1.86	1.71	0.86	0.98
Height(B58C)	rs2638953	12	-1.60	-2.50	0.76	0.98
Height(B58C)	rs2066807	12	-0.12	-0.57	0.71	0.97
Height(B58C)	rs1351394	12	3.30	3.17	0.74	0.94
Height(B58C)	rs10748128	12	-2.99	-3.06	0.82	0.94
Height(B58C)	rs11107116	12	-2.59	-2.66	0.88	0.96
Height(B58C)	rs7971536	12	2.31	2.37	0.72	0.88
Height(B58C)	rs11830103	12	-1.51	-1.55	0.55	0.92
Height(B58C)	rs7332115	13	-2.02	-1.91	0.88	0.97
Height(B58C)	rs3118905	13	3.30	3.97	0.81	0.95
Height(B58C)	rs7319045	13	1.55	1.66	0.72	0.92
Height(B58C)	rs1950500	14	2.67	2.51	0.96	0.95
Height(B58C)	rs2093210	14	2.30	1.93	0.65	0.93
Height(B58C)	rs1570106	14	-0.09	-0.71	0.78	0.96
Height(B58C)	rs862034	14	-2.22	-2.25	0.73	0.94
Height(B58C)	rs7155279	14	3.19	2.71	0.67	0.96
Height(B58C)	rs16964211	15	2.23	2.18	0.83	0.96
Height(B58C)	rs7178424	15	0.59	0.50	0.89	0.97
Height(B58C)	rs10152591	15	1.60	1.73	0.94	0.96
Height(B58C)	rs12902421	15	-0.25	-1.00	0.44	0.67
Height(B58C)	rs5742915	15	-0.90	-0.56	0.90	0.92
Height(B58C)	rs11259936	15	-3.58	-3.23	0.83	0.98
Height(B58C)	rs16942341	15	0.36	2.09	0.30	0.55
Height(B58C)	rs2871865	15	3.16	3.33	0.47	0.85
Height(B58C)	rs4965598	15	3.27	3.34	0.73	0.93

Phenotype	RsID	Chr	HMM-Imputation	ImpG-Summary	r^2_{hat}	r^2_{pred}
Height(B58C)	rs11648796	16	-0.20	-0.29	0.78	0.87
Height(B58C)	rs26868	16	-1.03	-1.25	0.76	0.92
Height(B58C)	rs1659127	16	-3.37	-3.01	0.72	0.86
Height(B58C)	rs8052560	16	-0.69	-1.71	0.50	0.68
Height(B58C)	rs4640244	17	1.44	1.32	0.86	0.92
Height(B58C)	rs3110496	17	-1.54	-1.74	0.85	0.93
Height(B58C)	rs3764419	17	0.57	1.02	0.55	0.93
Height(B58C)	rs17780086	17	0.70	0.57	0.37	0.97
Height(B58C)	rs1043515	17	-3.03	-2.61	0.74	0.93
Height(B58C)	rs4986172	17	2.76	2.79	0.90	0.94
Height(B58C)	rs2072153	17	-1.33	-1.19	0.66	0.96
Height(B58C)	rs4605213	17	-1.11	-1.07	0.56	0.87
Height(B58C)	rs227724	17	-1.84	-1.56	0.85	0.92
Height(B58C)	rs2079795	17	1.21	0.96	0.79	0.95
Height(B58C)	rs2665838	17	-1.54	-2.12	0.30	0.79
Height(B58C)	rs11867479	17	-0.63	-0.91	0.91	0.93
Height(B58C)	rs4800452	18	-4.60	-4.81	0.79	0.97
Height(B58C)	rs9967417	18	1.21	1.91	0.55	0.90
Height(B58C)	rs17782313	18	-1.16	-1.40	0.82	0.97
Height(B58C)	rs12982744	19	0.08	0.22	0.75	0.91
Height(B58C)	rs7507204	19	-0.96	-0.88	0.53	0.82
Height(B58C)	rs891088	19	-1.58	-1.50	0.86	0.95
Height(B58C)	rs4072910	19	1.46	1.18	0.53	0.81
Height(B58C)	rs2279008	19	2.02	1.93	0.79	0.93
Height(B58C)	rs17318596	19	-2.16	-2.25	0.85	0.95
Height(B58C)	rs1741344	20	1.61	1.65	0.92	0.94
Height(B58C)	rs2145272	20	2.37	2.96	0.78	0.95
Height(B58C)	rs7274811	20	3.43	3.94	0.90	0.95
Height(B58C)	rs143384	20	-3.78	-4.37	0.49	0.81
Height(B58C)	rs237743	20	-1.90	-1.96	0.69	0.93
Height(B58C)	rs2834442	21	-2.04	-2.28	0.80	0.95

Supplementary Table 6: Association statistics (χ^2) in the IHCS data at known associated SNPs on Chromosome 6 using several strategies for genotype calling from low coverage sequencing

Position	Typed	Indep	Indep+MAF	ImpG-Seq	Beagle
30140525	0.29	3.79	3.21	0.22	0.58
30364508	0.77	0.86	0.20	0.55	0.61
30756066	0.01	0.27	0.20	1.15	0.06
30785273	0.53	0.33	0.18	2.10	0.25
30787593	0.53	2.10	2.45	1.45	0.61
30823630	1.32	0.78	2.34	0.32	1.68
30848253	4.15	0.84	1.08	0.35	3.15
30895990	2.34	0.56	0.80	0.56	2.85
30983683	2.49	0.63	0.66	0.06	2.20
31001143	2.74	0.26	0.74	0.59	3.00
31083813	0.40	1.12	1.05	1.12	0.31
31084435	0.71	1.66	1.86	0.15	0.77
31085770	4.11	0.55	0.24	0.15	4.30
31087934	0.40	0.77	0.77	0.20	0.31
31091862	0.71	0.63	0.07	1.49	0.74
31095801	1.55	0.49	0.18	0.33	1.58
31100942	0.29	2.15	1.99	1.03	0.71
31124849	0.04	0.51	0.34	1.96	0.01
31125777	0.06	0.98	0.82	1.69	0.00
31130593	1.61	0.73	0.45	2.52	1.85
31133943	1.68	0.72	1.07	2.99	1.82
31170514	0.16	0.38	0.38	0.03	0.04
31170528	0.09	1.58	1.58	0.81	0.06
31240692	4.15	0.94	1.05	0.56	4.27
31241032	0.43	0.55	0.41	1.59	0.16
31269173	3.99	0.22	0.09	5.31	6.10
31274380	5.70	0.43	0.42	2.32	8.08
31317347	4.86	0.32	0.00	0.66	3.30
31320538	1.51	1.73	1.62	2.99	0.58
31331829	1.95	0.38	0.27	0.45	2.02
31336568	0.05	0.00	0.06	0.00	0.08
31353593	8.84	0.02	0.03	0.02	10.91
31362930	8.84	2.91	2.17	2.53	8.25
31387557	3.88	5.13	6.27	10.32	4.15
31388214	3.57	0.39	0.42	8.32	4.03
31447588	4.74	0.07	1.19	0.90	3.65
31544189	2.41	1.07	1.24	0.68	1.48
31564821	0.45	0.03	0.05	0.03	1.00
31572927	0.48	0.30	0.15	0.01	1.45
31575276	0.48	2.05	1.64	2.05	1.45
31920873	0.21	0.02	0.13	0.36	0.23
32026808	0.01	0.63	0.30	0.43	0.53
32066765	0.00	1.23	1.57	1.23	0.01

Position	Typed	Indep	Indep+MAF	ImpG-Seq	Beagle
32074804	0.01	0.39	0.03	0.39	0.00
32161324	1.68	0.01	0.06	0.00	0.40
32266506	0.89	0.17	1.04	0.03	1.68
32401327	0.89	2.05	2.48	0.09	0.71
Average	1.85	0.93	0.96	1.34	1.96

Method	Odds Ratio				
	1.0	1.2	1.5	1.7	2.0
	All SNPs				
Beagle	0.999	0.892	0.872	0.870	0.868
ImpG-Summary	0.937	0.835	0.823	0.827	0.836
ImpG-SummaryLD	0.999	0.872	0.851	0.852	0.855
ImpG-Raw	0.999	0.873	0.849	0.847	0.845
	Common SNPs (over 5%)				
Beagle	0.999	0.900	0.885	0.883	0.881
ImpG-Summary	0.956	0.850	0.841	0.845	0.855
ImpG-SummaryLD	0.999	0.882	0.867	0.868	0.872
ImpG-Raw	1.000	0.883	0.865	0.863	0.861
	Low frequency SNPs (1 to 5%)				
Beagle	0.997	0.808	0.667	0.640	0.620
ImpG-Summary	0.881	0.685	0.539	0.512	0.491
ImpG-SummaryLD	0.997	0.768	0.597	0.565	0.542
ImpG-Raw	0.998	0.768	0.596	0.564	0.540

Supplementary Table 7: Relative effective sample size at imputed SNPs (ratio of the average χ^2 association statistics attained at imputed versus typed SNPs) in simulated case-control studies at different effect sizes ($R > 1$). The column corresponding to $R=1$ shows the average χ^2 association statistic under the null model of no association. ImpG-Raw denotes Gaussian imputation with individual level data (see Main text).

Method	Rand	Great Britain
All SNPs		
Beagle	0.872	0.868
ImpG-Summary	0.823	0.818
ImpG-SummaryLD	0.851	0.845
ImpG-Raw	0.849	0.841
Common SNPs (over 5%)		
Beagle	0.885	0.880
ImpG-Summary	0.841	0.835
ImpG-SummaryLD	0.867	0.860
ImpG-Raw	0.865	0.857
Low frequency SNPs (1 to 5%)		
Beagle	0.667	0.671
ImpG-Summary	0.539	0.549
ImpG-SummaryLD	0.597	0.603
ImpG-Raw	0.596	0.598

Supplementary Table 8: Relative effective sample size at imputed SNPs (ratio of the average χ^2 association statistics attained at imputed versus typed SNPs) when imputation is performed in a random subsample of the 1000 Genomes European data or over only Great Britain haplotypes (odds ratio is set to 1.5). ImpG-Raw denotes Gaussian imputation with individual level data (see Main text).

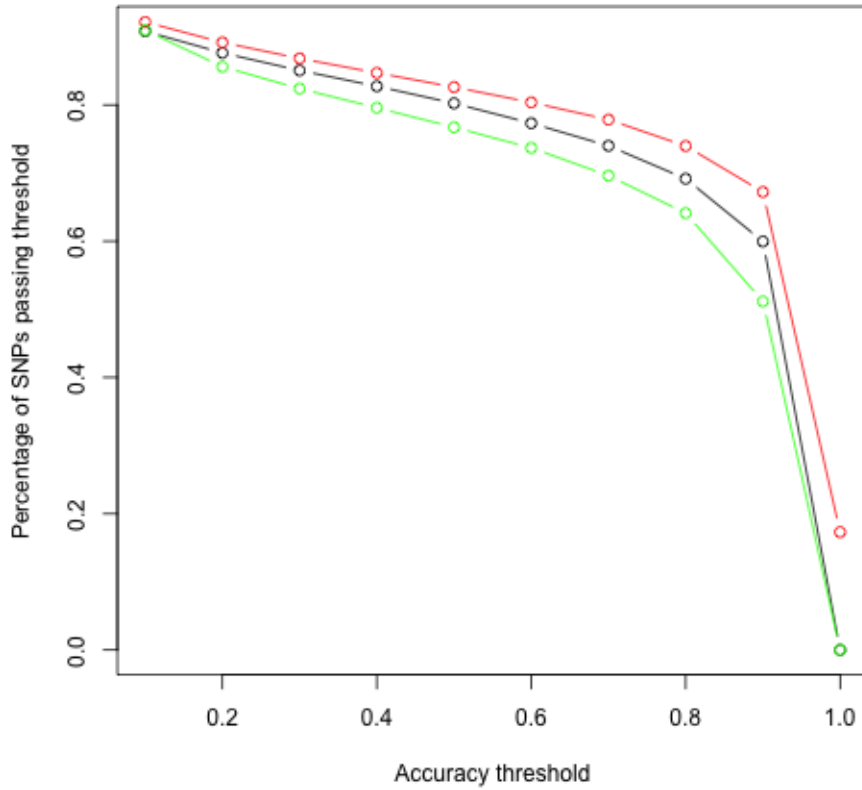
Phenotype	GENIC	INTRON	INTERGENIC	All
HDL(before)	1.080	1.031	0.981	1.007
HDL(after)	1.101	1.052	1.000	1.027
HDL(1000G,before)	1.030	0.960	0.916	0.937
HDL(1000G,after)	1.124	1.048	1.000	1.023
LDL(before)	1.068	1.031	0.975	1.002
LDL(after)	1.095	1.058	1.000	1.027
LDL(1000G,before)	1.019	0.959	0.901	0.929
LDL(1000G,after)	1.131	1.065	1.000	1.031
TC(before)	1.083	1.031	0.972	1.002
TC(after)	1.114	1.061	1.000	1.030
TC(1000G,before)	1.034	0.966	0.905	0.934
TC(1000G,after)	1.143	1.068	1.000	1.032
TG(before)	1.059	1.040	0.966	1.002
TG(after)	1.096	1.077	1.000	1.037
TG(1000G,before)	1.007	0.968	0.893	0.926
TG(1000G,after)	1.128	1.083	1.000	1.036

Supplementary Table 9: Genomic control before and after correction for inflation observed at intergenic set of SNPs.

Phenotype	GENIC	INTRON	All
HDL	7.63E-05	2.87E-02	2.30E-01
HDL(1000G)	4.75E-08	1.69E-02	2.44E-01
LDL	3.63E-04	5.02E-02	3.39E-01
LDL(1000G)	1.45E-06	1.73E-02	2.27E-01
TC	4.85E-05	2.28E-02	2.51E-01
TC(1000G)	1.33E-07	2.14E-02	2.01E-01
TG	1.04E-04	7.62E-03	2.58E-01
TG(1000G)	8.91E-07	7.10E-03	1.75E-01

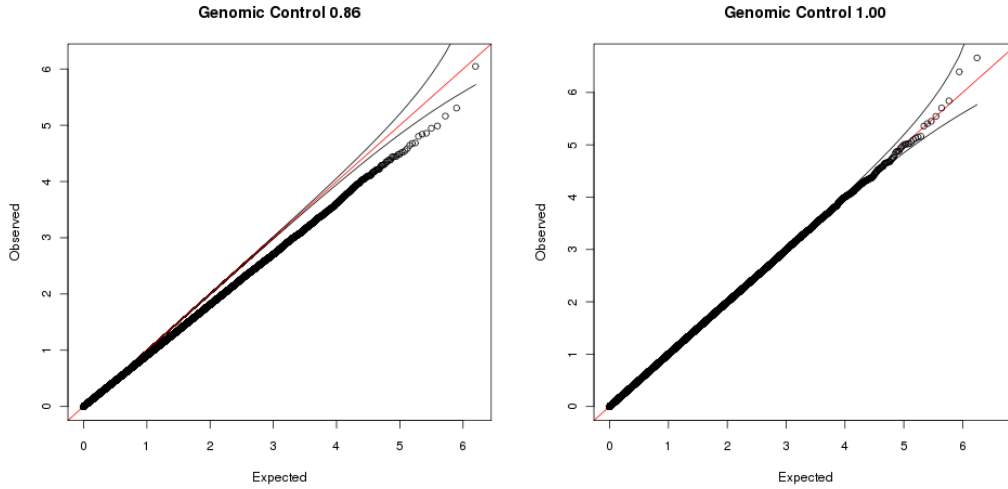
Supplementary Table 10: Comparison between chi-square distribution to the INTERGENIC class of SNPs (-log10). Kolmogorov-Smirnov (KS) Tests statistic over 100 random draws each of 10,000 random SNPs across the genome was computed with median reported above. We note that the KS test used is known to be overly conservative when distributions differ only in the extreme tails.

2 Supplementary Figures

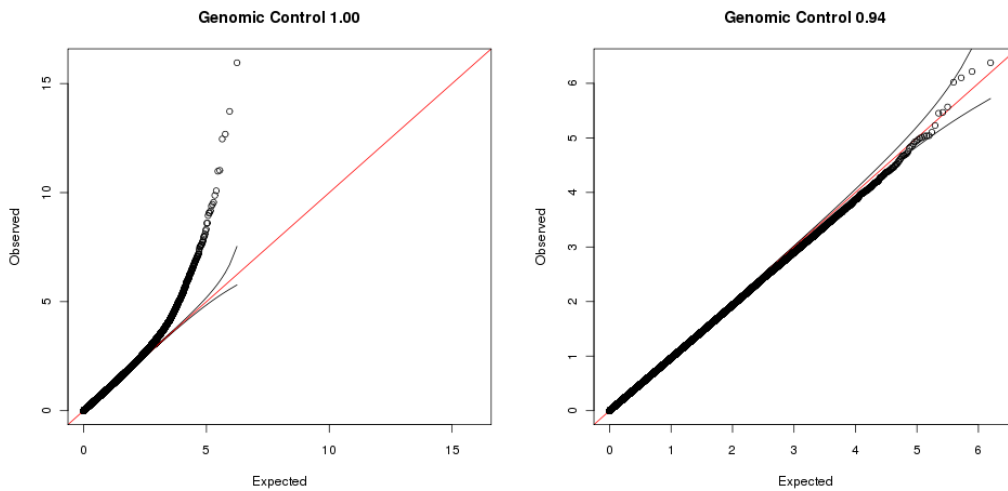


Supplementary Figure 1: Percentage of SNPs passing different thresholds on accuracy using the true accuracy (r^2 , black), estimated under HMM (r^2_{hat} , red) and estimated from MVN (r^2_{pred} , green). We observe a Pearson correlation of 0.92 between r^2_{hat} and r^2 as compared to 0.90 between r^2_{pred} and r^2 . 77%, 80% respectively 74% of SNPs attain accuracy higher than 0.6 under the r^2 , r^2_{hat} or r^2_{pred} estimates of accuracy.

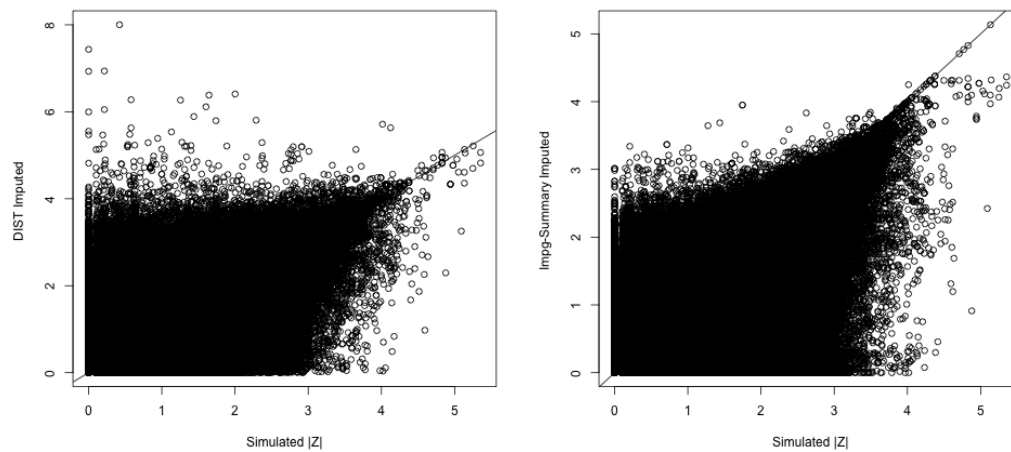
Variance unadjusted statistics (left), ImpG-SummaryLD (right)



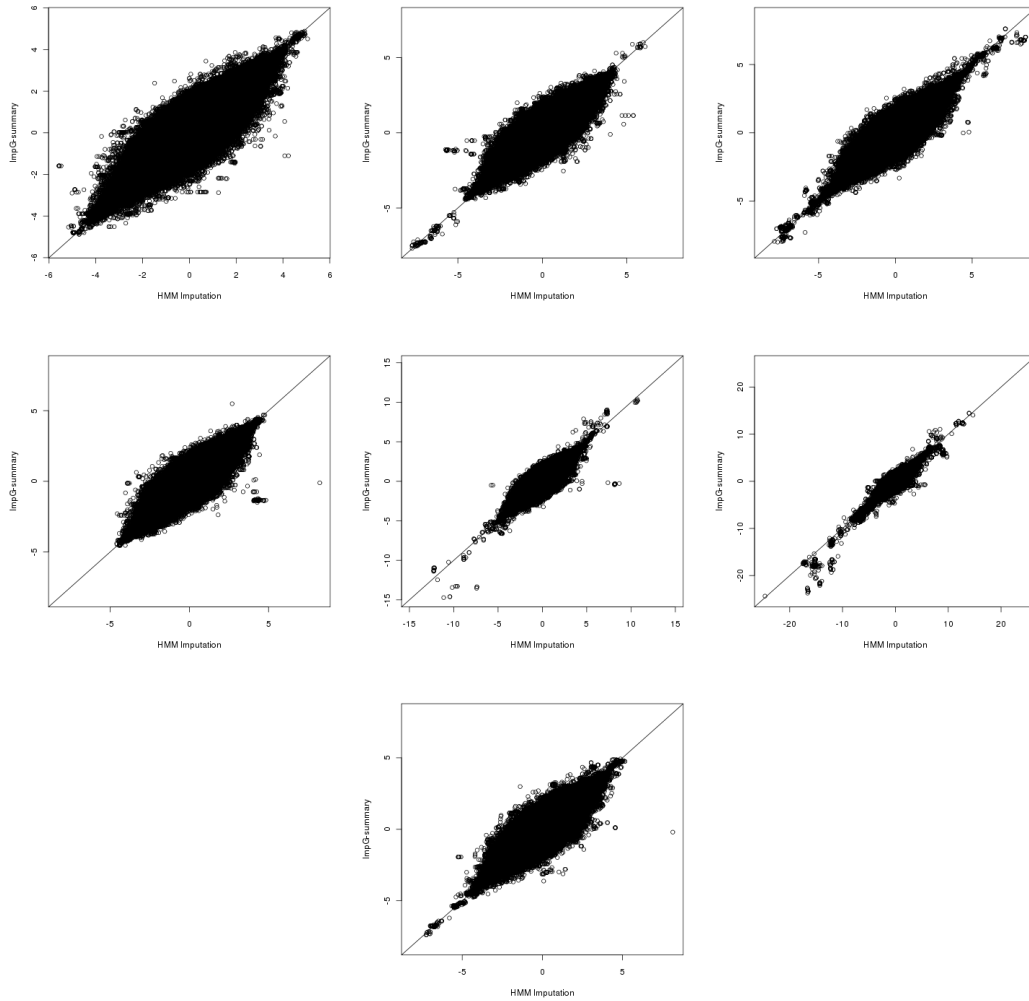
ImpG-Summary($\lambda = 0.000$) (left), ImpG-Summary ($\lambda = 0.100$) (right)



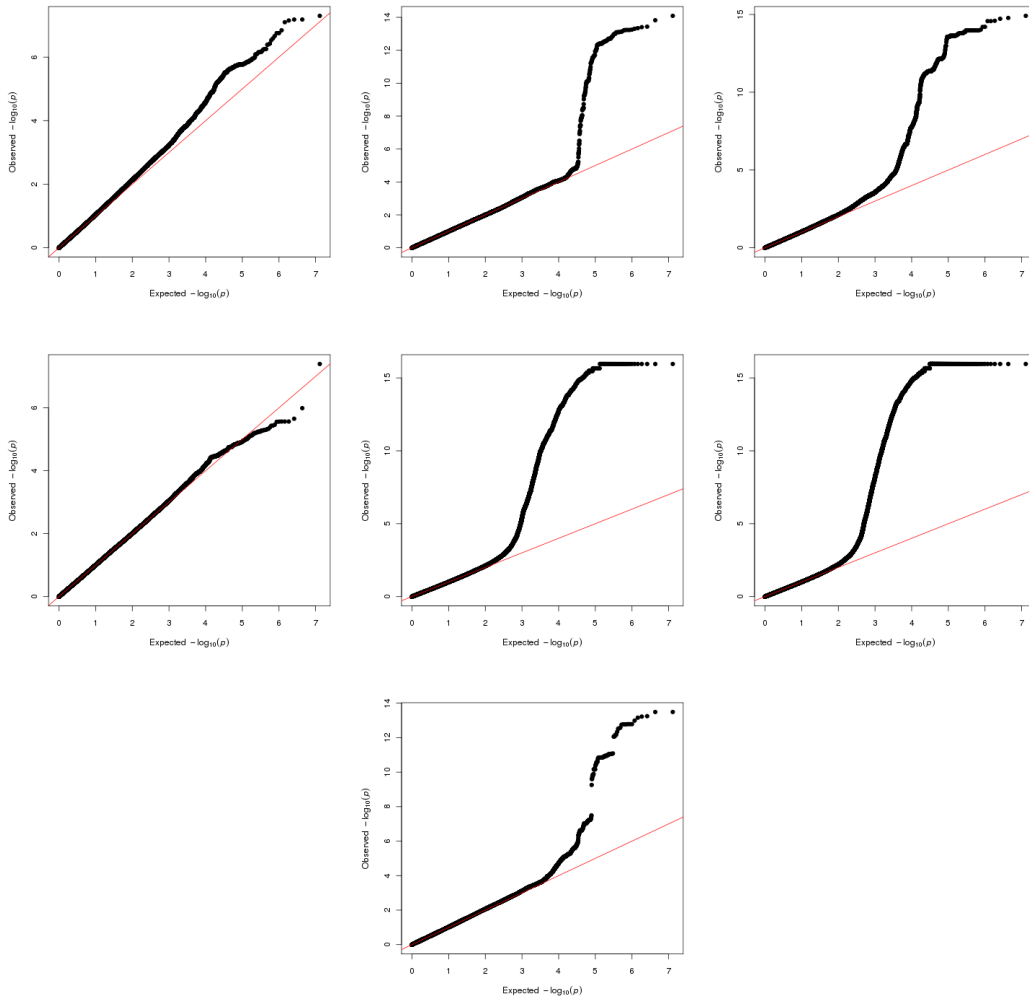
Supplementary Figure 2: Expected versus observed minus log 10 p-values in null simulations ($R=1$) for Gaussian imputation from summary data. Top left denotes variance unadjusted statistics, top right denotes variance adjusted statistics using the LD matrix at typed variants inferred from the sample, bottom left denotes variance adjusted statistics using the LD matrix over typed variants inferred from reference panel while bottom right denotes statistics adjusted using LD learned from reference panels with the sample noise factor. All results displayed over confidently imputed statistics ($r^2_{pred} > 0.6$).



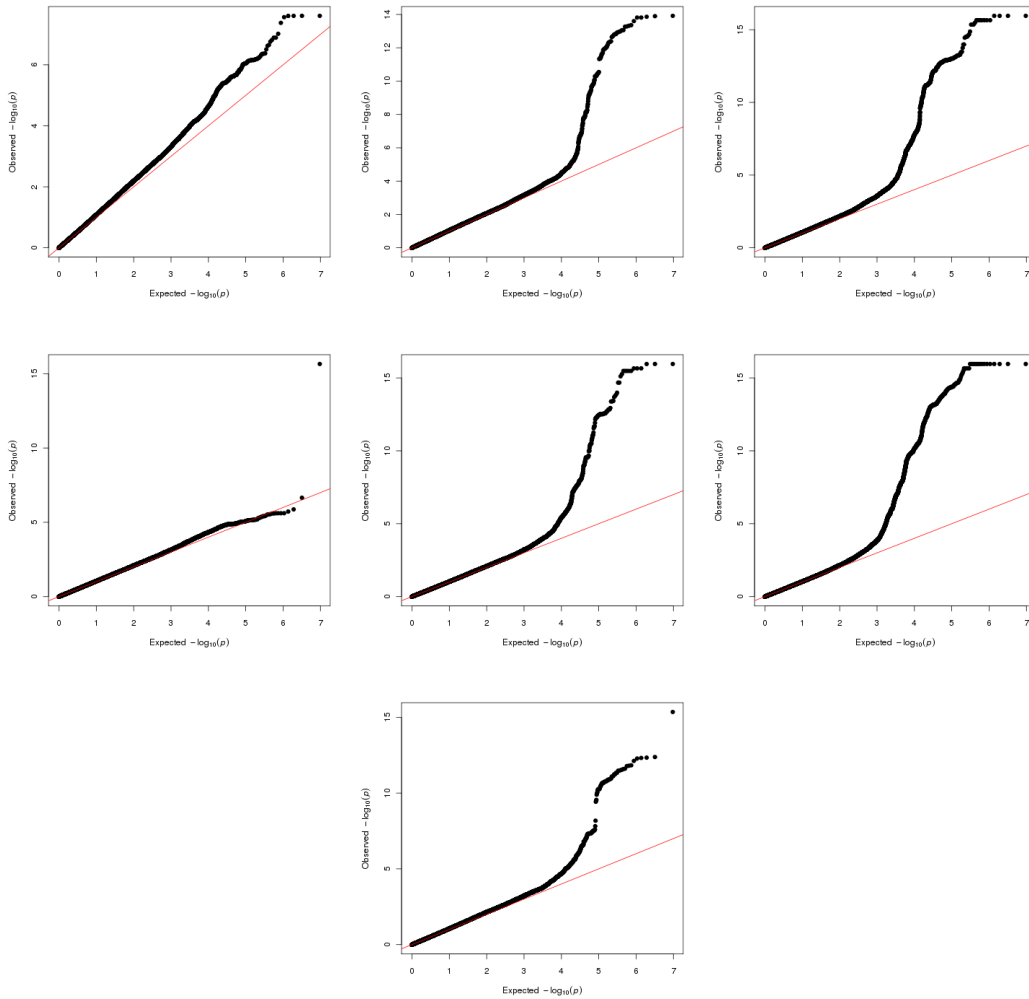
Supplementary Figure 3: Gaussian imputation results on null simulations from 1000 Genomes data. The 381 European samples were randomly split in half, with one half used as reference and the other half used to simulate case control data sets by randomly assigning case control labels (85 cases and 85 controls). SNPs present on the Illumina 610 platform and that attained a MAF > 5% in both cases and controls (464,897) were used to impute all variants polymorphic (MAF > 1% in the case-control data (5,961,997 in total) Left shows DIST (v0.1.4) results at an info score > 0.6 (5,620,505 in total) while right plots ImpG-Summary results at a r^2_{pred} > 0.6 score (5,469,489 in total).



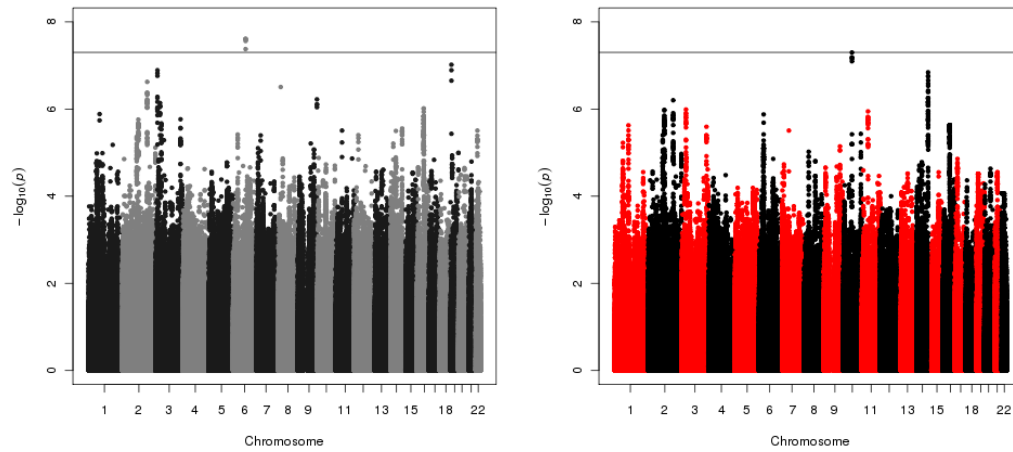
Supplementary Figure 4: HMM-imputed (x-axis) versus ImpG-summary (y-axis) association statistics (z-scores) of for all phenotypes in WTCCC Data. Data only at SNPs accurately called in both ImpG-Summary and HMM-imputation.



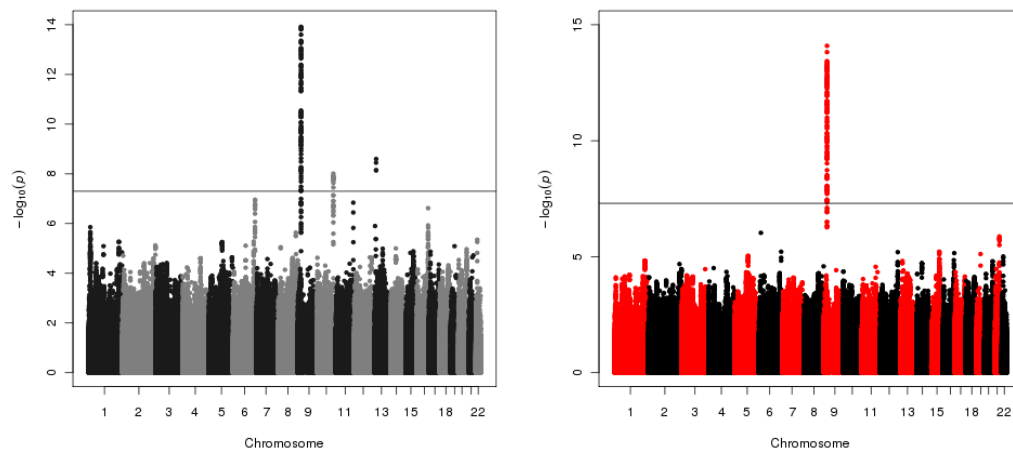
Supplementary Figure 5: ImpG-summary: Expected versus observed association statistics of for each of the 7 WTCCC phenotypes.



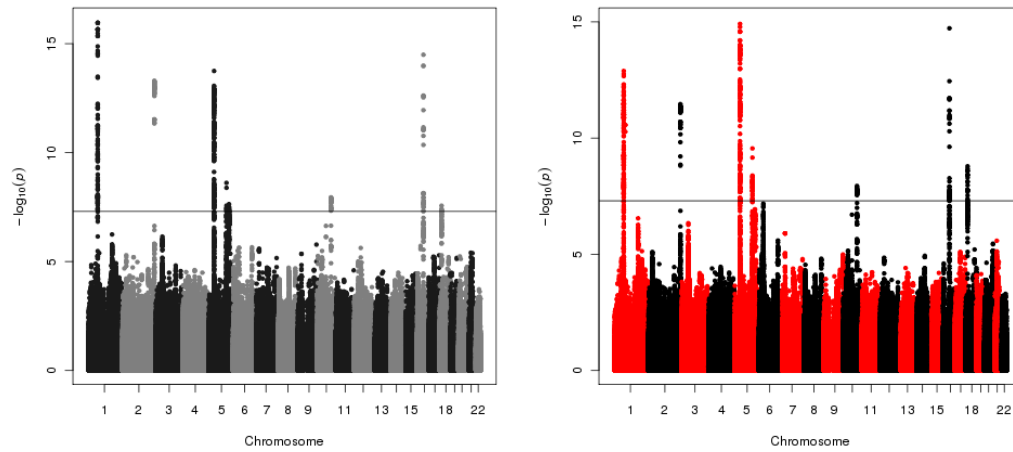
Supplementary Figure 6: Impute2: Expected versus observed association statistics of for each of the 7 WTCCC phenotypes.



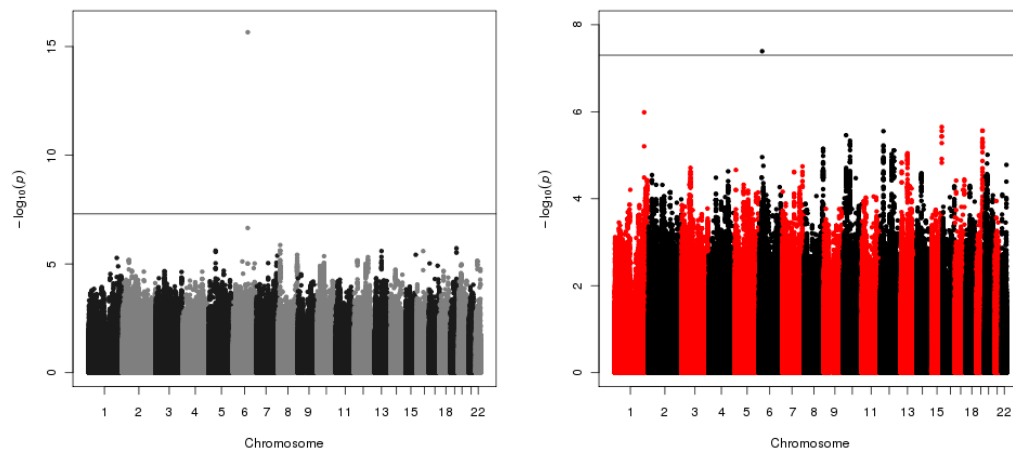
Supplementary Figure 7: Manhattan plot BD phenotype in WTCCC data. HMM(left), ImpG-Summary(right).



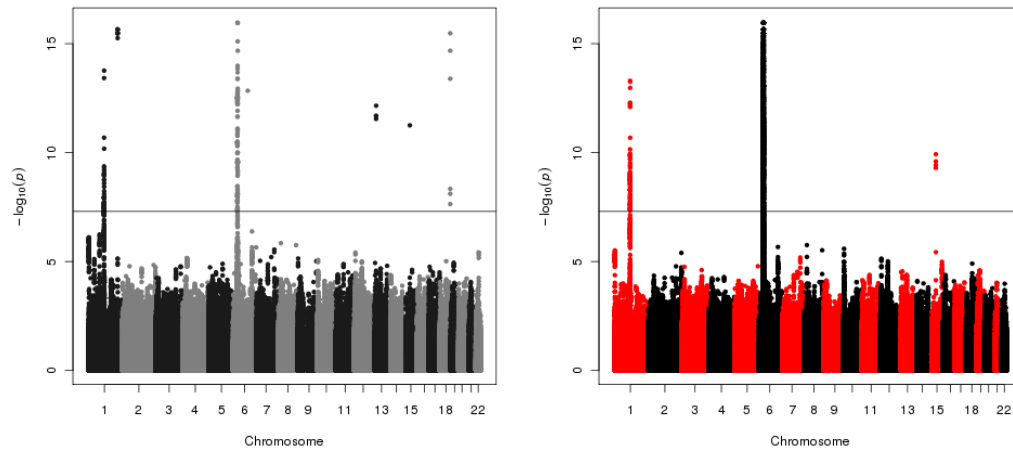
Supplementary Figure 8: Manhattan plot CAD phenotype in WTCCC data. HMM(left), ImpG-Summary(right).



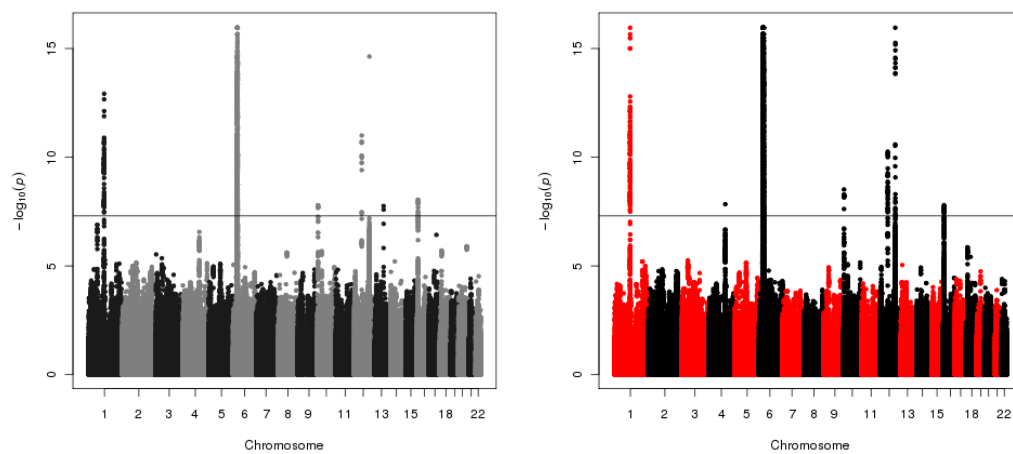
Supplementary Figure 9: Manhattan plot CD phenotype in WTCCC data. HMM(left), ImpG-Summary(right).



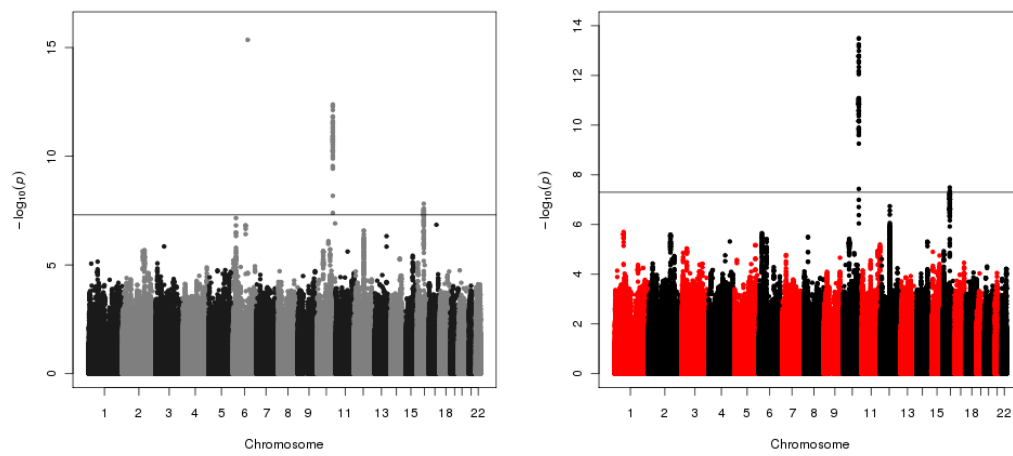
Supplementary Figure 10: Manhattan plot HT phenotype in WTCCC data. HMM(left), ImpG-Summary(right).



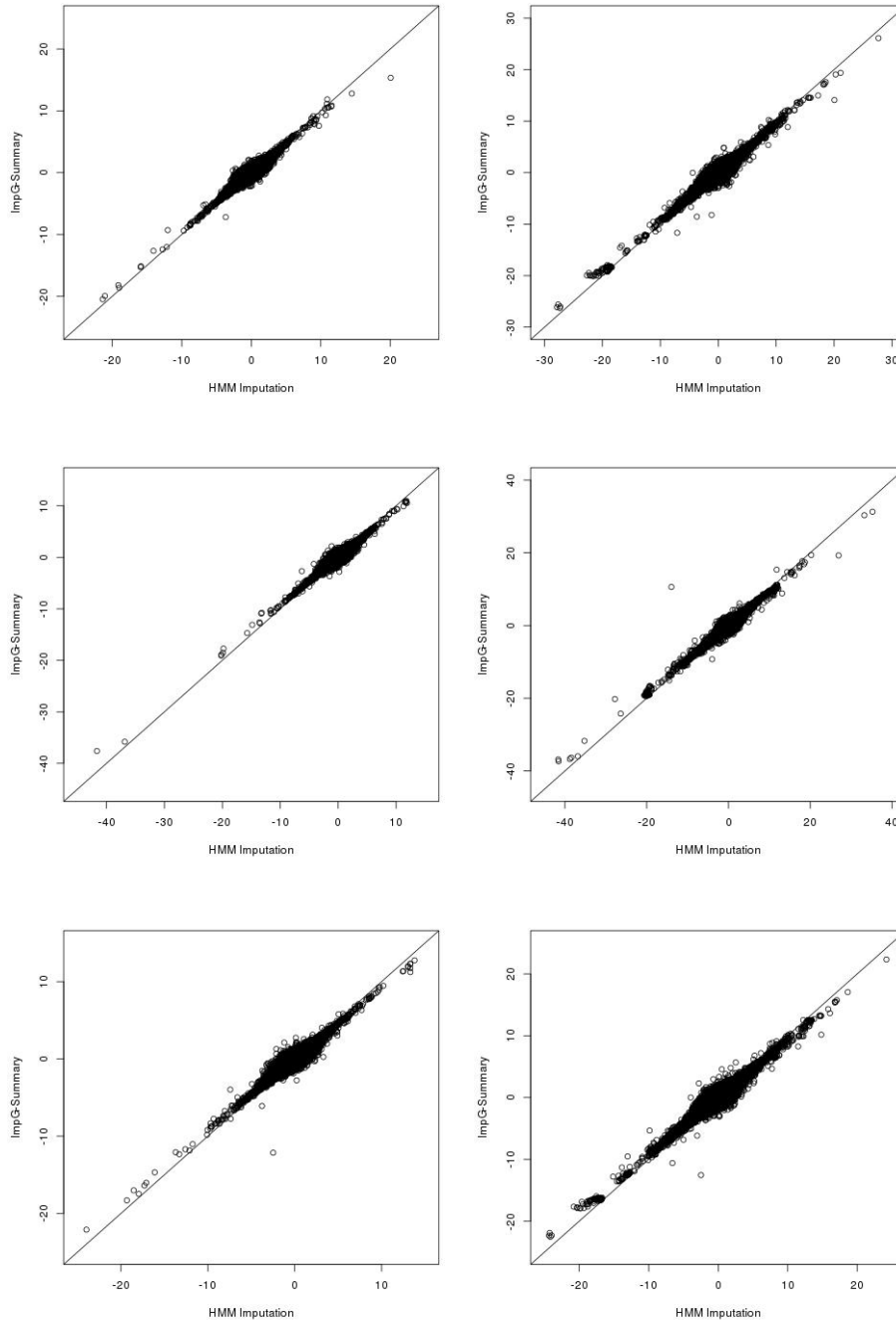
Supplementary Figure 11: Manhattan plot RA phenotype in WTCCC data. HMM(left), ImpG-Summary(right).



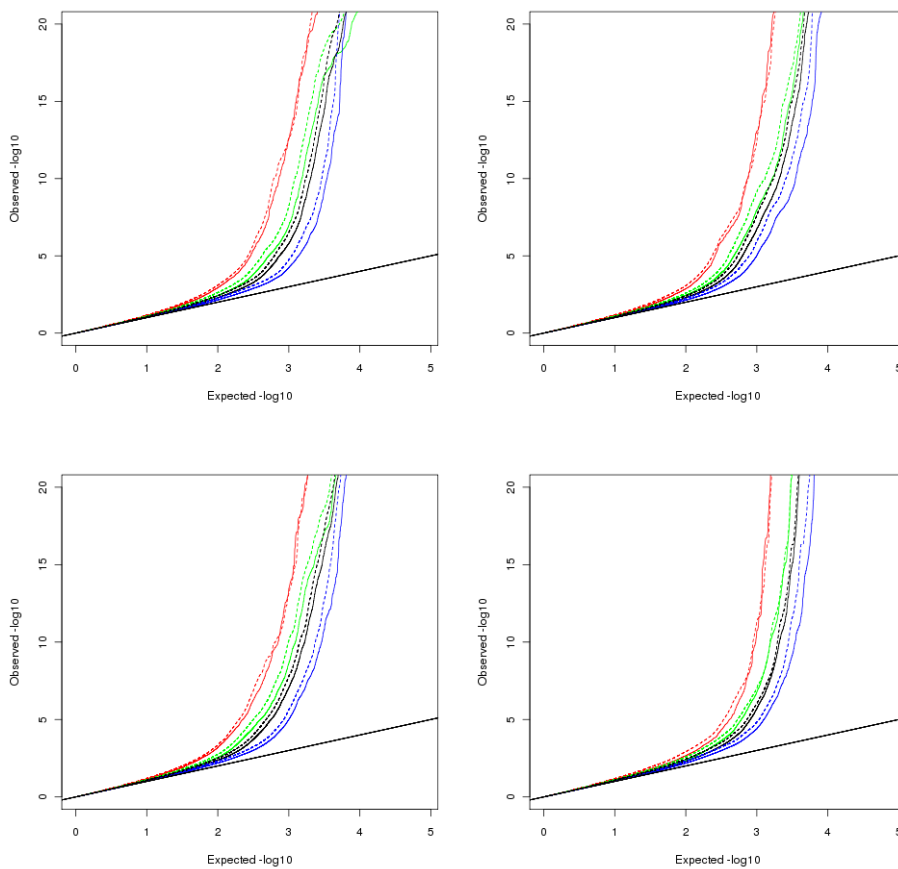
Supplementary Figure 12: Manhattan plot T1D phenotype in WTCCC data. HMM(left), ImpG-Summary(right).



Supplementary Figure 13: Manhattan plot T2D phenotype in WTCCC data. HMM(left), ImpG-Summary(right).



Supplementary Figure 14: HMM-imputed (x-axis) versus ImpG-Summary (y-axis) association statistics (z-scores) for the LDL,HDL, and TC phenotypes. Left denotes imputation of 10% of the z-scores using the remaining 90% while right shows imputation results starting from all variants present on the Illumina 610 array.



Supplementary Figure 15: QQ-plots for LDL,HDL, TC and TG phenotypes. Red denotes GENIC class, green the INTRON class, blue the INTERGENIC class with black denoting results at all SNP set. Dashed lines for ImpG-Summary 1000 Genomes imputed data with solid lines for original data.