# Genomewide association study of 14,000 cases of seven common diseases and 3,000 shared controls

## Supplementary Information

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## Data Quality

One important step in the analysis of genome-wide SNP data is determining a set of quality-assurance filters identifying problem SNPs while discarding as few high quality SNPs as possible. To this end the WTCCC Design and Analysis Group (DAG) investigated a number of different statistics related to genotype clustering, including ratios of cluster mean and variance within and across sample collections (2 control groups plus 7 diseases). As noted in the main text, the best "metric" we found for CHIAMO for identifying difficult-to-call SNPs is the proportion of missing data.

One interesting feature of our QC analyses was the identification of several hundred SNPs which resemble Supplementary Figure 24. For these SNPs, some collections show three tight clusters, whereas others show six distinct clusters: two for each genotype. In fact, all such SNPs show the three cluster pattern in UKBS, RA and CAD and the six cluster pattern in 58C, BD, CD, HT, T1D and T2D. Furthermore, investigation of which specific samples appear in the clusters closer to the origin of the graph revealed that these samples were always the same, and came from early plates in the experiment run at the Affymetrix R&D facility, whereas the samples in the more distantly spaced clusters (and all samples from UKBS, RA and CAD) were processed at the Affymetrix Services Lab. (Based on our QC metrics both laboratories generated data of similar quality.)

We note this observation for two reasons: first that specific laboratory conditions can significantly affect the raw data generated on the Affymetrix 500K chip, and second that such experimental aberrations might be incorrectly followed up as possible copy number variants or other

biological processes of interest. While we have ruled out any such explanations, we are left with questions about the experimental process such as why only a few SNPs are affected in this fashion. Note that CHIAMO had no difficulty in correctly calling genotypes when there are these six clusters present, so this artefact had no effect on our analyses.

The plots of missing data rates per sample (Supplementary Figure 25) show a change-point roughly midway through our study, where there is a small but noticeable increase in overall rates. Although we investigated several possibilities, the reasons for this are not clear. There are also plate effects in missing data rates. Again, these phenomena do not affect our analyses.

## Interpreting Cluster Plots

Genotype calling errors can easily lead to spurious associations. These can be attributed either to errors made by the calling algorithm or to poor data quality. The latter can make genotype calling very difficult, or in some cases even impossible.

The calling algorithm we use, CHIAMO, correctly calls the vast majority of SNPs. However, the large number of SNPs in the study means that even a small error rate or a small amount of poor quality data can lead to non-trivial numbers of false-positive associated SNPs. Thus, all SNPs that showed strong association were subject to cluster plot inspection to verify their genotype calls.

A cluster plot is a graphical representation of the results of both the genotyping and genotype calling of a SNP. It is a scatter plot of normalised summary probe intensities from the genotyping, with each point representing one individual. Each point is then coloured to indicate how the genotype calling algorithm decided to

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classify that individual (either as a homozygote for one of the two alleles, a heterozygote, or a "null" (missing) call).

The aim of examining a cluster plot is twofold: to determine whether the given SNP has been genotyped well — in particular, whether we see clear, distinct, clusters on the plot that would correspond to the three genotypes — and also to determine whether the calling algorithm has called the clusters correctly. If both of these are true, we can usually be confident that the genotype counts are accurate. If these are not true, any associations that we observe at such SNPs may well be caused by the resulting incorrect genotype counts.

SNPs observed to have a cluster plot error are generally excluded from the analysis. However, depending on what kind of error it is and any other evidence of association, some method of error recovery could be attempted — e.g. re-running CHIAMO, re-genotyping using a different platform, or imputation of genotypes.

One particularly challenging but relatively rare scenario relates to differential missingness. Some samples may be hard to call, especially if they lie on cluster boundaries, so instead of calling them a certain genotype the algorithm may call them as "null" (i.e. they will be missing data). Ordinarily, this isn't a problem and very few individuals will be called null. However, if clusters are close together, or even overlapping, many of the individuals on the adjacent boundaries will be called null (and these represent sensible calls given the uncertainty). Often, only two of the clusters are close together (the heterozygote and one of the homozygotes), which leads to most of the missing individuals to be those that preferentially have one of the two alleles, resulting in biased allele frequency estimates. If this happens differentially between cases and controls it can lead to spurious associations. We used a posterior probability threshold in CHIAMO of 0.9, treating the genotype as missing when the most probable call fell below this threshold. With this choice of threshold the call rate was high. Counterintuitively, we found that increasing the threshold in an attempt to improve data quality was counter-productive, leading to increased false positives because of differential missingness.

Despite the multiple potential sources of error, CHIAMO and BRLMM get nearly all the calls correct (Supplementary Table 3). Using CHIAMO as described, typically only about 100 cluster plots required inspection per disease for a genomewide scan.

## Interpreting Signal Plots

Signal plots can help us learn about the believability and characteristics of putative disease associations. Most real susceptibility loci should show elevated signals at multiple nearby SNPs unless the recombination rate in the region is very high or the SNP density very low. This is because sets of SNPs that are near a disease locus will often be correlated and consequently share an allele frequency disparity between cases and controls. This effect should decline with genetic distance (and decreasing LD) but also depends on factors like minor allele frequency. A single elevated signal is often the spurious result of data or analysis artifacts, such as miscalled genotypes at a SNP.

Once a plausible hit region has been identified, we can learn more about it by delimiting its boundaries. This provides some basic information about the part of the genome where the association signal was found and guides follow-up studies of interesting regions. We specify hit region boundaries by looking for positions flanking a hit SNP where the signal returns to background levels; if this coincides with a recombination hotspot, as it often does, we choose that as the boundary. Historical recombinations — particularly those concentrated in hotspots —- will tend to decrease correlations between marker and disease loci. The gene and sequence conservation tracks on our signal plots also provide useful information about genomic context in the neighborhood of a putative susceptibility locus: highly conserved tracts and known genes in the hit region suggest obvious candidates for further scrutiny. Inclusion of imputed SNPs gives an additional level of resolution and, as in some of our examples, can potentially identify a stronger signal of association at a SNP not assayed directly.

## Bayes Factors

Consider a SNP with two alleles coded 0 and 1. Suppose we have genotypes at this SNP in a set of $N$ individuals ($N_1$ cases and $N_2$ controls). We use $Y_i$ to denote the binary disease phenotype of individual $i$ (cases have $Y_i = 1$, controls have $Y_i = 0$). Let $Z_i$ denote the count of alleles coded as 1 for individual $i$. The data at the SNP can be summarised in the following table:

| $Z$ | 0 | 1 | 2 |
|---|---|---|---|
| Cases | $s_0$ | $s_1$ | $s_2$ |
| Controls | $r_0$ | $r_1$ | $r_2$ |

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We use $M_0$ to denote a model of no association, $M_1$ for a model with an additive effect on the log-odds scale and $M_2$ for a general 3 parameter model of association. The Bayes Factor between models $M_1$ and $M_0$ is defined as

$$BF_1 = \frac{P(D|M_1)}{P(D|M_0)} = \frac{\int P(D|\theta_1, M_1)P(\theta_1|M_1)d\theta_1}{\int P(D|\theta_0, M_0)P(\theta_0|M_0)d\theta_0}$$

where $D$ is used to denote the data, $\theta_1$ and $\theta_0$ are the parameters of the models $M_1$ and $M_0$. It can be clearly seen that instead of maximising the likelihood (as is the case for frequentist tests) under the two models the parameters are integrated out of the likelihood with a weighting given by the prior distribution on the parameters.

For both models we use a logistic regression model for the likelihood

$$P(D|\theta) = \prod_{i=1}^{N} p_i^{Y_i}(1 - p_i)^{1-Y_i}$$

where for model $M_1$ we have

$$\theta_1 = (\mu, \gamma) \qquad \log \frac{p_i}{1 - p_i} = \mu + \gamma Z_i,$$

and for model $M_0$ we have

$$\theta_0 = (\mu) \qquad \log \frac{p_i}{1 - p_i} = \mu.$$

We now need to specify the prior distribution $P(\theta_1|M_1) = P(\mu, \gamma|M_1)$. The parameter $\mu$ represents the baseline odds of disease. This parameter will be influenced by the numbers of cases and controls in the dataset. In a case-control design the numbers of cases in the sample have been elevated artificially which will have a large effect on likely values of $\mu$. For this reason we wish to use a prior distribution that allows flexibility in the specification of our beliefs on $\mu$ so we use a $\mathrm{N}(\alpha_1, \beta_1)$ distribution. In practice we have used $\mu \sim \mathrm{N}(0, 1)$.

The parameter $\gamma$ is the increase in log-odds of disease for every copy of the risk allele and $e^{\gamma}$ is the additive model odds ratio. We have some good prior information about likely values of this parameter. For example, it is widely believed that the genetic variants underlying common disease will have risk allele odds-ratios in the range 1–2 with substantially more weight on the values between 1–1.5. Note that this implies a protective allele odds-ratio in the range 0.5–1 with substantially more weight on values between 0.67–1. After some experimentation we settled on a flexible prior distribution for $\gamma$ of a $\mathrm{N}(\alpha_2, \beta_2)$ distribution. For example, Figure 1 shows a density plot for the additive model odds-ratio

($e^{\gamma}$) from a sample of 1,000,000 draws from the prior $\gamma \sim \mathrm{N}(0, 0.2)$.

Overall, the prior distribution on the parameters has the form

$$P(\theta_1|M_1) \propto \frac{1}{\beta_1} e^{-\frac{(\mu-\alpha_1)^2}{2\beta_1^2}} \frac{1}{\beta_2} e^{-\frac{(\gamma-\alpha_2)^2}{2\beta_2^2}}.$$

For $P(\theta_0|M_0) = P(\mu|M_0)$ we used the same prior on $\mu$ as in the model $M_1$. That is,

$$P(\theta_0|M_0) \propto \frac{1}{\beta_1} e^{-\frac{(\mu-\alpha_1)^2}{2\beta_1^2}}.$$

It is well understood that the priors on the parameters of the model can have a non-negligible impact on the value of the Bayes Factor[1] even as the amount of data gets large. In line with this we have found that using different priors on $\mu$ for the two models can substantially change the Bayes Factor. We have little strong prior information about $\mu$ and as noted above the case-control ratio will have a large effect on the values that best fit the data. For these reasons we use a reasonably diffuse prior distribution on this parameter that is the same for both models. This acts to focus the comparison between the models on the parameter $\gamma$ which is the main parameter of interest.

To evaluate the marginal likelihood for the model $P(D|M_1)$ we need to evaluate the integral

$$\int P(D|\theta_1, M_1)P(\theta_1|M_1)d\theta_1.$$

We do this using a Laplace Approximation[2] in which the posterior distribution is approximated using a Gaussian distribution centred on its mode. More specifically, we use

$$\log P(D|M_1) \approx \log P(D|\hat{\theta}_1, M_1) + \log P(\hat{\theta}_1|M_1)$$
$$+ \frac{d}{2} \log(2\pi) - \frac{1}{2} \log |A|$$

where $\hat{\theta}_1$ is the value of $\theta_1$ that maximises $P(D|\theta_1, M_1)P(\theta_1|M_1)$, and is known as the *maximum a posteriori* (MAP) estimate of $\theta_1$. Also, $A$ is the negative Hessian of $P(D|\theta_1, M_1)P(\theta_1|M_1)$ evaluated at $\hat{\theta}_1$ and $d$ is the dimension of $\theta_1$. We use Newton-Raphson optimisation to find $\hat{\theta}_1$ but if this fails to converge we use a line-search method. Both approaches are numerically efficient for this low dimensional integral.

In addition, we note that the evaluation of this marginal likelihood will depend upon the way the alleles at the SNP have been coded 0 and 1. Thus, to calculate the

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Prior distribution on γ
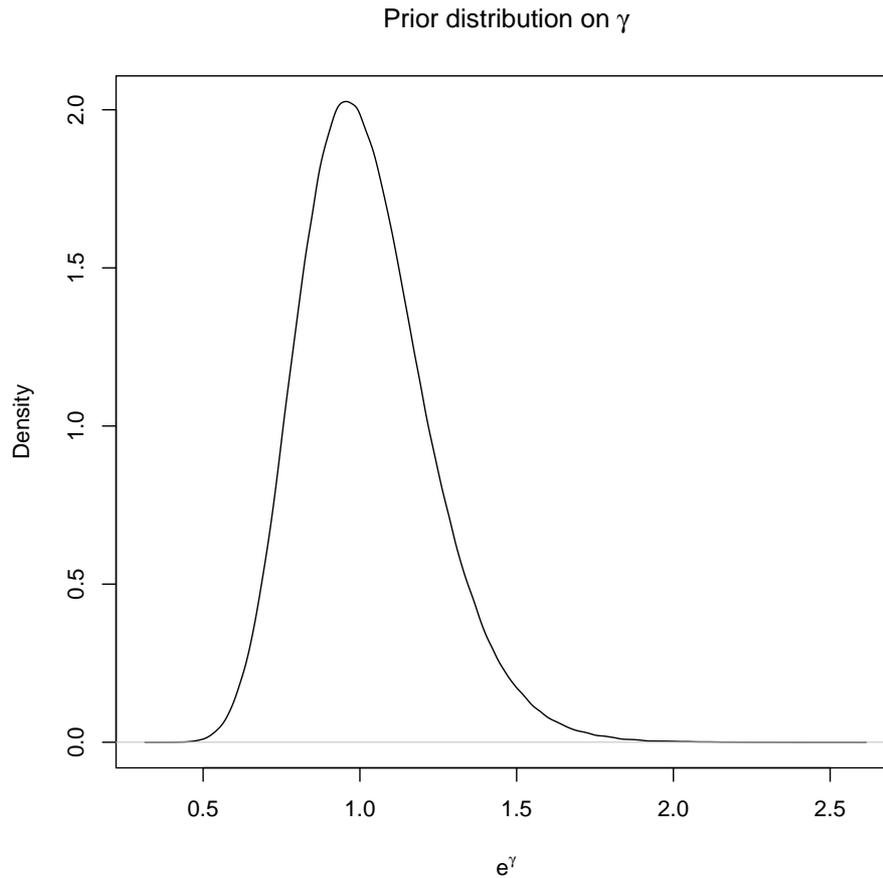


Figure 1: Density plot of the empirical distribution of $e^\gamma$ from a sample of size $10^6$ from the distribution $\gamma \sim N(0, 0.2)$

marginal likelihood for the additive model of the SNP we average over the two possible codings with equal weight. We have used a similar formulation for dominant and recessive models[?].

The general 3 parameter model, $M_2$, is slightly more complicated in that we require a prior distribution on an additional parameter. We use the following model for the log-odds

$$\log \frac{p_i}{1 - p_i} = \mu + \gamma I(Z_i = 1) + 2\phi\gamma I(Z_i = 2)$$

which has an additive genetic effect parametrised by $\gamma$ and then an additional recessive effect parametrised by $\phi$. In this model the additive model occurs when $\phi = 1$. We use a Gaussian prior, $N(\alpha_3, \beta_3)$ for $\phi$. In practice we use a $N(1, 1)$ for $\phi$ which results in a symmetric departure from the additive model and we use the same prior for $\gamma$ i.e. $N(0, 0.2)$ as we did above when we considered the additive model. As with the additive model we use a Laplace approximation to evaluate the required integral

we average the marginal likelihood over the two possible codings for the SNP.

Other priors that are more computationally efficient are possible[3]. For example, for the general 3 parameter model if we use the formulation

$$\log \frac{p_i}{1 - p_i} = \mu I(Z_i = 0) + \gamma I(Z_i = 1) + \phi I(Z_i = 2)$$

in which each genotype is given its own log-odds parameter then the likelihood can be re-written as

$$P(D|\theta_2, M_2) = p_0^{s_0}(1-p_0)^{r_0} p_1^{s_1}(1-p_1)^{r_1} p_2^{s_2}(1-p_2)^{r_2}$$

where $p_0 = \frac{e^\mu}{1+e^\mu}$, $p_1 = \frac{e^\gamma}{1+e^\gamma}$ and $p_2 = \frac{e^\phi}{1+e^\phi}$. This has the form of an independent Binomial Likelihood for each of the three penetrance parameters $p_0$, $p_1$ and $p_2$. Thus we could use a conjugate Beta prior for these parameters which facilitates the exact calculation of the integrals. That is, if we let

$$P(\theta_2|M_2) = \prod_{g=0}^{2} \frac{1}{\beta(\psi_g, \eta_g)} p_g^{\psi_g - 1}(1 - p_g)^{\eta_g - 1}$$

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where $\beta(\psi_g, \eta_g) = \frac{\Gamma(\psi_g)\Gamma(\eta_g)}{\Gamma(\psi_g+\eta_g)}$ then

$$P(D|M_2) = \prod_{g=0}^{2} \frac{\beta(s_g + \psi_g, r_g + \eta_g)}{\beta(\psi_g, \eta_g)}.$$

Similar expressions can be derived for the marginal likelihoods for dominant and recessive models using this class of conjugate priors. For the null model $M_0$ of no association we obtain a marginal likelihood of

$$P(D|M_0) = \frac{\beta(s_0 + s_1 + s_2 + \psi_0, r_0 + r_1 + r_2 + \eta_0)}{\beta(\psi_0, \eta_0)}$$

where a $\text{Beta}(\psi_0, \eta_0)$ is used for the baseline penetrance.

It is interesting to consider what the conjugate Beta priors on penetrance actually mean in terms of odds-ratios. It can be shown that a $\text{Beta}(a, b)$ prior on a probability $p$ is equivalent to a Generalised Logistic distribution on the log-odds $(\log \frac{p}{1-p})$ with mean $\Psi^{(0)}(a) - \Psi^{(0)}(b)$ and variance $\Psi^{(1)}(a) + \Psi^{(1)}(b)$ where $\Psi^{(r)}$ is the polygamma function[4]. For example, a uniform distribution, $p \sim \text{Beta}(1, 1)$, results in a distribution for log-odds centred on 0 with a variance of $\pi^2/3$. This implies that the prior on the difference in log-odds between the heterozygote genotype and the baseline homozygote genotype has mean 0 and variance $2\pi^2/3$. This is considerably more diffuse than the $N(0, 0.2)$ prior we use in the additive model above. Using simulation from this prior we found that it corresponds to a prior distribution on the risk-allele odds ratio with a mean of approximately 80, which is rather larger than might be expected for common human diseases. This suggests that for the General, Dominant and Recessive models in which Beta priors are applicable it might be more reasonable to set the hyper-parameters $a$ and $b$ to be greater than 1. This would bring the priors closer to those we have suggested above.

# CHIAMO

## Normalisation

The raw data for the $s$th SNP of the $i$th individual/array can be denoted as $I_{isk} = (I_{isk}^{PA}, I_{isk}^{PB}, I_{isk}^{MA}, I_{isk}^{MB})$. These denote the $k$th perfect match probe intensities for the A and B alleles and the mismatch probes probe intensities for the A and B alleles respectively, where $k = 1, \ldots, K$ and $K \in \{6, 10\}$. We create a set of normalised intensities, $I'$, using the standard pre-processing step of quantile normalisation to reduce variability across chips[5,6]. To carry out this step on the 17,000 arrays in the WTCCC study we wrote our own software to improve efficiency.

Second, we log transform the quantile normalised intensities $Y = \log(I')$ to reduce the skewness of the intensities[6].

We use $Y_{iks} = (Y_{iks}^{PA}, Y_{iks}^{PB}, Y_{iks}^{PA}, Y_{iks}^{PB})$ to denote the vector of log-normalised intensities for the $k$th probe quartet of individual $i$ at SNP $s$. We use the following transformation to correct for the average background hybridisation across the $A$ and $B$ alleles

$$Y_{iks}^A = \begin{cases} Y_{iks}^{PA} - \frac{1}{2}\left(Y_{iks}^{MA} + Y_{iks}^{MB}\right) & \text{if } Y_{iks}^{PA} \geq Y_{iks}^{MB} \\ 0 & \text{if } Y_{iks}^{PA} < Y_{iks}^{MB} \end{cases}$$

$$Y_{iks}^B = \begin{cases} Y_{iks}^{PB} - \frac{1}{2}\left(Y_{iks}^{MA} + Y_{iks}^{MB}\right) & \text{if } Y_{iks}^{PB} \geq Y_{iks}^{MB} \\ 0 & \text{if } Y_{iks}^{PB} < Y_{iks}^{MB}. \end{cases}$$

We then pool signals across probes using a simple arithmetic mean to create a pair of intensities $X_{is} = (X_{is}^A, X_{is}^B)$ for individual $i$ at SNP $s$,

$$X_{is}^A = \frac{1}{n_s}\sum_{k=1}^{n_s} Y_{iks}^A, \qquad X_{is}^B = \frac{1}{n_s}\sum_{k=1}^{n_s} Y_{iks}^B,$$

where $n_s$ is the number of probe quartets at SNP $s$. Through visual inspection of thousands of SNP intensity plots we found that our normalisation scheme produced tighter clusters with fewer outlying observations than a median polish approach[6].

## A Bayesian Hierarchical Mixture Model

We use $X_{ij}$ to denote the bi-variate intensity vector for $j$th individual in $i$th collection. We use $N_i$ to denote the number of individuals in the $i$th collection and $C$ to denote the number of collections. The basic model for the set of intensities within each collection is a 4-class Gaussian mixture model. We have a class for each of the genotypes $\{AA, AB, BB\}$ as well as a $NULL$ outlier class to capture the clear outlying observations in each collection and to add robustness to the model fit of the other 3 genotype classes. We use $Z_{ij}$ to denote the genotype call for the $j$th individual in the $i$th collection where $Z_{ij} \in \{0, 1, 2, 3\} \equiv \{AA, AB, BB, NULL\}$. The mean and covariance matrix of the $k$th cluster in $i$th collection are denoted by $\mu_{ik}$ and $\Sigma_{ik}$ where

$$\mu_{ik} = (\mu_{ikA}, \mu_{ikB}) \quad \text{and} \quad \Sigma_{ik} = \begin{pmatrix} \sigma_{iAA}^2 & \sigma_{iAB}^2 \\ \sigma_{iAB}^2 & \sigma_{iBB}^2 \end{pmatrix}$$

so that

$$X_{ij}|Z_{ij}, \mu_{iZ_{ij}}, \Sigma_{iZ_{ij}} \sim \text{MVN}(\mu_{iZ_{ij}}, \Sigma_{iZ_{ij}}).$$

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All individuals are conditionally independent given the class labels, means and covariances which gives

$$p(X|Z, \mu, \Sigma) = \prod_{i=1}^{C} \prod_{j=1}^{N_i} p(X_{ij}|Z_{ij}, \mu_{iZ_{ij}}, \Sigma_{iZ_{ij}}). \quad (1)$$

The class labels $Z_{ij}$ depend upon a vector of class proportions for the $i$th collection which we denote as $\lambda_i = \{\lambda_{i0}, \lambda_{i1}, \lambda_{i2}, \lambda_{i3}\}$. We use a multinomial distrbution for each of the class labels such that

$$Z_{ij}|\lambda_i \sim \text{Multinomial}(1, \lambda_i),$$

and assume independence of labels within and across collections conditional upon collection genotype proportions

$$p(Z|\lambda) = \prod_{i=1}^{C} \prod_{j=1}^{N_i} p(Z_{ij}|\lambda_i). \quad (2)$$

The proportions of the classes 1–3 correspond to the genotype proportions in the collection. These proportions depend upon the allele frequency and the proportion of $NULL$ data in the $i$th collection which we denote $\alpha_i$ and $\eta_i$ respectively. Since we expect most SNPs to conform closely but not exactly to the Hardy-Weinberg Law we use a Dirichlet distribution with a variance parameter $\theta$ to model the dependence of the class proportions on $\alpha_i$ and $\eta_i$ as follows

$$\lambda_i|\alpha_i, \theta, \eta_i \sim \text{Dirichlet}((1 - \eta_i)\alpha_i^2\theta,$$
$$(1 - \eta_i)2\alpha_i(1 - \alpha_i)\theta,$$
$$(1 - \eta_i)(1 - \alpha_i)^2\theta,$$
$$\eta_i\theta ).$$

We assume independence of the genotype proportions across collections conditional on the collection allele frequencies and proportions of $NULL$ data

$$p(\lambda|\alpha, \eta) = \prod_{i=1}^{C} p(\lambda_i|\alpha_i, \eta_i, \theta). \quad (3)$$

The parameter $\theta$ is a fixed constant that controls the degree to which the data should conform to the Hardy-Weinberg Law. We have used $\theta = 10$.

We use a model for the means $\mu_i$ of each collection that is based on the following parametrisation

$$\mu = \{\mu_i; i = 1, \dots, C\}$$
$$\Rightarrow \mu' = \{c_i, l_i, g_i, f_i, d_i, \mu_{i3}; i = 1, \dots, C\}.$$

We use $c_i$, $l_i$ and $g_i$ to denote the midpoint, length and negative gradient of the line joining the centres of the homozygote clusters $\mu_{i0}$ and $\mu_{i2}$. We let $e_i$ be the point of

intersection of the line between $\mu_{i0}$ and $\mu_{i2}$ and a perpendicular line through $\mu_{i1}$. We use $f_i$ to denote the distance from $e_i$ to $\mu_{i0}$ expressed as a fraction of the length $l_i$. More specifically,

$$f_i = \frac{(\mu_{i0} - \mu_{i2}).(\mu_{i0} - \mu_{i1})}{(\mu_{i0} - \mu_{i2}).(\mu_{i2} - \mu_{i0})}.$$

Finally, we use $d_i$ to denote the distance from $\mu_{i1}$ to $e_i$ expressed as a fraction of its maximum possible distance. This maximum distance is the length of $h_i - e_i$ where $h_i$ is defined such that $\mu_{i1}$ cannot have an x-coordinate larger than the x-coordinate of $\mu_{i0}$ or a y-coordinate larger than the y-coordinate of $\mu_{i2}$. The centre of the $NULL$ class is fixed to a constant and is described in more detail below.

Given this parametrisation we model the variable components of $\mu'$ using a hierarchical structure that links the parameters of each collection together conditional upon a set of mean and variance parameters

$$\begin{aligned} p(\mu') &= \prod_{i=1}^{C} p(c_i|c_\mu, c_{\sigma^2})p(c_\mu)p(c_{\sigma^2}) \\ &\times p(l_i|l_\mu, l_{var})p(l_\mu)p(l_{var}) \\ &\times p(g_i|g_\mu, g_{var})p(g_\mu)p(g_{var}) \\ &\times p(f_i|f_\mu, f_{var})p(f_\mu)p(f_{var}) \\ &\times p(d_i|d_\mu, d_{var})p(d_\mu)p(d_{var}). \quad (4) \end{aligned}$$

The prior structure on the parameters $c_i$, $l_i$, $f_i$ and $d_i$ is as follows:

$$\begin{aligned} c_i &\sim \text{N}(c_\mu, c_{\sigma^2}I_2), \\ c_\mu &\sim \text{N}((1,1), 1), \\ c_{\sigma^2} &\sim \text{Scale} - \text{Inv} - \chi^2(0.0001, 100), \\ l_i &\sim \text{Gamma}\Big(\frac{l_\mu^2}{l_{var}}, \frac{l_\mu}{l_{var}}\Big), \\ g_i &\sim \text{Gamma}\Big(\frac{g_\mu^2}{g_{var}}, \frac{g_\mu}{g_{var}}\Big), \\ l_\mu &\sim \text{Gamma}(20, 20), \\ l_{var} &\sim \text{Gamma}(1, 100), \\ g_\mu &\sim \text{Gamma}(10, 10), \\ g_{var} &\sim \text{Gamma}(1, 100), \\ f_i &\sim \text{Beta}\Big(f_\mu \frac{1 - f_{var}}{f_{var}}, (1 - f_\mu)\frac{1 - f_{var}}{f_{var}}\Big), \\ d_i &\sim \text{Beta}\Big(d_\mu \frac{1 - d_{var}}{d_{var}}, (1 - d_\mu)\frac{1 - d_{var}}{d_{var}}\Big), \\ f_\mu &\sim \text{Beta}(30, 30), \\ f_{var} &\sim \text{Beta}(1, 100), \\ d_\mu &\sim \text{Beta}(2, 8), \\ d_{var} &\sim \text{Beta}(1, 100). \end{aligned}$$

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We use the following reparameterization of the covariance matrices $\Sigma_i$

$$
\begin{aligned}
\Sigma &= \{\Sigma_i; i = 1, \ldots, C\} \\
\Rightarrow \Sigma' &= \{\sigma_i^2, \phi_i, r_{i0}, r_{i1}, r_{i2}, \Sigma_{i3}; i = 1, \ldots, C\},
\end{aligned}
$$

where

$$
\begin{aligned}
\Sigma_{i0} &= \begin{pmatrix} \sigma_i^2 & r_{i0}\phi_i\sigma_i^2 \\ r_{i0}\phi_i\sigma_i^2 & \phi_i^2\sigma_i^2 \end{pmatrix}, \\
\Sigma_{i1} &= \begin{pmatrix} \sigma_i^2 & r_{i1}\sigma_i^2 \\ r_{i1}\sigma_i^2 & \sigma_i^2 \end{pmatrix}, \\
\Sigma_{i2} &= \begin{pmatrix} \phi_i^2\sigma_i^2 & r_{i2}\phi_i\sigma_i^2 \\ r_{i2}\phi_i\sigma_i^2 & \sigma_i^2 \end{pmatrix}.
\end{aligned}
$$

The prior structure on $\Sigma'$ is as follows

$$
\begin{aligned}
p(\Sigma') &= \prod_{i=1}^{C} p(\sigma_i | \sigma_\mu, \sigma_{var}) p(\sigma_\mu) p(\sigma_{var}) \\
&\times p(\phi_i | \phi_\mu, \phi_{var}) p(\phi_\mu) p(\phi_{var}) \\
&\times \prod_{j=1}^{3} p(r_{ij} | r_{j\mu}, r_{jvar}) \\
&\times p(r_{j\mu}) p(r_{jvar}),
\end{aligned} \tag{5}
$$

$$
\begin{aligned}
\sigma_i &\sim \mathrm{Gamma}\left(\frac{\sigma_\mu^2}{\sigma_{var}}, \frac{\sigma_\mu}{\sigma_{var}}\right), \\
\sigma_\mu &\sim \mathrm{Gamma}(1, 4), \\
\sigma_{var} &\sim \mathrm{Gamma}(1, 100), \\
\phi_i &\sim \mathrm{Beta}\left(\phi_\mu \frac{1 - \phi_{var}}{\phi_{var}}, (1 - \phi_\mu)\frac{1 - \phi_{var}}{\phi_{var}}\right), \\
\sigma_\mu &\sim \mathrm{Beta}(1, 4) \\
\sigma_{var} &\sim \mathrm{Beta}(1, 100), \\
r_{ij} &\sim \mathrm{Beta}\left(r_{j\mu}\frac{1 - r_{jvar}}{r_{jvar}}, (1 - r_{j\mu})\frac{1 - r_{jvar}}{r_{jvar}}\right), \\
r_{0\mu} &\sim \mathrm{Beta}(1, 50), \\
r_{1\mu} &\sim \mathrm{Beta}(10, 1), \\
r_{2\mu} &\sim \mathrm{Beta}(1, 50), \\
r_{0var} &\sim \mathrm{Beta}(1, 100), \\
r_{1var} &\sim \mathrm{Beta}(1, 100), \\
r_{2var} &\sim \mathrm{Beta}(1, 100).
\end{aligned}
$$

We fix the parameters of the outlier class to be a very flat density to capture outlier observation in an approximately uniform way across the intensity space.

$$
\mu_{i3} = (1, 1), \quad \Sigma_{i3} = \begin{pmatrix} 100 & 0 \\ 0 & 100 \end{pmatrix}.
$$

We model the dependency of allele frequencies across collections by conditioning on an unknown 'global' or mean allele frequency $\alpha_\mu$ and an allele frequency variance parameter $\alpha_{var}$ such that

$$
\alpha_i \sim \mathrm{Beta}\left(\alpha_\mu \frac{1 - \alpha_{var}}{\alpha_{var}}, (1 - \alpha_\mu)\frac{1 - \alpha_{var}}{\alpha_{var}}\right).
$$

For the WTCCC we use $\alpha_{var} = 0.005$ and $\alpha_\mu \sim \mathrm{Beta}(1, 1)$. Further, we allow for additional prior information on the allele frequency of the collections through the specification of an extra fixed allele frequency $\alpha'$ with distribution

$$
\alpha' \sim \mathrm{Beta}\left(\alpha_\mu \frac{1 - \alpha'_{var}}{\alpha'_{var}}, (1 - \alpha_\mu)\frac{1 - \alpha'_{var}}{\alpha'_{var}}\right).
$$

In the current implementation we have set $\alpha'$ equal to the empirical allele frequency of the SNP from the CEU HapMap population if available and set $\alpha'_{var} = 0.01$. Overall, the distribution for $\alpha$ is given by

$$
p(\alpha) = \prod_{i=1}^{C} p(\alpha_i | \alpha_\mu, \alpha_{var}) p(\alpha_\mu) p(\alpha' | \alpha_\mu). \tag{6}
$$

We model dependency of the $NULL$ class proportions across collections by conditioning on an unknown mean proportion $\eta_\mu$ and a variance parameter $\eta_{var}$ such that

$$
\eta_i \sim \mathrm{Beta}\left(\eta_\mu \frac{1 - \eta_{var}}{\eta_{var}}, (1 - \eta_\mu)\frac{1 - \eta_{var}}{\eta_{var}}\right),
$$

so that

$$
p(\eta) = \prod_{i=1}^{C} p(\eta_i | \eta_\mu, \eta_{var}) p(\eta_\mu) p(\eta_{var}), \tag{7}
$$

$$
\eta_\mu \sim \mathrm{Beta}(3, 100), \quad \eta_{var} \sim \mathrm{Beta}(5, 100).
$$

Overall, the posterior distribution is constructed using equations (1), (2), (3), (4), (5), (6) and (7) to give

$$
\begin{aligned}
p(Z, &\mu, \Sigma, \lambda, \alpha, \eta | X) \propto \\
&p(X | Z, \mu, \Sigma)\, p(\mu')\, p(\Sigma') \\
&\times p(Z | \lambda)\, p(\lambda | \alpha, \eta)\, p(\alpha)\, p(\eta).
\end{aligned} \tag{8}
$$

## Software

A C++ implementation of the algorithm called CHIAMO* is available. Separate normalization software is also available. Please email Jonathan Marchini at `marchini@stats.ox.ac.uk` in the first instance to obtain this software.

---

*chiamo means 'I call' in Italian and is derived from the verb chiamare.

7

# Membership

The following individuals were responsible for the stated activities within the WTCCC

**Study Working Group (2003-2005):** Lon R. Cardon, David G. Clayton, Panos Deloukas, Peter Donnelly, Marcus Pembrey, David P. Strachan, John A. Todd, David R. Bentley (Chair);

**Publications Committee:** Nick Craddock, Peter Donnelly, Willem H. Ouwehand, Nilesh J. Samani, Mark I. McCarthy (Chair);

**Writing Committee:** David G. Clayton, Nick Craddock, Panos Deloukas, Mark I. McCarthy, Peter Donnelly (Chair);

**Joint Steering Committee:** Simon Cawley, Alan Dance*, Hossein Fakhrai-Rad, Rui Mei*, Raji Pillai (Affymetrix); Suzannah J. Bumpstead, Claire Bryan, David G. Clayton, Lon R. Cardon, Panos Deloukas*, Sarah Nutland, Simon Potter, Helen E. Stevens, John A. Todd*, Neil M. Walker, Pamela Whittaker (*=voting member).

## Membership of BRAGGS and BCSC

### BRAGGS

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### Breast Cancer Susceptibility Collaboration (UK)

The Breast Cancer Susceptibility Collaboration (UK) consists of the following contributors:

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1. O'Hagan, A. and Forster, J. *Bayesian Inference.* Arnold, (2004).

2. Jordan, M. I., editor. *Learning in Graphical Models.* Kluwer Academic Publishers, (1998).

3. Balding, D. J. A tutorial on statistical methods for population association studies. *Nature Reviews Genetics* **7**, 781–791 (2006).

4. Jong-Wuu, W., Wen-Liang, H., and Lee, H. Some moments and limit behaviours of the generalized logistic distribution with applications. *Proc. Natl. Sci, Counc. ROC(A)* **24**(1), 7–14.

5. Bolstad, B. M., A., I. R., strand, M., and Speed, T. P. A comparison of normalization methods for high density oligonucleotide array data based on variance and bias. *Bioinformatics* **19**, 185–193 (2003).

6. Rabbee, N. and Speed, T. A genotype calling algorithm for affymetrix snp arrays. *Bioinformatics* **22**(1), 7–12 (2006).

8
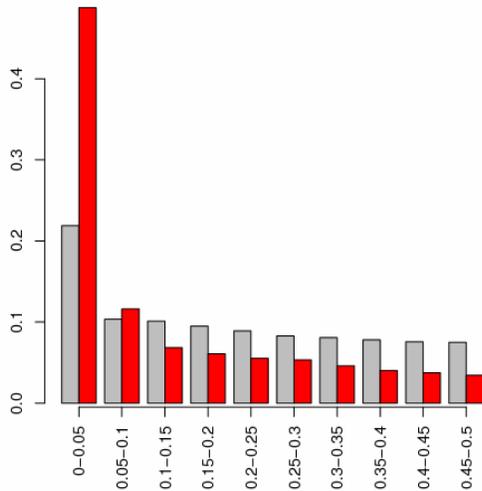
**Supplementary Figure 1 | Minor allele frequency (MAF) spectrum of SNPs included and excluded from the study.** Red bars show the proportion of SNPs excluded from the study (see text and Methods) in 10 MAF bins. Grey bars show the frequency spectrum of included SNPs.

a)



b)
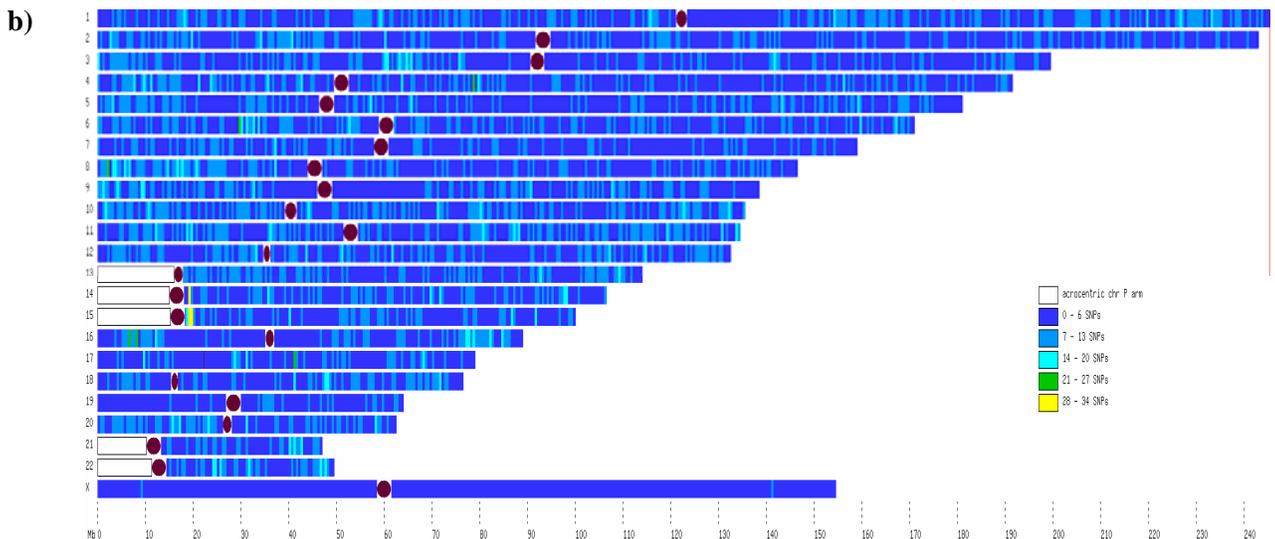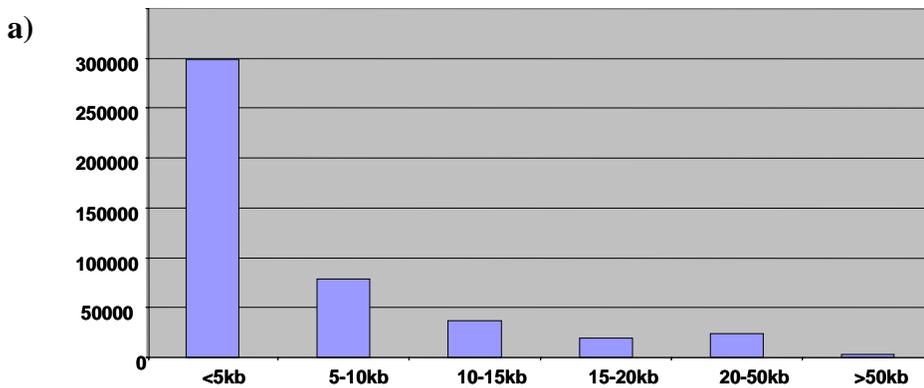


**Supplementary Figure 2 | Marker density on the Affymetrix 500k chip.** Distribution of SNP markers on the 500K Affymetrix array based on QC. a) Distribution of inter-marker distances for the ~459,000 autosomal SNPs Passing QC filters. b) Chromosomal distribution of SNPs failing QC criteria in 500 kb windows. Each window is coloured according to SNP density as follows 0-6, blue; 7-13, light blue; 14-20 turquoise; 21-27, green; and 28-34 yellow. Centromeres are depicted as black ovals and the p-arm of the acrocentric chromosomes as white rectangles.
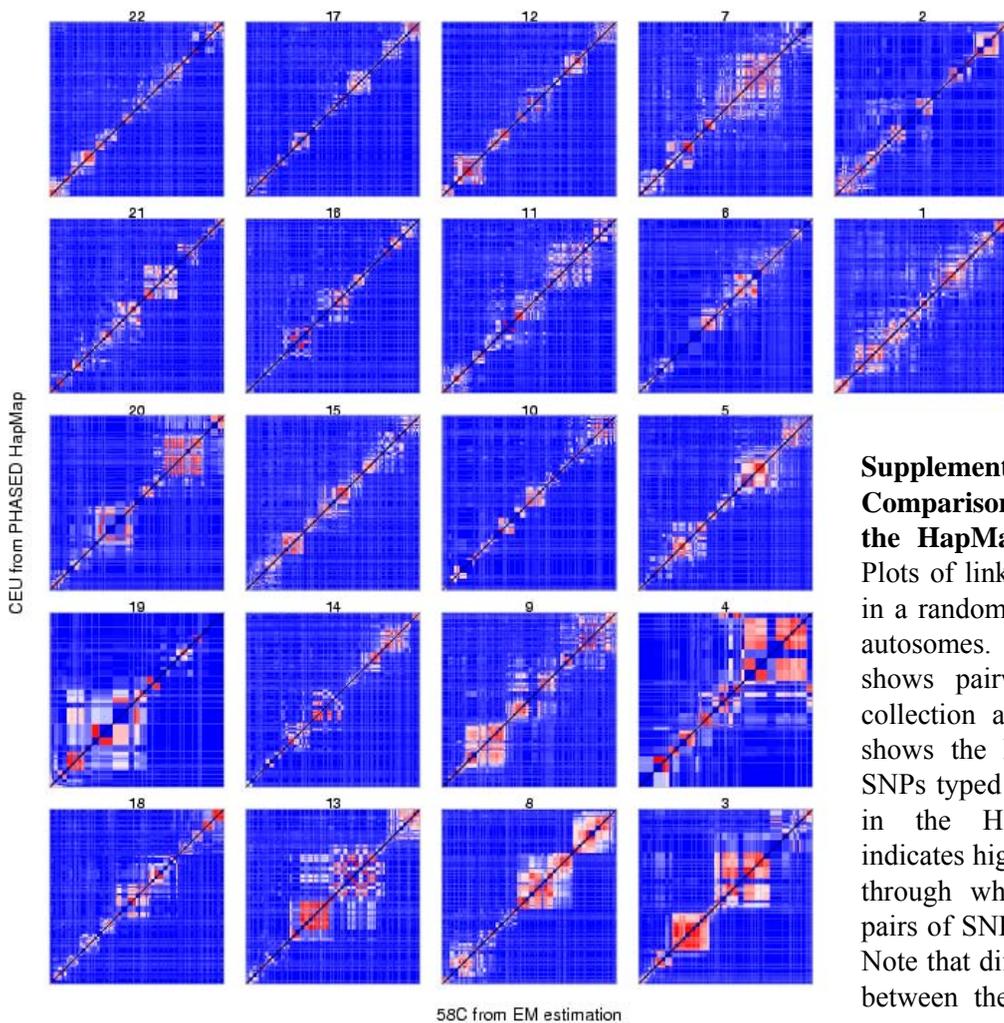
**Supplementary Figure 3 | Comparison of patterns of LD in the HapMap and the WTCCC.** Plots of linkage disequilibrium (r2) in a random 1Mb from each of the autosomes. The lower diagonal shows pairwise LD in the 58C collection and the upper diagonal shows the LD between the same SNPs typed in the CEU population in the HapMap sample. Red indicates high r2, strong correlation, through white and then blue for pairs of SNPs with low correlation. Note that difference in SNP density between the regions can alter the appearance. See Methods.



**Supplementary Figure 4 | Geographical region definitions.** Geographical regions are defined by postcode and their boundaries do not necessarily coincide with current administrative boundaries. For example, part of Wales falls within the SY postcode which is assigned to the "Midlands" region (however this is an area of low population density). The correspondence between postcode and region is shown in the relevant section of the Supplementary Information.

**Supplementary Figure 5 | Multidimensional Scaling (MDS).** WTCCC and HapMap samples plotted for the first two principal components obtained by multidimensional scaling of a matrix of pairwise IBS values between samples. Samples near the YRI cluster were subsequently identified in sample records as Afro-Caribbean; the large cluster one-third of the way between CEU and CHB+JPT were subsequently identified as South Asian (India/Pakistan). Samples showing evidence of non-European ancestry were excluded from further analyses (grey crosses).
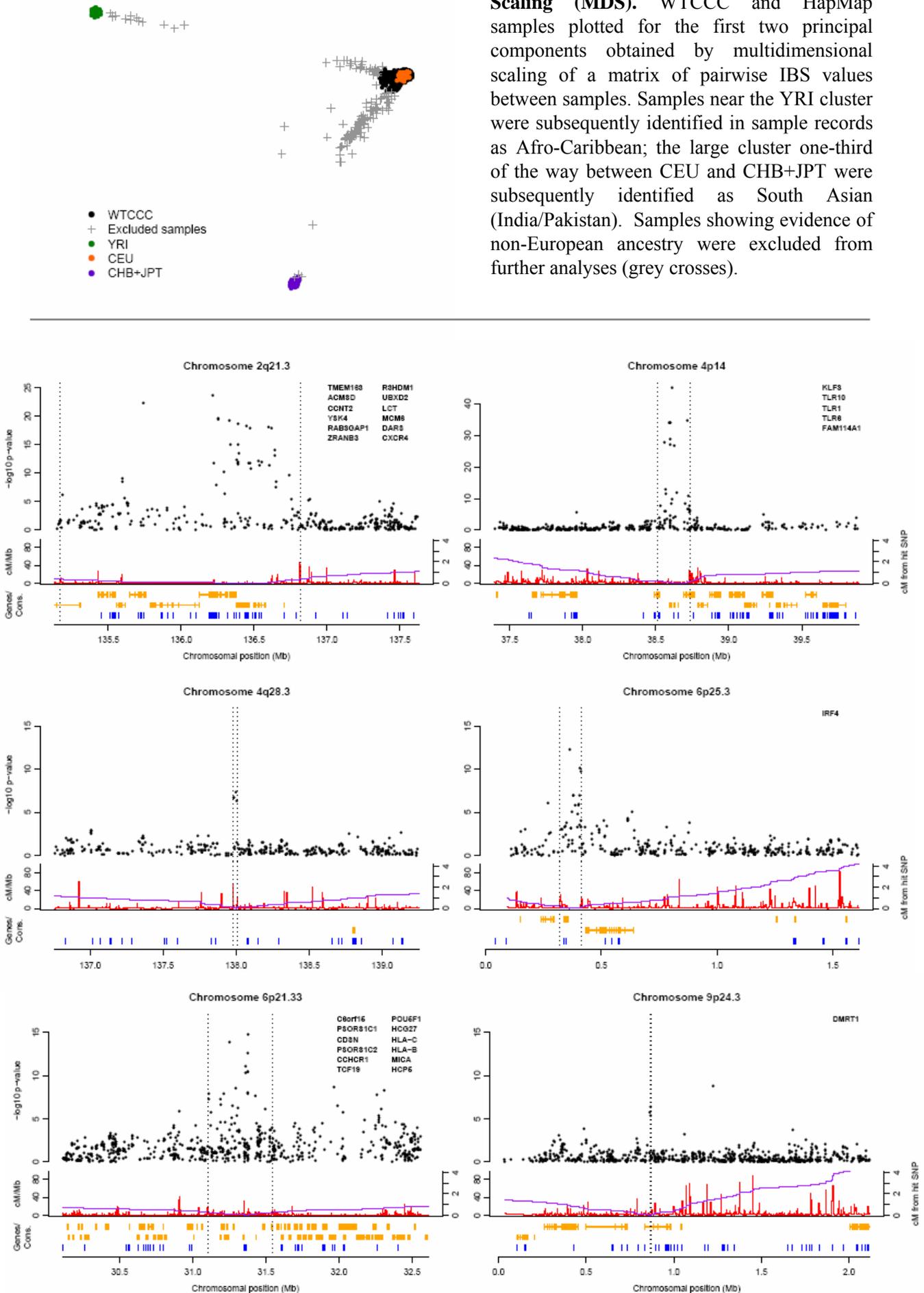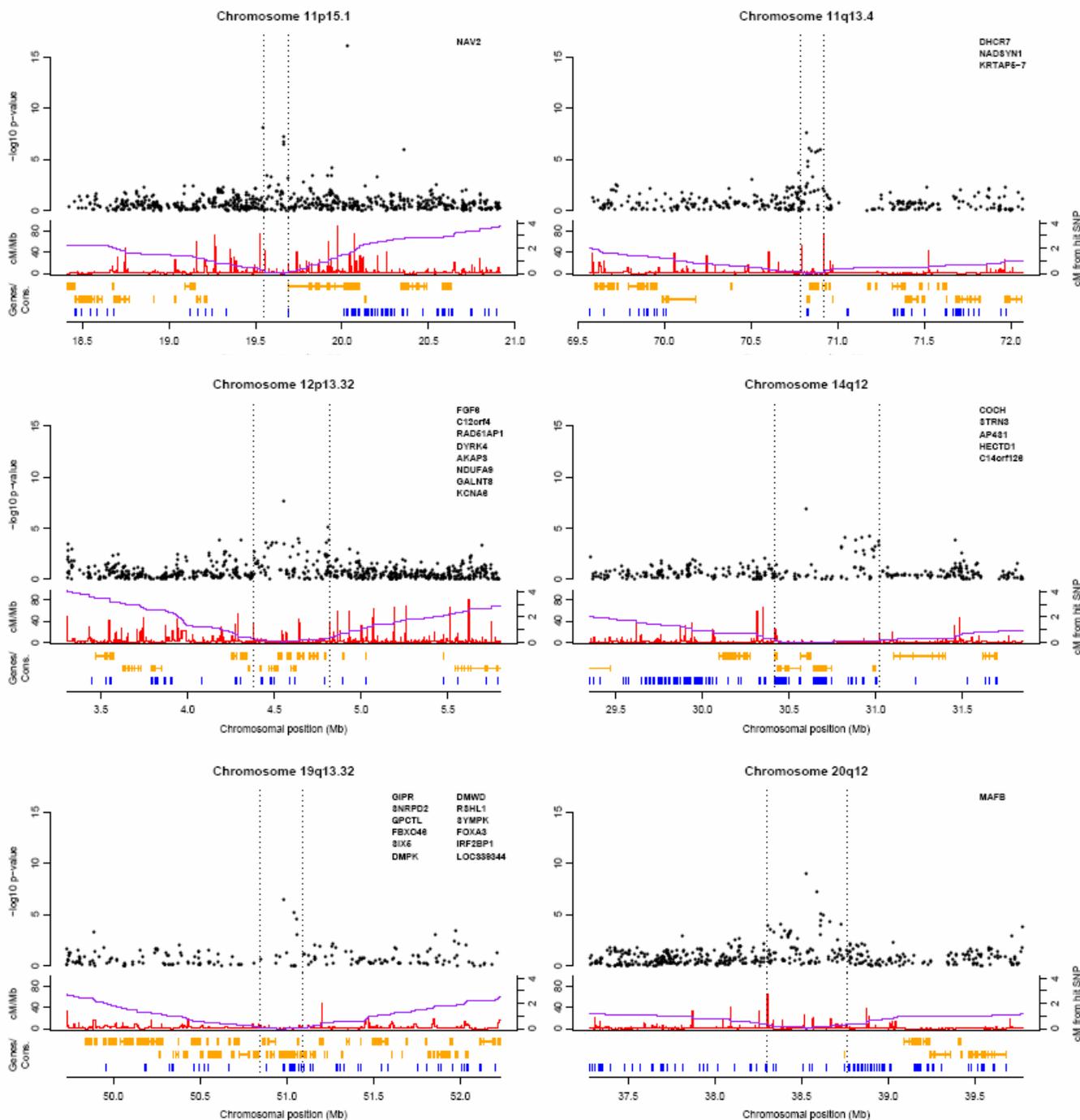
**Supplementary Figure 6 | Signal plots for regions of strong geographic differentiation.** Characteristics of genomic regions with strong evidence for geographic differentiation between WTCCC samples. Region boundaries (vertical dotted lines) were chosen to coincide with locations where test statistics returned to background levels and, where possible, recombination hotspots. Top panel: -log10 p-values for an 11 d.f. test for allele frequency differences between geographic regions. See Methods. Note that the y-axis scales used for regions 2q21 and 4p14 differ from each other and from the scale used in all other plots in this figure. Middle panel: Fine-scale recombination rate (cM/Mb). The purple line shows the cumulative genetic distance (in cM) from the hit SNP. Bottom panel: Known genes and sequence conservation in 17 vertebrates. Genes (orange) in the hit region are listed in the upper righthand part of each plot in chromosomal order, starting at the lefthand edge of the region. The top track shows plus-strand genes and the middle track shows minus-strand genes. Sequence conservation (bottom track) scores are based on the phylogenetic hidden Markov model phastCons. Highly conserved regions (phastCons score ≥600) are shown in blue. Further instruction on interpreting these plots can be found in the Supplementary Information.

**Supplementary Figure 7 | Geographic frequency of highly differentiated SNPs.** Minor allele frequencies (%) by geographical region for the 13 SNPs listed in Main Table 1 (data from all 9 collections). Figures in each geographical region give the frequency of the (British-wide) minor allele. Shading goes from darker to lighter as this frequency decreases.
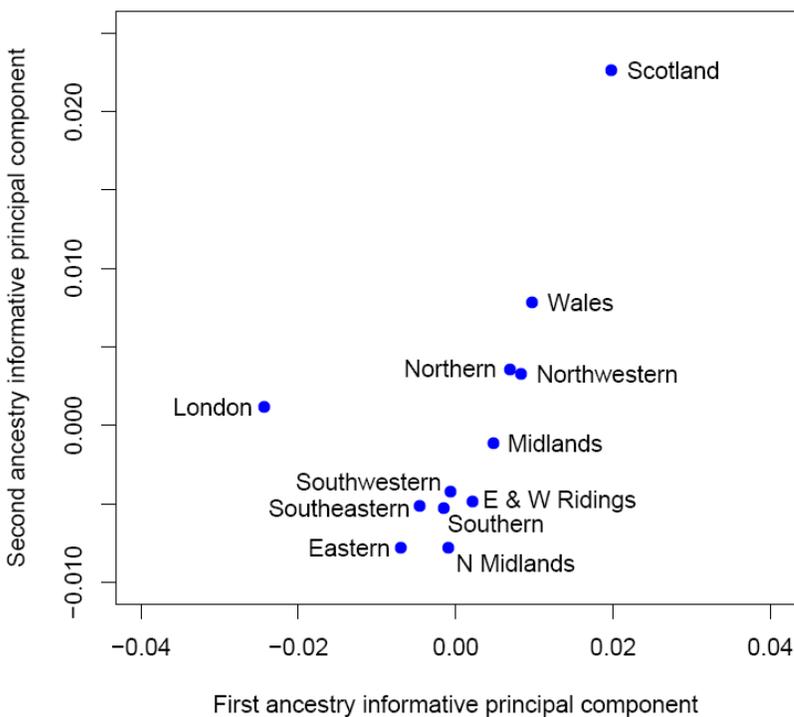


**Supplementary Figure 8 | UK geographic population structure.** Means, by geographical region, of the two principal components we judged to be informative of ancestral population admixture. Note that the means reflect the geographical configuration of the regions to some extent, confirming that the principal components are informative about geographical population structure. However, the distributions of principal component scores for individuals from each region overlap very extensively (data not shown), indicating that the population structure is very weak.
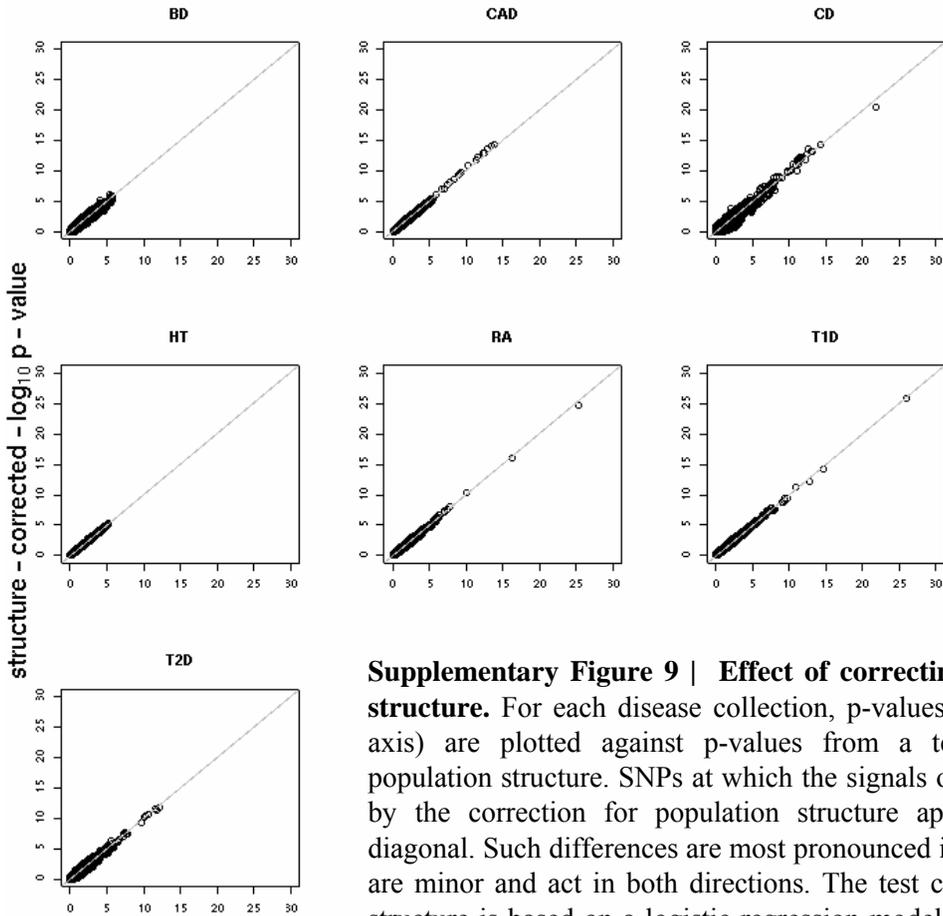
**Supplementary Figure 9 | Effect of correcting tests for population structure.** For each disease collection, p-values from the trend test (x-axis) are plotted against p-values from a test which corrects for population structure. SNPs at which the signals of association is affected by the correction for population structure appear as points off the diagonal. Such differences are most pronounced in CD, BD and T2D, but are minor and act in both directions. The test correcting for population structure is based on a logistic regression model which includes the two ancestry informative principal components as covariates (while the trend test is equivalent to a score test in a logistic regression model with no covariates).
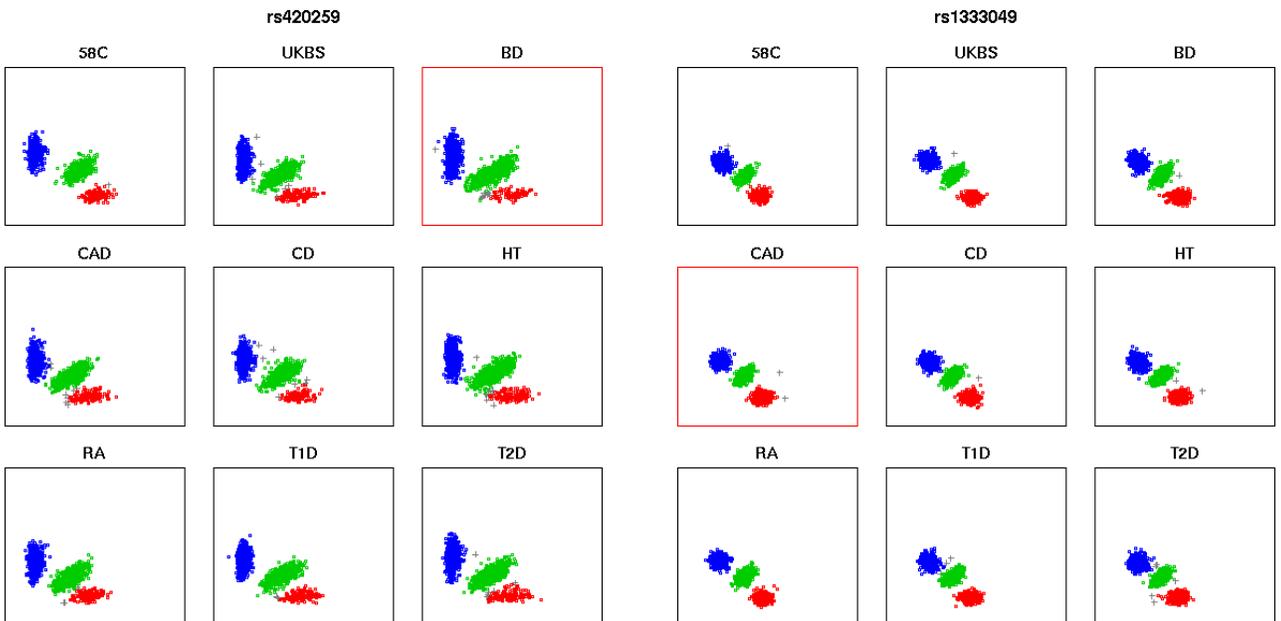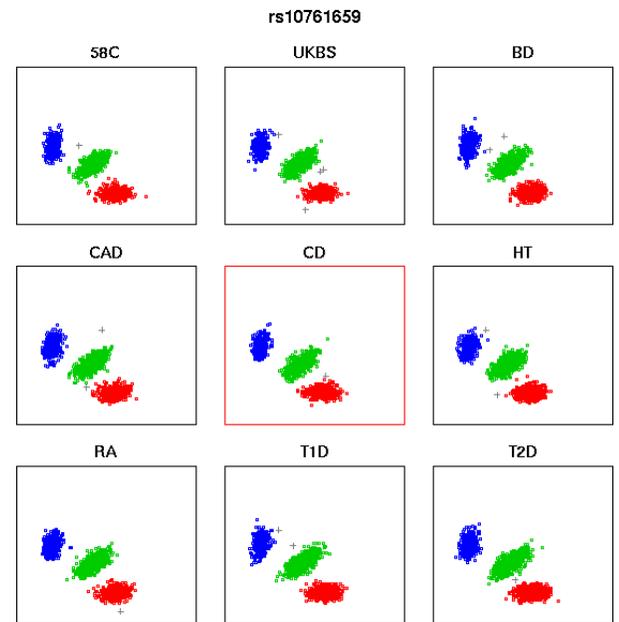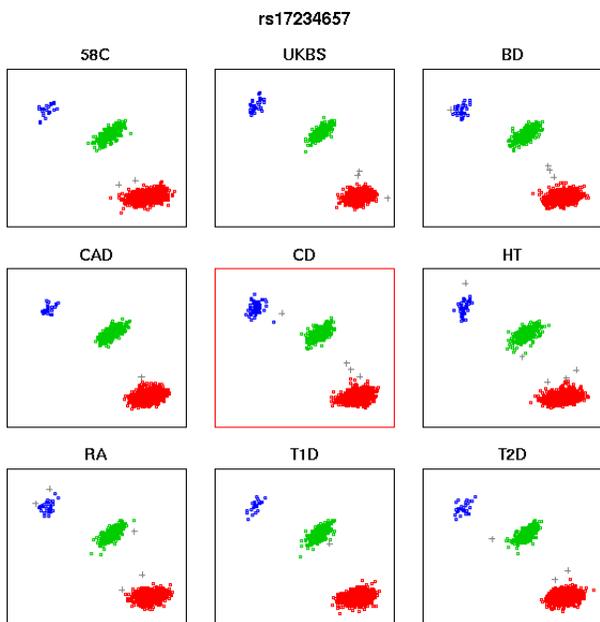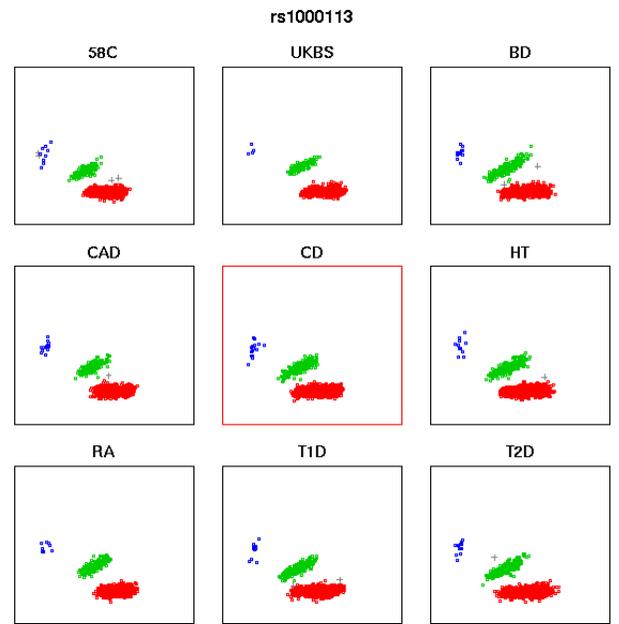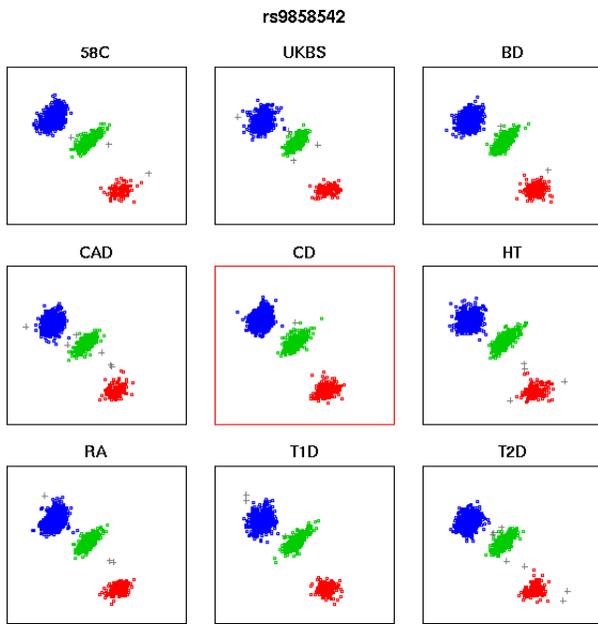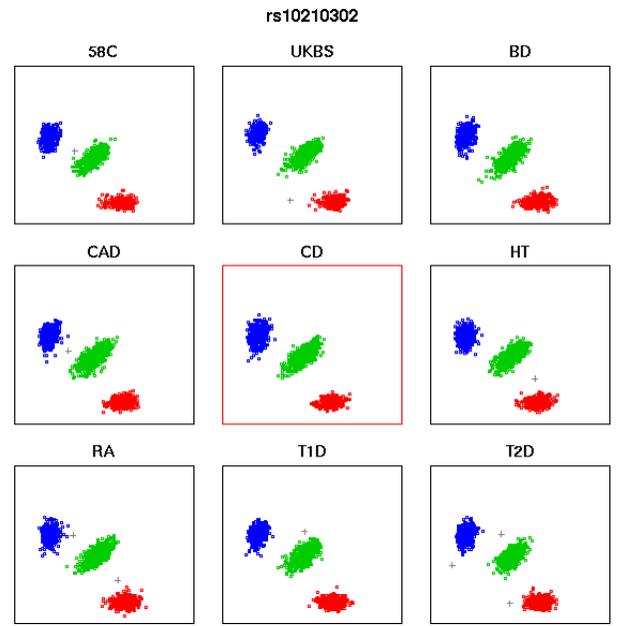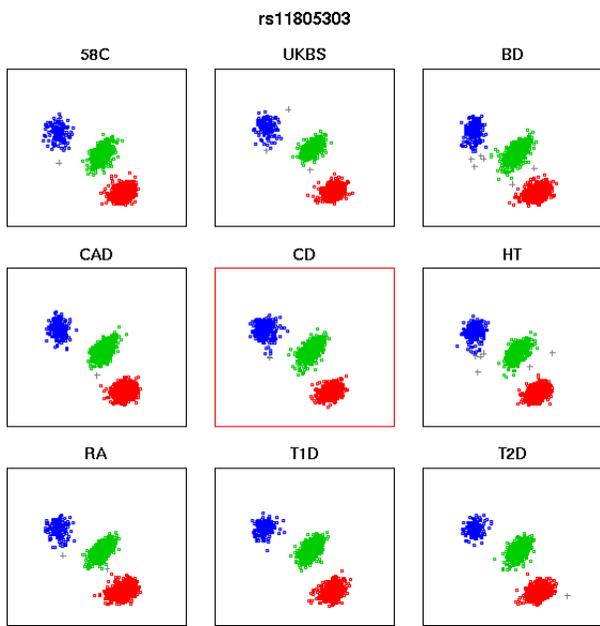
rs10883365

| 58C | UKBS | BD |
| CAD | CD | HT |
| RA | T1D | T2D |

rs17221417

| 58C | UKBS | BD |
| CAD | CD | HT |
| RA | T1D | T2D |

rs2542151

| 58C | UKBS | BD |
| CAD | CD | HT |
| RA | T1D | T2D |

rs6679677

| 58C | UKBS | BD |
| CAD | CD | HT |
| RA | T1D | T2D |

rs6679677

| 58C | UKBS | BD |
| CAD | CD | HT |
| RA | T1D | T2D |

rs11171739

| 58C | UKBS | BD |
| CAD | CD | HT |
| RA | T1D | T2D |
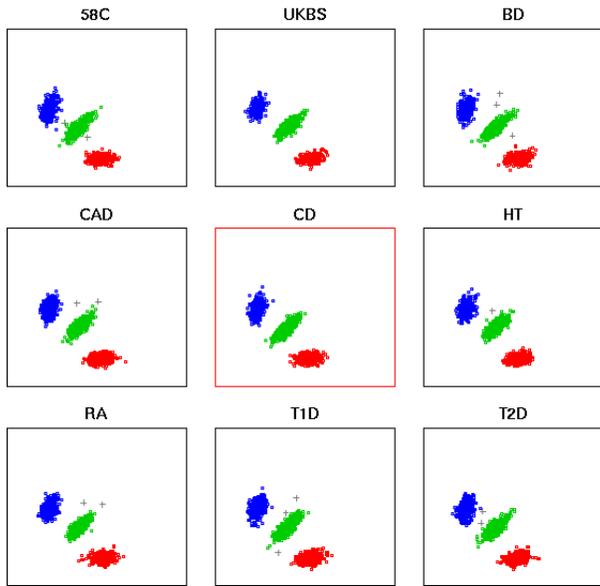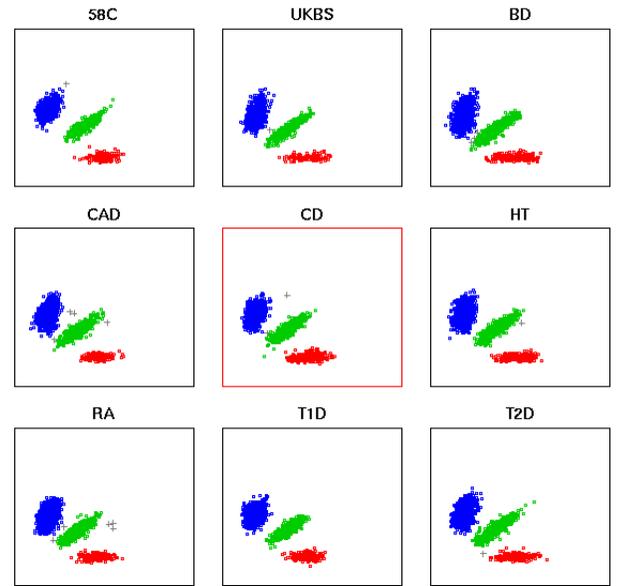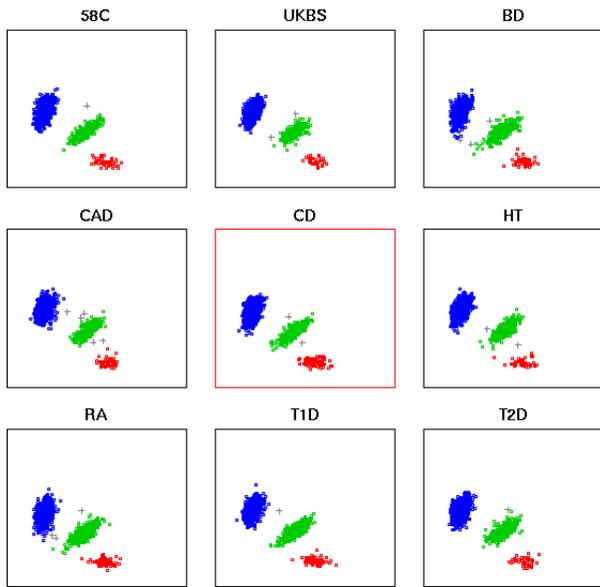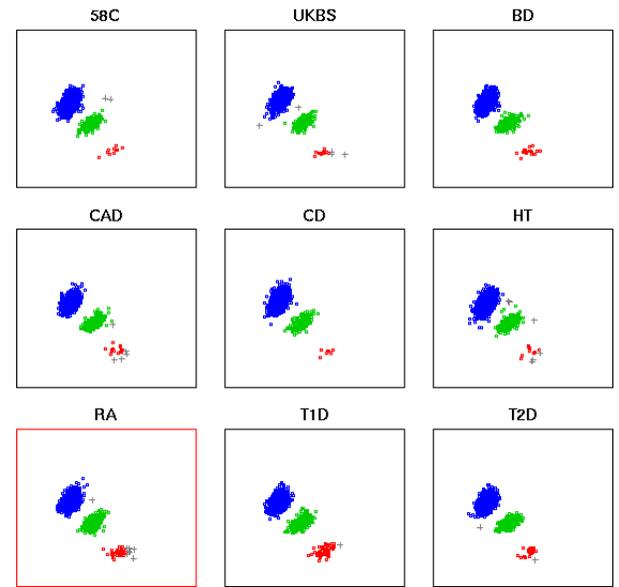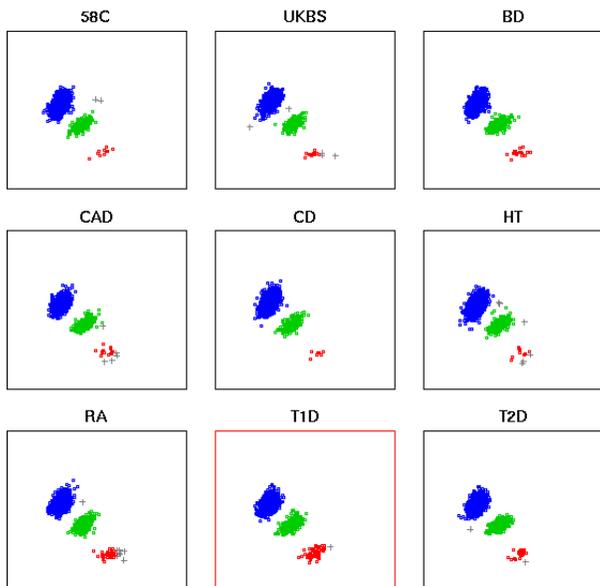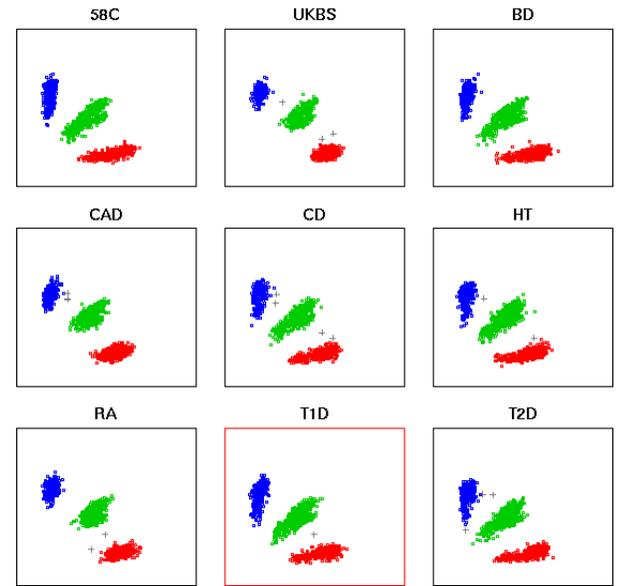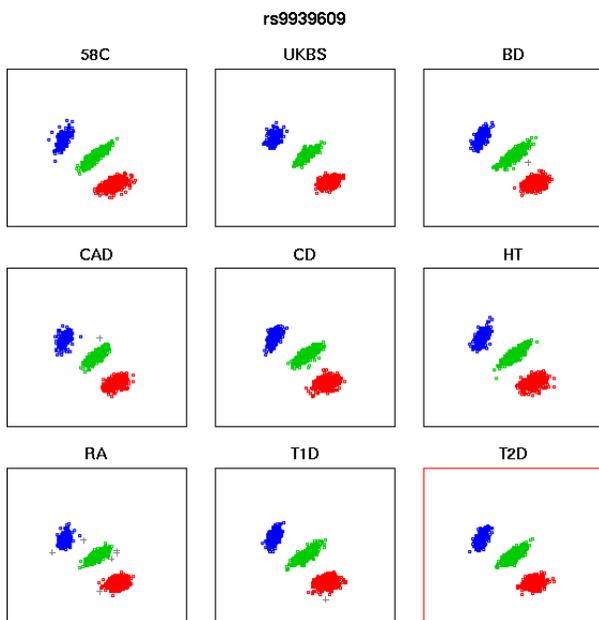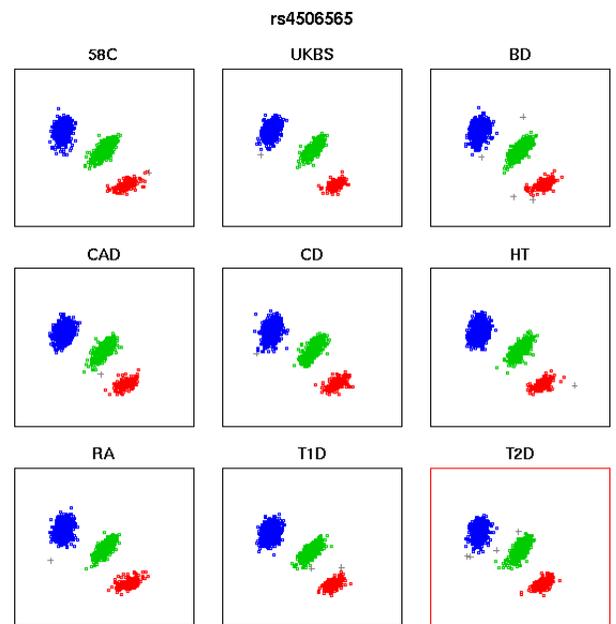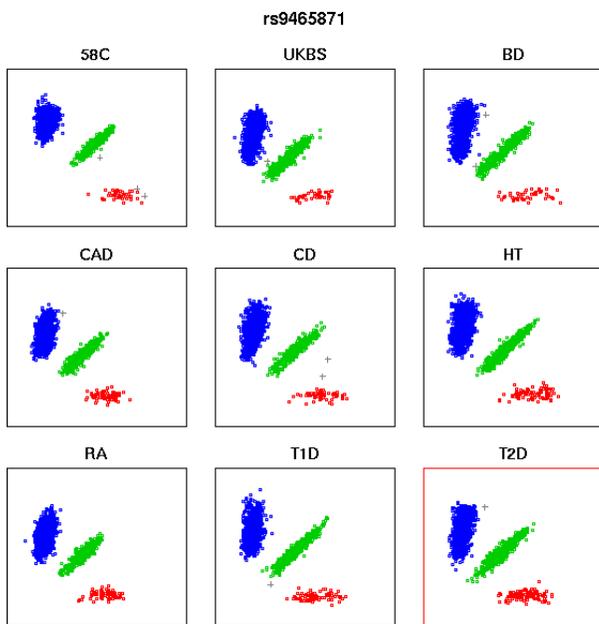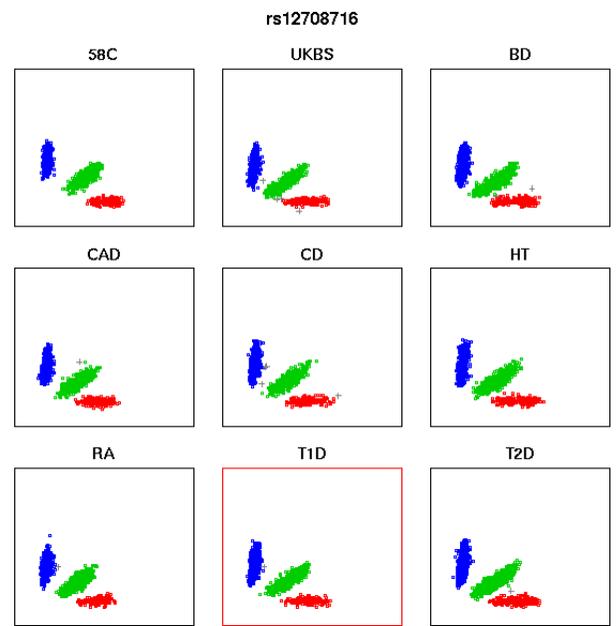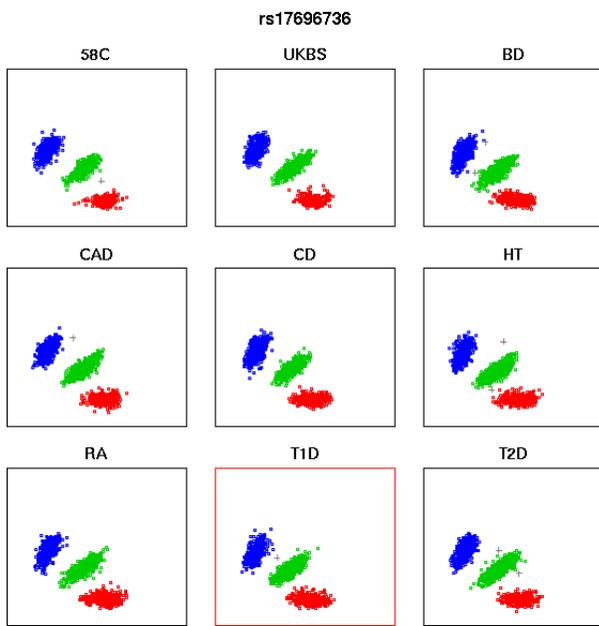
**Supplementary Figure 10 | Cluster plots for SNPs showing strong association to disease status.** For an example SNP, scatter plots of normalized probe intensities for each individual, coloured by the CHIAMO genotype call for that individual, with each collection shown in a separate plot. Homozygotes for the two different alleles are in blue and red, and heterozygotes in green. Genotypes called as missing are shown as grey crosses. Note that the density of each genotype cloud is high and that subjects on the exclusion list are not plotted. See Supplementary Information.

**RA hit region, chromosome 7**
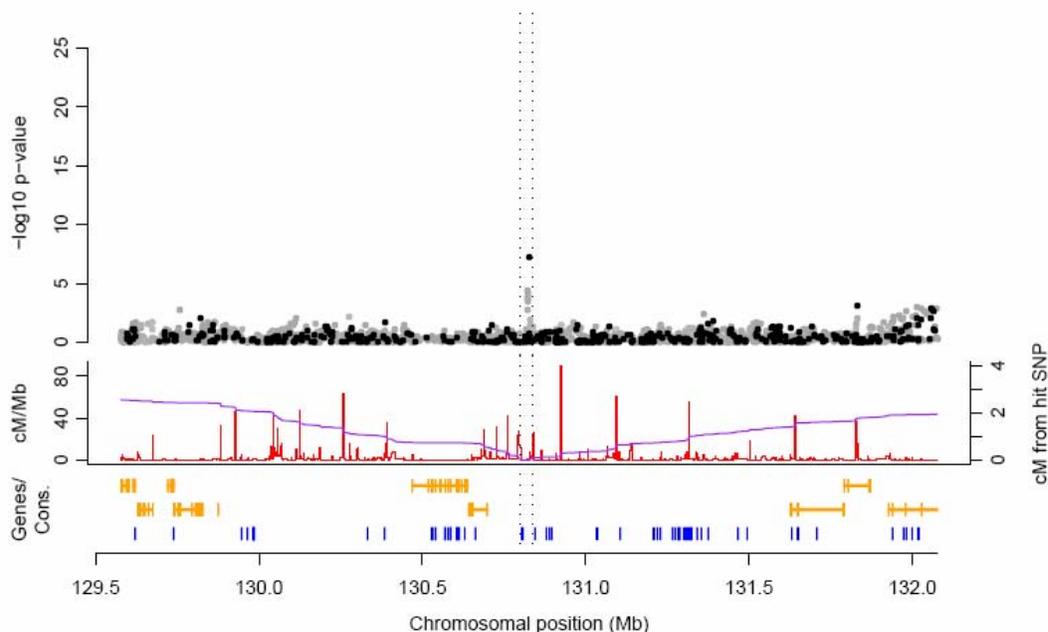
**Supplementary Figure 11 | Signal plot for region identified by the sex-differentiated test.** Characteristics of genomic region surrounding the hit SNP identified by the sex-differentiated test. Since further analysis suggested that the association was considerably stronger in females, this figure displays the results of an analysis which uses only females. Region boundaries (vertical dotted lines) were chosen to coincide with the recombination hotspots immediately flanking the hit SNP. Top panel: -log10 p-values for the (1 d.f.) trend test calculated using only females. Black points represent SNPs typed in the study, and grey points represent SNPs whose genotypes were imputed. SNPs imputed with higher confidence are shown in darker grey. Middle panel: Fine-scale recombination rate (cM/Mb). The purple line shows the cumulative genetic distance (in cM) from the hit SNP. Bottom panel: Known genes and sequence conservation in 17 vertebrates. No genes (orange) lie in the hit region, so none is listed on the plot. The top track shows plus-strand genes and the middle track shows minus-strand genes. Sequence conservation (bottom track) scores are based on the phylogenetic hidden Markov model phastCons . Highly conserved regions (phastCons score ≥600) are shown in blue. Further instruction on interpreting these plots can be found in the Supplementary Information.



**T1D hit region, chromosome 4**

**T1D hit region, chromosome 12**
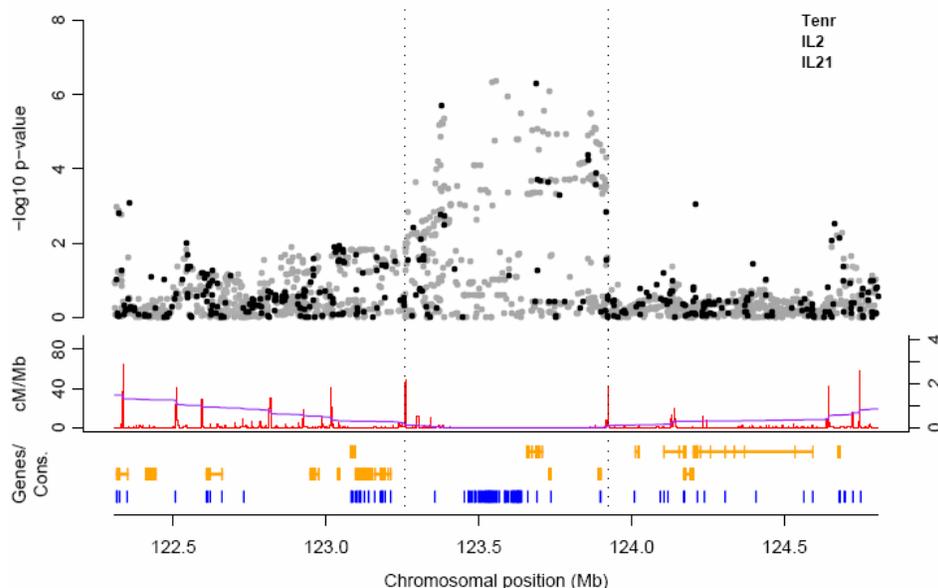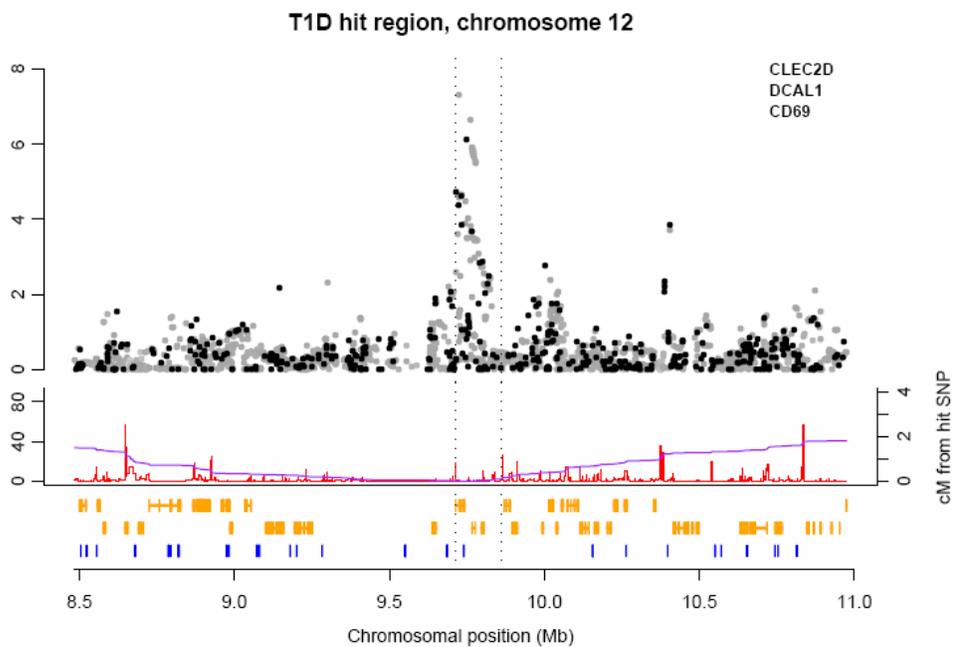
**Supplementary Figure 12 | Signal plots for regions identified through imputation.** Characteristics of genomic regions that reached a p-value threshold of 5x10-7 only at imputed SNPs. Region boundaries (vertical dotted lines) were chosen to coincide with locations where test statistics returned to background levels and, where possible, recombination hotspots. Top panel: -log10 p-values for the frequentist test with the smallest p-value at the imputed hit SNP. Black points represent SNPs typed in the study, and grey points represent SNPs whose genotypes were imputed. SNPs imputed with higher confidence are shown in darker grey. Middle panel: Fine-scale recombination rate (cM/Mb). The purple line shows the cumulative genetic distance (in cM) from the hit SNP. Bottom panel: Known genes and sequence conservation in 17 vertebrates. Genes (orange) in the hit region are listed in the upper righthand part of each plot in chromosomal order, starting at the lefthand edge of the region. The top track shows plus-strand genes and the middle track shows minus-strand genes. Sequence conservation (bottom track) scores are based on the phylogenetic hidden Markov model phastCons . Highly conserved regions (phastCons score ≥600) are shown in blue. Further instruction on interpreting these plots can be found in the Supplementary Information.

**Supplementary Figure 13 | Signal plots for regions identified by pooling T1D and RA cases.** Characteristics of genomic regions surrounding hit SNPs found by combining case groups. Region boundaries (vertical dotted lines) were chosen to coincide with locations where test statistics returned to background levels and, where possible, recombination hotspots. Top panel: -log10 p-values for the trend test in pooled cases (black dots), T1D cases (blue crosses), and RA cases (red triangles). Middle panel: Fine-scale recombination rate (cM/Mb). The purple line shows the cumulative genetic distance (in cM) from the hit SNP. Bottom panel: Known genes and sequence conservation in 17 vertebrates. Genes (orange) in the hit region are listed in the upper righthand part of each plot in chromosomal order, starting at the lefthand edge of the region. The top track shows plus-strand genes and the middle track shows minus-strand genes. Sequence conservation (bottom track) scores are based on the phylogenetic hidden Markov model phastCons . Highly conserved regions (phastCons score ≥600) are shown in blue. Further instruction on interpreting these plots can be found in the Supplementary Information.

**Supplementary Figure 14 | Signal plots for regions identified by pooling T1D, RA, and CD cases.**
Characteristics of genomic regions surrounding hit SNPs identified by combining case groups. Region boundaries (vertical dotted lines) were chosen to coincide with locations where test statistics returned to background levels and, where possible, recombination hotspots. Top panel: -log10 p-values for the trend test in pooled cases (black dots), T1D cases (blue crosses), RA cases (red triangles), and CD cases (green squares). Middle panel: Fine-scale recombination rate (cM/Mb). The purple line shows the cumulative genetic distance (in cM) from the hit SNP. Bottom panel: Known genes and sequence conservation in 17 vertebrates. Genes (orange) in the hit region are listed in the upper righthand part of each plot in chromosomal order, starting at the lefthand edge of the region. The top track shows plus-strand genes and the middle track shows minus-strand genes. Sequence conservation (bottom track) scores are based on the phylogenetic hidden Markov model phastCons . Highly conserved regions (phastCons score ≥600) are shown in blue. Further instruction on interpreting these plots can be found in the Supplementary Information.



**Supplementary Figure 15 | Estimated odds ratios for strong associations.** Bar chart showing the estimated odds ratio for the SNPs outside HLA in Table 3. The left-hand bar for each SNP shows the estimated odds for each additional copy of the risk allele in a disease model which is additive on the log-odds scale. The central and right-hand bars show odds ratios estimated separately for the heterozygote and the homozygote for the risk allele. Note that because of the "winner's curse" odds ratios will tend to be overestimated for loci discovered in our study. The loci are ordered by the height of the left-hand bar.
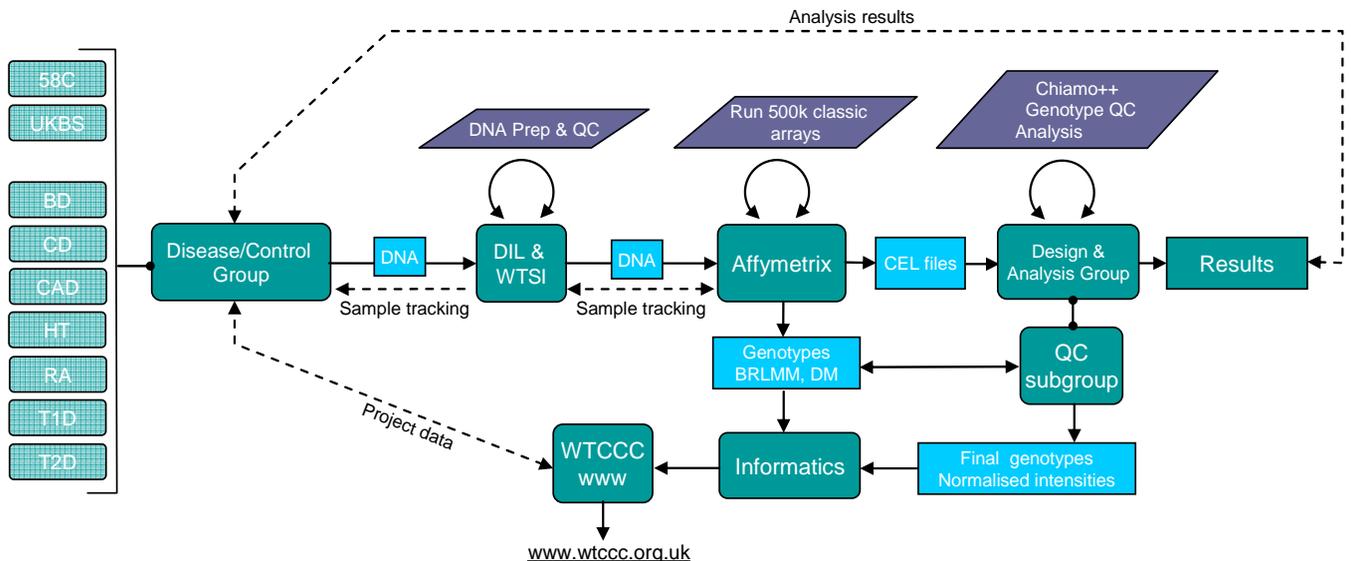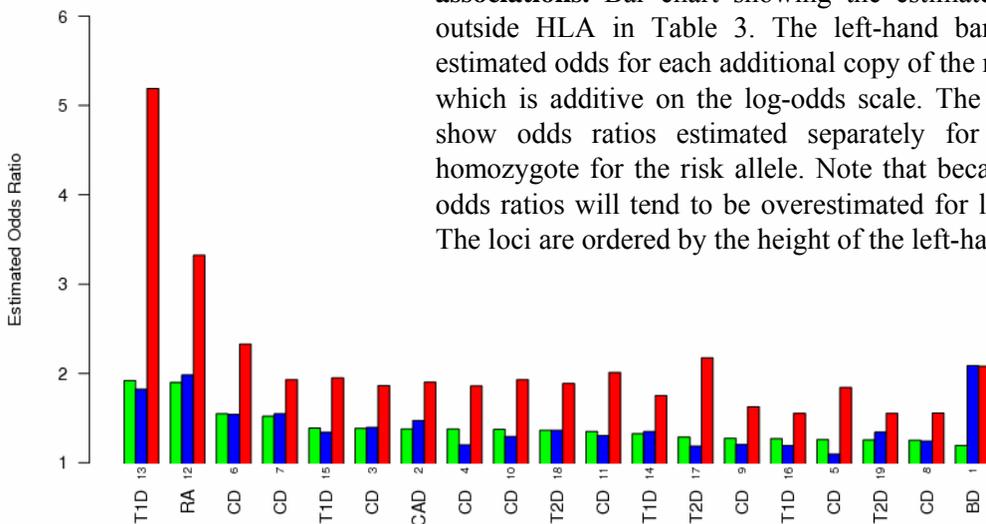
**Supplementary Figure 16 | Workflow for the WTCCC**. Initial DNA processing, QC and tracking steps were undertaken at the Wellcome Trust/JDRF Diabetes and Inflammation Laboratory (DIL) and the Wellcome Trust Sanger Institute (WTSI) in the United Kingdom. Re-arrayed plates of DNA were shipped to Affymetrix in the United States for outsourced genotyping. Raw intensity information from the Affymetrix platform was shipped back to the UK for genotype calling (CHIAMO) by the WTCCC Design and Analysis Group (DAG). The size and volume of this information exceeded the capacity for transfer over the internet and necessitated shipping of physical hard disks. The BRLMM and DM genotype calls were not used by the WTCCC, but are shown to emphasize their availability for external access via the Data Access Committee.
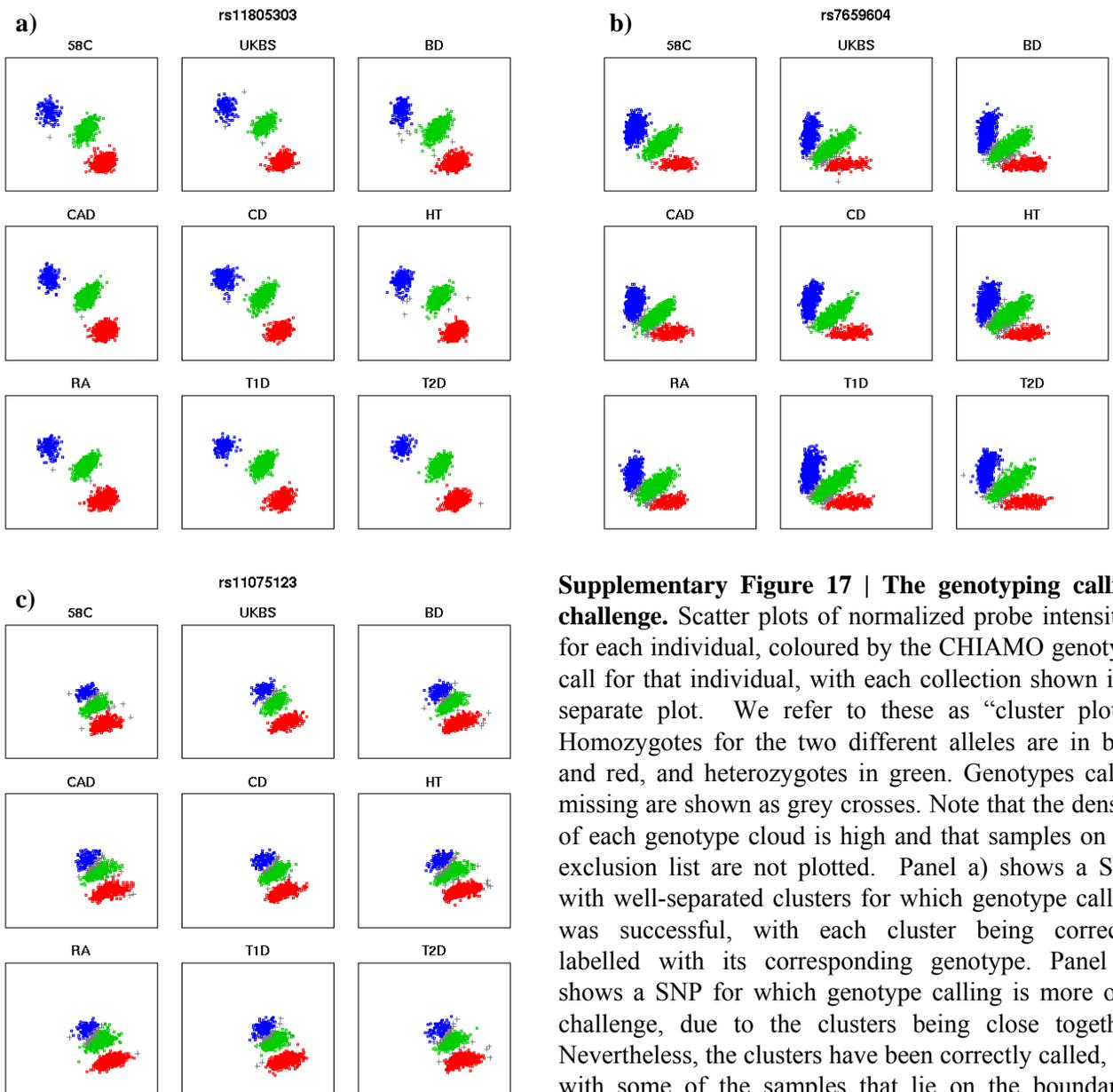


**Supplementary Figure 17 | The genotyping calling challenge.** Scatter plots of normalized probe intensities for each individual, coloured by the CHIAMO genotype call for that individual, with each collection shown in a separate plot. We refer to these as "cluster plots". Homozygotes for the two different alleles are in blue and red, and heterozygotes in green. Genotypes called missing are shown as grey crosses. Note that the density of each genotype cloud is high and that samples on the exclusion list are not plotted. Panel a) shows a SNP with well-separated clusters for which genotype calling was successful, with each cluster being correctly labelled with its corresponding genotype. Panel b) shows a SNP for which genotype calling is more of a challenge, due to the clusters being close together. Nevertheless, the clusters have been correctly called, but with some of the samples that lie on the boundaries between clusters being called as missing (they are shown as grey crosses). Panel c) shows a SNP for which genotype calling is problematic, due to two clusters being very close together but separated from the third cluster. While the clusters have been correctly called, many samples with signals lying between the two adjacent clusters are called as missing, causing bias in allele frequency estimates.
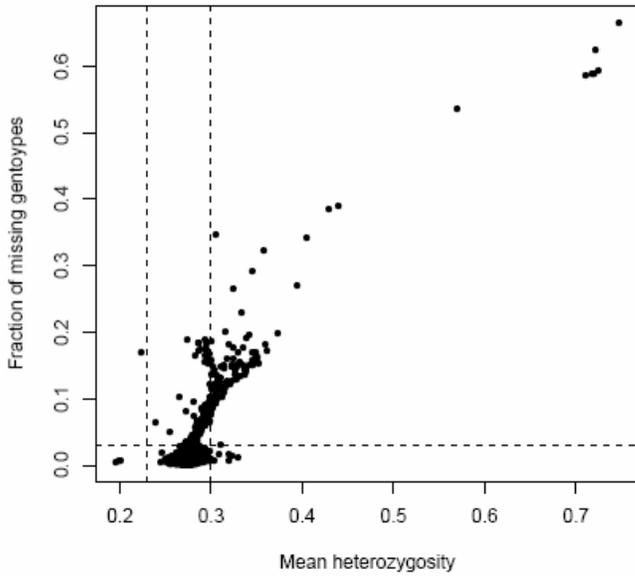
**Supplementary Figure 18 | Individual missing data and heterozygosity.** Scatter plot of the proportion of SNPs called heterozygote (x-axis) against the proportion called missing at a posterior probability threshold of 0.9 (y-axis) for each individual in the study. Dotted lines delimit the threshold used for exclusion of individuals from further analysis.
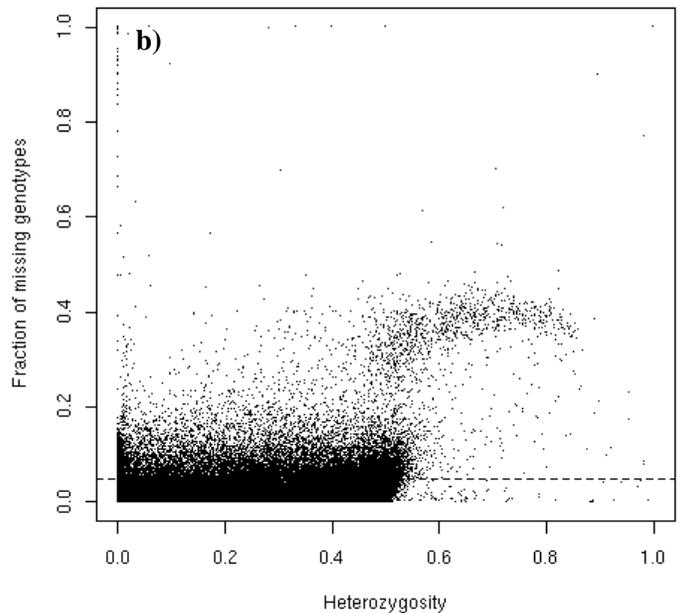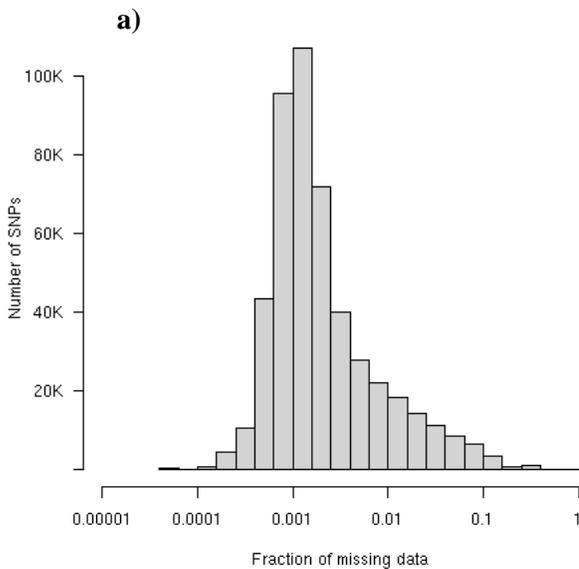


**Supplementary Figure 19 | Missing data and heterozygosity per SNP.** a) Histogram of proportion of individuals called missing for each SNP (i.e with posterior probability < 0.9) b) Scatter plot of the proportion of individuals called heterozygote (x-axis) against the proportion called missing at a posterior probability threshold of 0.9 (y-axis) for each SNP assayed. The dotted line shows the threshold over which a SNP was excluded from further analyses.
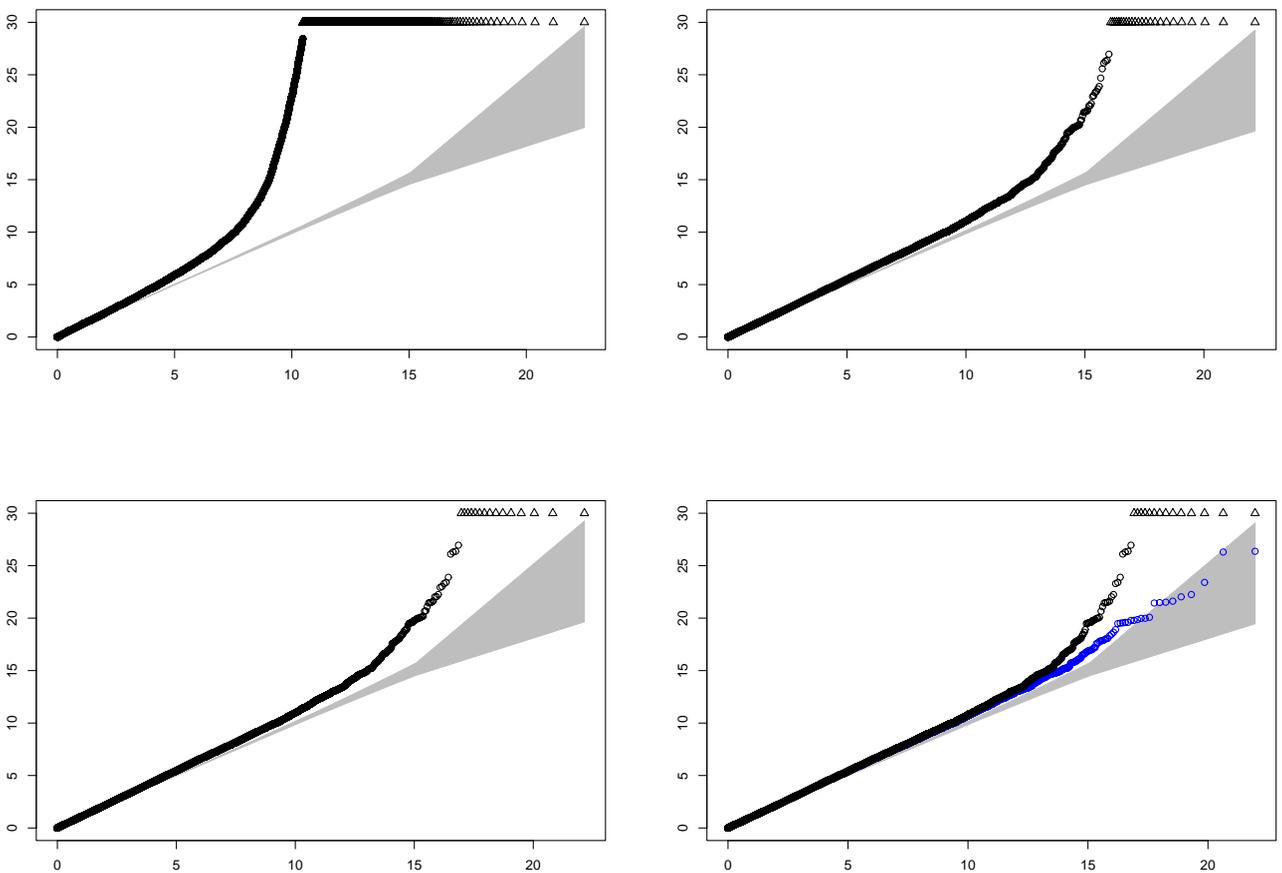
**Supplementary Figure 20 | Quantile-quantile plots at four different stages of filtering.** Each panel shows a QQ plot for the trend test results in T2D for the following subsets of SNPs ($\lambda$ estimates for each subset in parentheses – see Methods for details), observed test statistics (y-axis) >30 are shown as triangles: top left, all SNPs ($\lambda$ = 1.17); top right, SNPs passing standard project filter described in text and having minor allele frequency > 1% ($\lambda$ = 1.09); bottom left, those passing the previous filter but excluding SNPs for which visual inspection of cluster plots revealed poor genotype calls ($\lambda$ = 1.09); bottom right is as bottom left, but the plot which excludes regions with strong evidence for association is superimposed in blue, as in Main Figure 3.
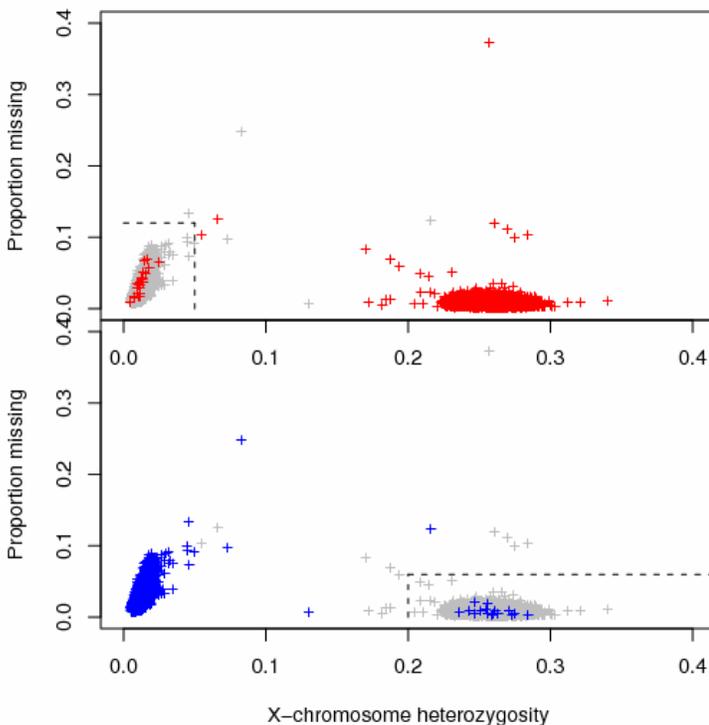


**Supplementary Figure 21 | Individual missing data and heterozygosity on the X chromosome.** Scatter plot of the proportion of SNPs called heterozygote (x-axis) against the proportion called missing (y-axis) for each individual in the study. For each collection the individuals are plotted twice; samples whose gender were initially reported as male are coloured blue and those reported as female are coloured red.
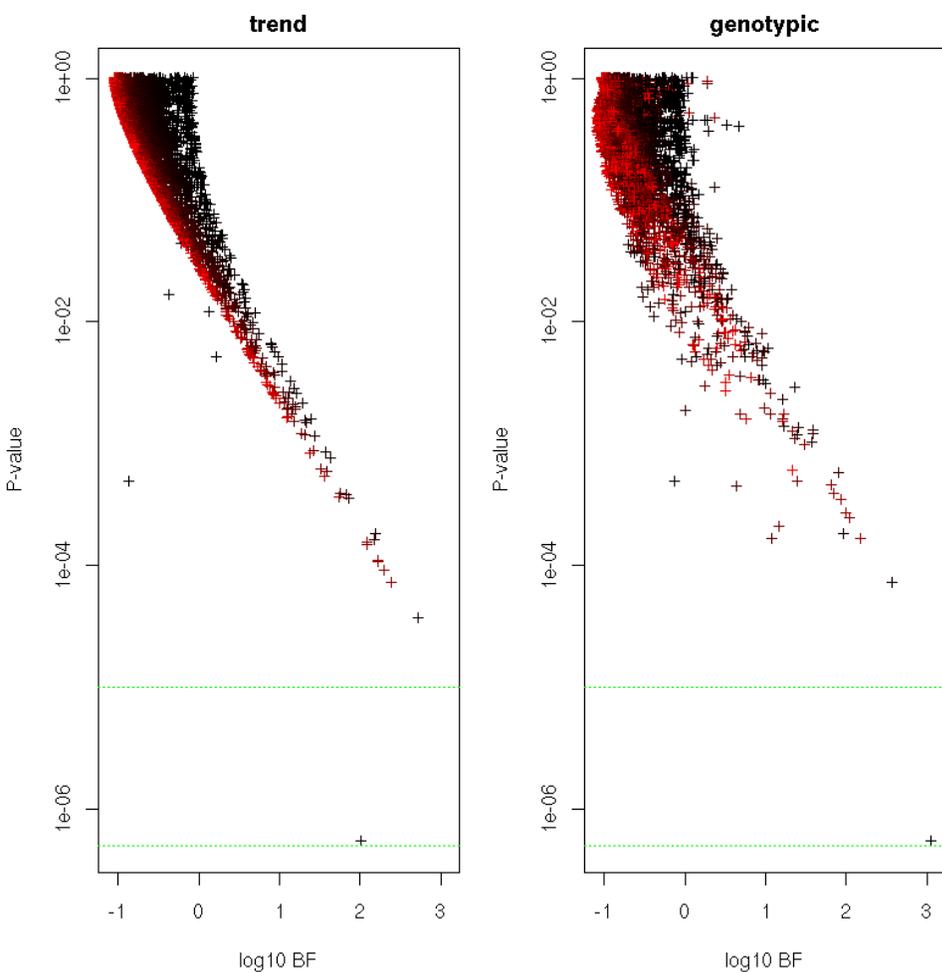
**Supplementary Figure 22 | Comparison of p-values and Bayes factors.** Scatter plot showing p-values and Bayes factors for all SNPs on chromosome 22 for BD. The points are coloured according to the minor allele frequency (MAF), ranging from fully black for a MAF of 0 to fully red for a MAF of 0.5. Two panels are shown, one for the trend test and the other for the genotypic test. The horizontal lines denote threshold values for inclusion on various tables.
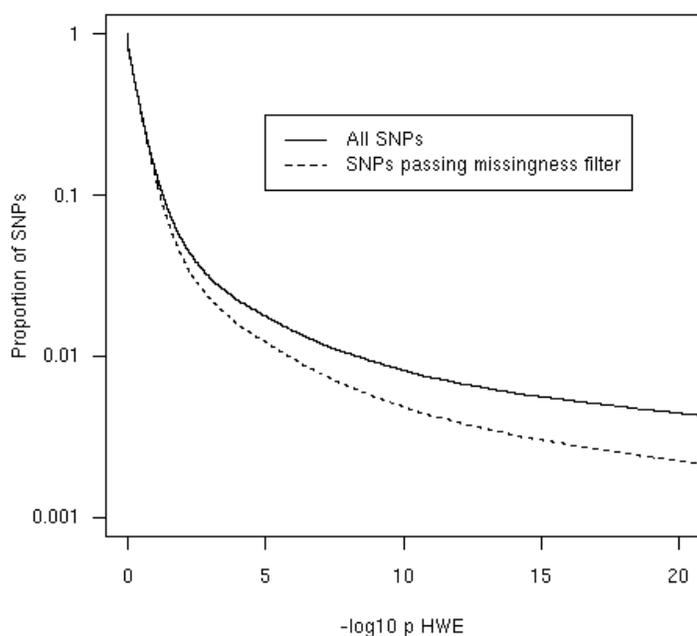


**Supplementary Figure 23 | Proportion of SNPs failing test for HWE in controls.** Proportion of SNPs with HWE p-values (in controls) below a given threshold. The solid line corresponds to all SNPs, while the dashed line corresponds to the SNPs which pass the call rate filter. SNPs which fail the call rate filter account for a substantial fraction of the extreme HWE p-values.

rs384848

58C    UKBS    BD

CAD    CD    HT

RA    T1D    T2D
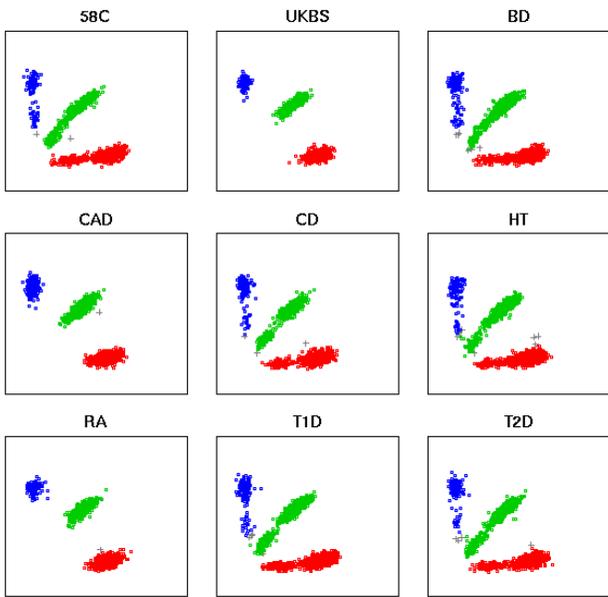
**Supplementary Figure 24 | Radial shift.** This cluster plot (see Supplementary Figure 19) shows the shift towards the origin that occurs in a subset of samples in a small number of SNPs. The shift did not occur in samples from the UKBS, CAD and RA collections. These collections differ from the others in that no samples were typed in the early stages of the study.



58C



BD

**CAD**



**CD**



**HT**

**RA**

**T1D**

**T2D**
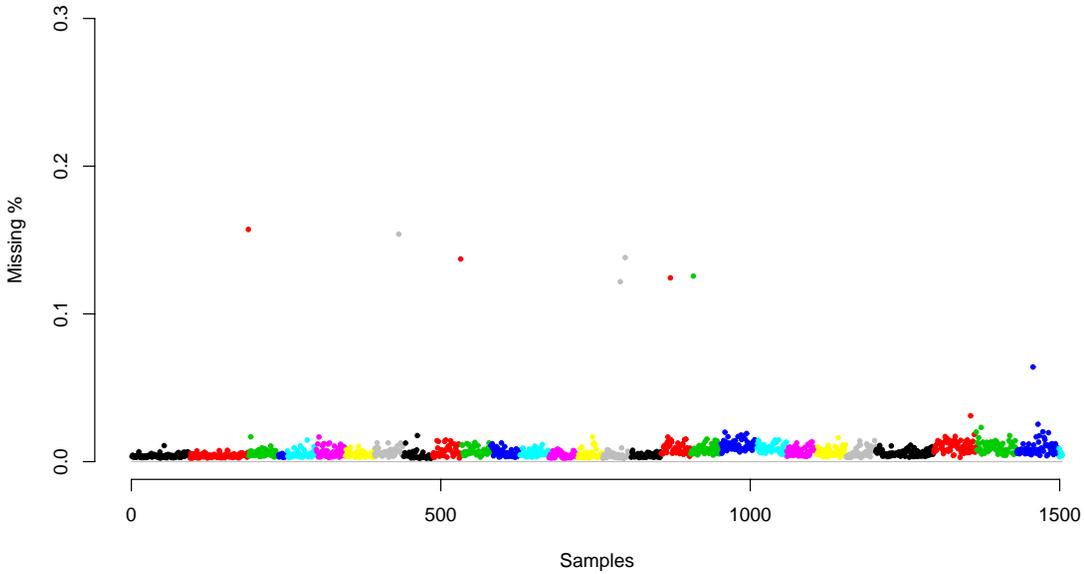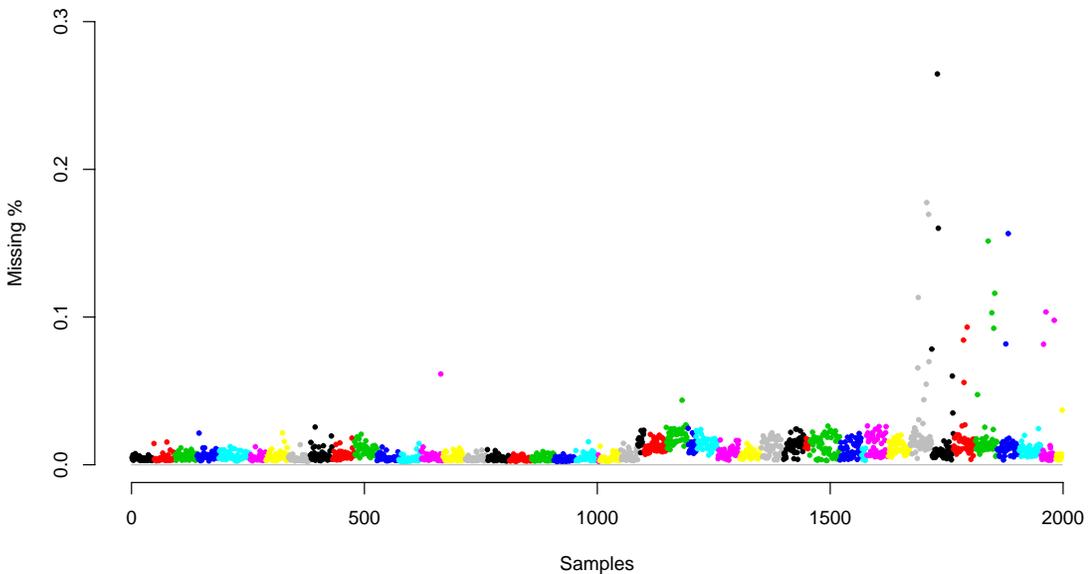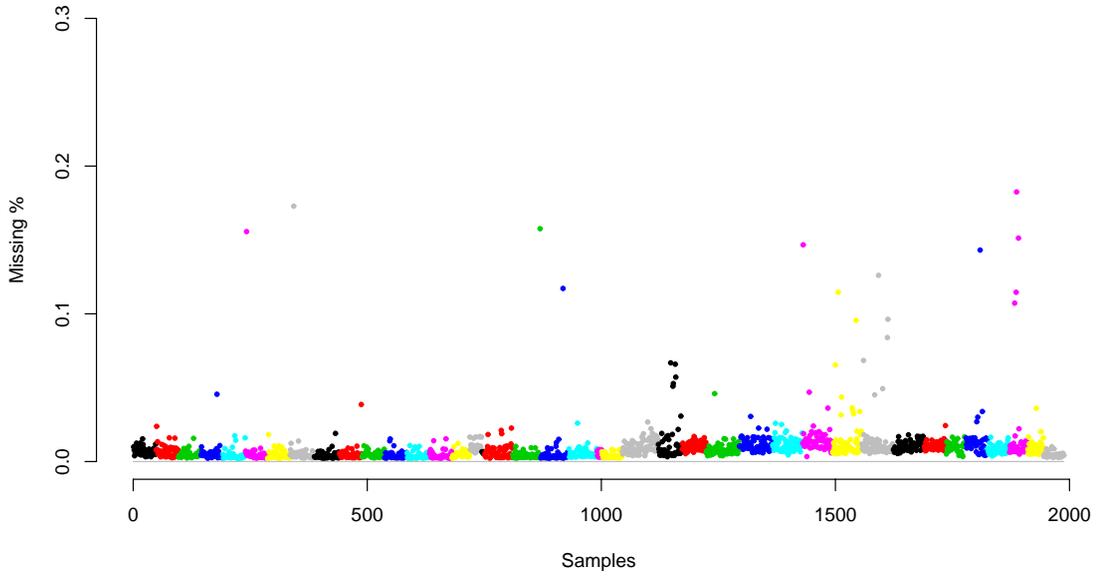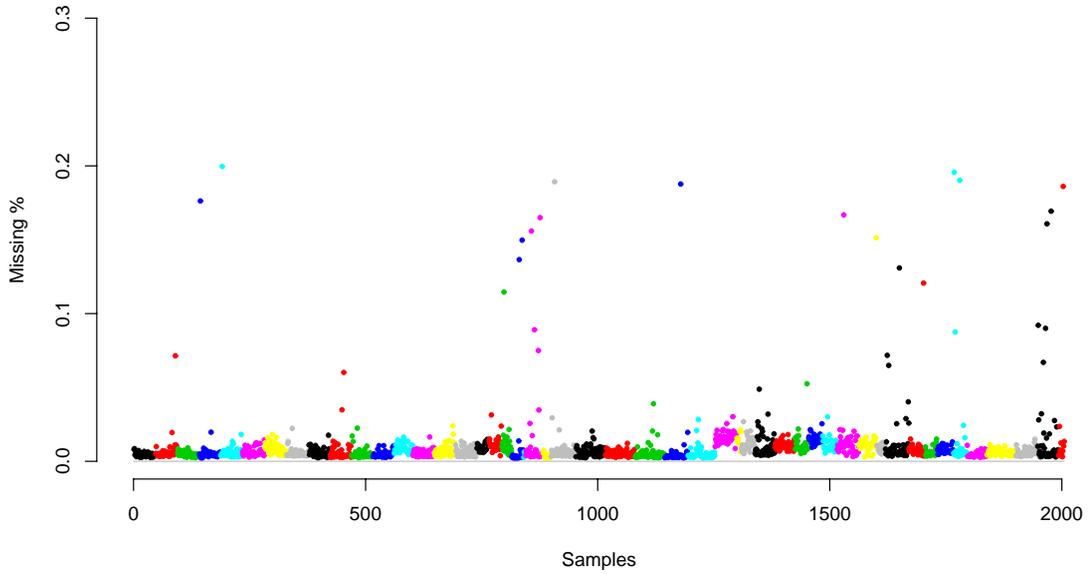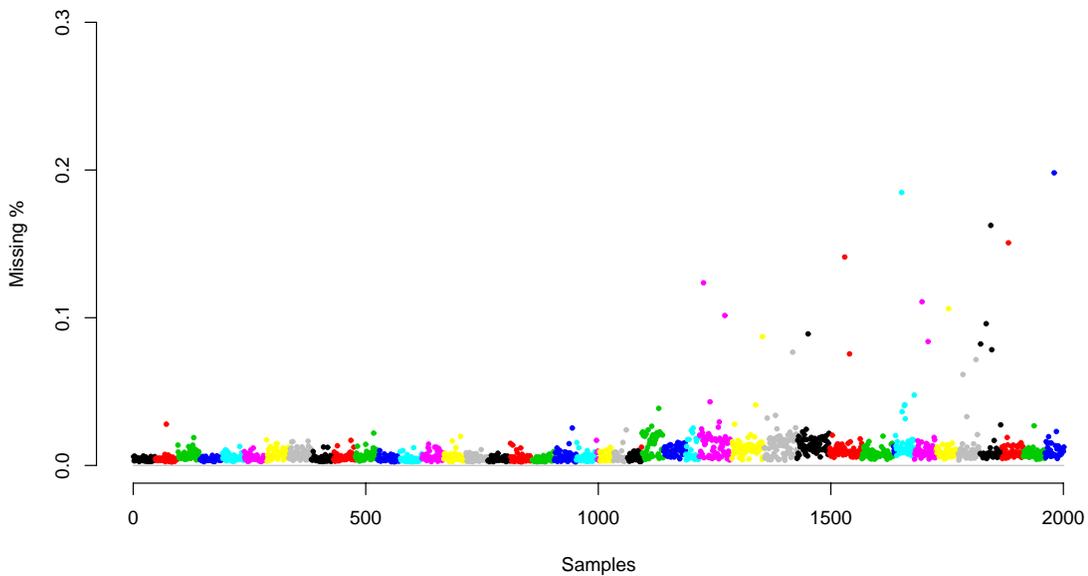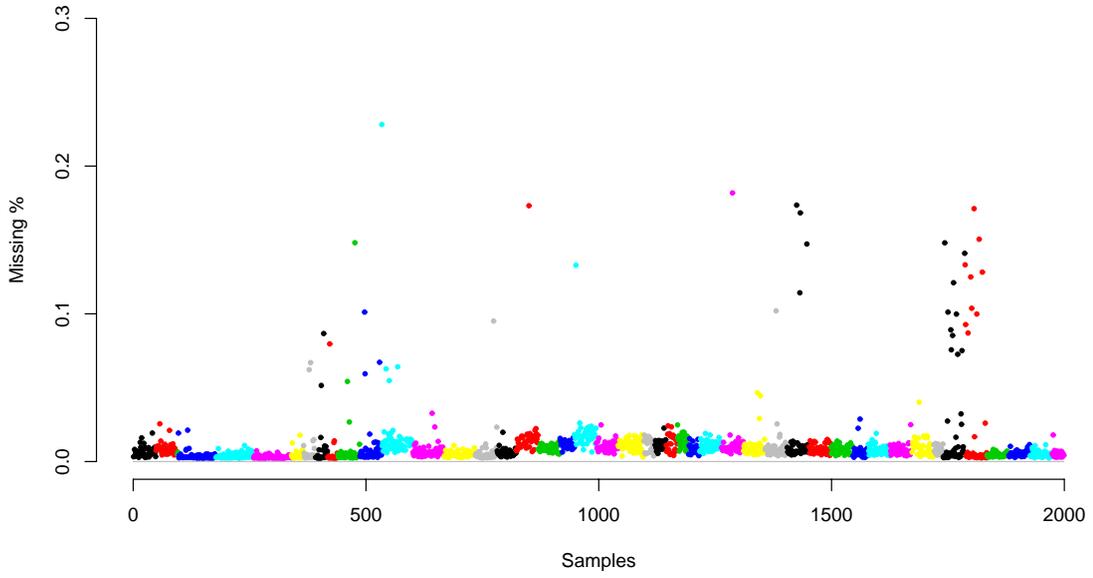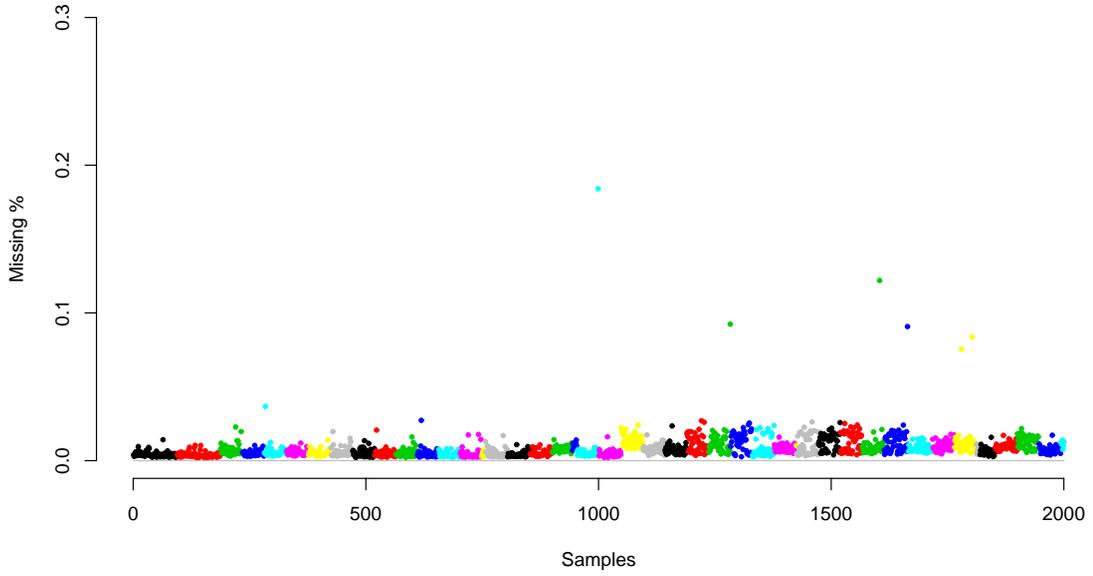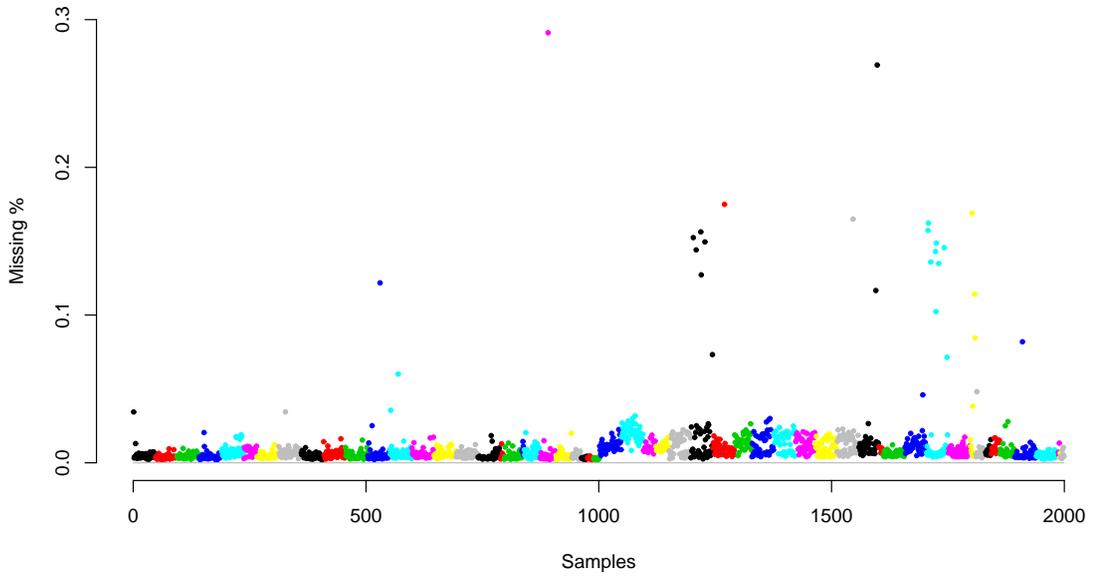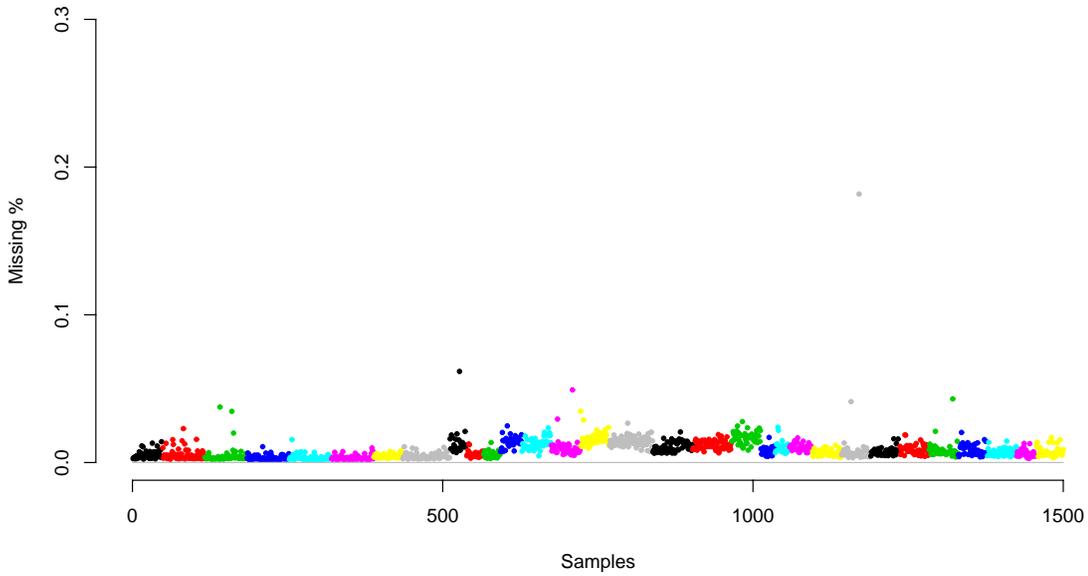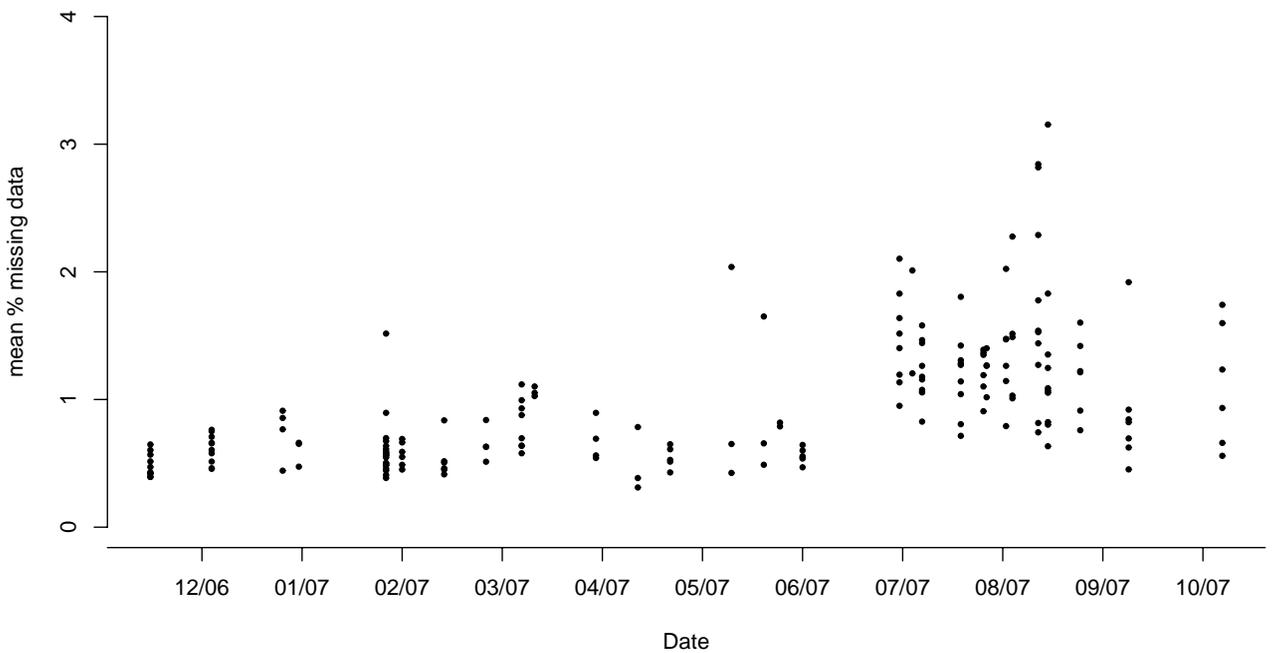
**Mean % Missing Data**



**Supplementary Figure 25 | Missing genotypes per collection over time.** The plots show the percentage of missing data for each individual in the unfiltered dataset for each collection. The individuals are coloured by plate, and plates of individuals are arranged left to right in ascending order of the time the plate was shipped to Affymetrix. The plot titled "Mean % Missing Data" shows the mean percentage of missing data for each plate of individuals in the unfiltered dataset. The plates of individuals are arranged by the date the plate was shipped to Affymetrix.

| | Collection | 58C | UKBS | BD | CAD | CD | HT | RA | T1D | T2D |
|---|---|---|---|---|---|---|---|---|---|---|
| | No Samples | 1480 | 1458 | 1868 | 1926 | 1748 | 1952 | 1860 | 1963 | 1924 |
| | % Male / % Female | 50/50 | 48/52 | 37/63 | 79/21 | 39/61 | 40/60 | 25/75 | 51/49 | 58/42 |
| **Geographic region - % samples** | Eastern | 11 | 12 | 3 | 10 | 25 | 16 | 20 | 17 | 26 |
| | E&WRidings | 9 | 6 | 1 | 26 | 0 | 1 | 10 | 10 | 0 |
| | London | 8 | 5 | 7 | 2 | 22 | 18 | 2 | 4 | 10 |
| | Midlands | 9 | 12 | 24 | 6 | 1 | 4 | 16 | 6 | 1 |
| | Northern | 8 | 10 | 9 | 10 | 20 | 3 | 3 | 8 | 15 |
| | North Midlands | 7 | 3 | 6 | 15 | 1 | 13 | 8 | 7 | 5 |
| | Northwestern | 11 | 11 | 3 | 8 | 1 | 3 | 19 | 11 | 3 |
| | Southeastern | 7 | 11 | 5 | 4 | 1 | 8 | 2 | 3 | 2 |
| | Southern | 8 | 8 | 6 | 4 | 14 | 5 | 12 | 8 | 18 |
| | Southwestern | 8 | 9 | 6 | 6 | 1 | 3 | 1 | 9 | 19 |
| | Scotland | 10 | 9 | 10 | 5 | 14 | 24 | 3 | 10 | 0 |
| | Wales | 5 | 5 | 21 | 5 | 0 | 1 | 1 | 7 | 1 |
| | Unknown | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 |
| **Age band % samples** | <40 | 0 | 37 | 30 | 1 | 40 | 8 | 28* | 65 | 5 |
| | 40-49 | 100 | 27 | 29 | 11 | 20 | 20 | 20* | 1 | 16 |
| | 50-59 | 0 | 28 | 24 | 37 | 18 | 31 | 20* | 0 | 33 |
| | 60-69 | 0 | 8 | 14 | 42 | 10 | 30 | 12* | 0 | 34 |
| | >70 | 0 | 0 | 3 | 9 | 7 | 11 | 5* | 0 | 11 |
| | Unknown | 0 | 0 | 0 | 0 | 4 | 0 | 14* | 33 | 1 |

**Supplementary Table 1 | Descriptive statistics.** For each collection: number of samples after QC filtering, percentage Male/Female, percentage of samples in each of 12 geographic regions (see Supplementary Information for region definitions) and percentage of samples in each age band for age at entry of individual into the study. *RA patients age-at-onset.

| Relative Risk | 1.3 | 1.5 | 1.7 |
|---|---|---|---|
| Power (p-value threshold 1x10$^{-6}$) | 0.461 | 0.813 | 0.91 |
| Power (p-value threshold 5x10$^{-7}$) | 0.429 | 0.798 | 0.902 |

**Supplementary Table 2 | Power of study design.** Estimate of the power of the study, with 3,000 controls and 2,000 cases using for SNPs above 5% MAF in HapMap. See Methods section for details.

a)

| | Percent discordance | |
|---|---|---|
| | Illumina filtering | Illumina and CHIAMO filtering |
| BRLMM vs. Illumina | 0.60 | 0.35 |
| CHIAMO vs. Illumina | 0.37 | 0.22 |
| BRLMM vs. CHIAMO | 0.39 | 0.18 |

b)

| | Percent missing data | | |
|---|---|---|---|
| | Illumina filtering | Illumina and CHIAMO filtering | Study-wide |
| **BRLMM** | 0.79 | 0.63 | 0.7 |
| **CHIAMO** | 0.60 | 0.33 | 0.3 |
| **Illumina** | 0.57 | 0.54 | --- |

**Supplementary Table 3 | Agreement of genotype calls.** Percent discordance and percent missing data (the percentage of genotypes for which an algorithm could not make a call with high certainty) for BRLMM, CHIAMO, and Illumina calling algorithms. The CHIAMO and BRLMM calls were made on Affymetrix 500K intensity data, and the Illumina calls were made on the Infinium platform for the same individuals from the 58C collection (Typed as part of WTCCC non-synonymous study, see www.wtccc.org.uk). Results are shown for 1,489 SNPs and 1,456 individuals that passed Illumina filters, and for 1,396 SNPs and 1,444 individuals that passed additional CHIAMO filters. Study-wide missing data figures are for 453,509 CHIAMO-filtered SNPs, of which the 1,396 used in the Illumina comparison are a subset.

| Collection | Missingness | Heterozygosity | External discordance | Non-European ancestry | Duplicate | Relative | Total |
|---|---|---|---|---|---|---|---|
| **58C** | 9 | 0 | 4 | 6 | 4 | 1 | **24** |
| **UKBS** | 8 | 0 | 5 | 14 | 0 | 15 | **42** |
| **BD** | 30 | 0 | 0 | 9 | 77 | 13 | **129** |
| **CAD** | 41 | 1 | 0 | 13 | 2 | 5 | **62** |
| **CD** | 43 | 4 | 6 | 54 | 131 | 18 | **256** |
| **HT** | 29 | 0 | 0 | 2 | 6 | 11 | **48** |
| **RA** | 47 | 1 | 0 | 26 | 53 | 9 | **136** |
| **T1D** | 7 | 2 | 1 | 18 | 6 | 3 | **37** |
| **T2D** | 36 | 1 | 0 | 11 | 16 | 11 | **75** |
| **Total** | **250** | **9** | **16** | **153** | **295** | **86** | **809** |

**Supplementary Table 4 | Exclusion summary by collection.** Six filters were applied for sample exclusion: 1. SNP call rate < 97% (missingness). 2. Heterozygosity > 30% or < 23% across all SNPs. 3. External discordance with genotype or phenotype data. 4. Individuals identified as having recent non-European ancestry by the Multidimensional Scaling analysis (see Methods). 5. Duplicates (the copy with more missing data was removed) 6. Individuals with too much IBS sharing (>86%); likely relatives. Where individuals could be excluded for more than one reason, they appear in the leftmost such column.

| Region | Postcodes |
|---|---|
| Northern | CA DH DL HG NE SR TS YO |
| East & West Ridings | BD DN HD HU HX LS S WF |
| North Midland | DE LE LN NG NN |
| Eastern | AL CB CM CO EN IG IP LU MK NR PE RM SG SS WD |
| Southeast | BN CT DA GU ME RH TN |
| Southern | BH DT HP OX PO RG SL SO SP |
| Southwest | BA BS EX GL GY PL SN TA TQ TR |
| Wales | CF LD LL NP SA |
| Midlands | B CV DY HR ST SY TF WR WS WV |
| Scotland | AB DD DG EH FK G HS IV KA KW KY ML PA PH TD ZE |
| London | BR CR E EC HA KT N NW SE SM SW TW UB W WC |
| Northwest | BB BL CH CW FY IM L LA M OL PR SK WA WN |

**Supplementary Table 5 | Postcode definition of geographic regions.** The prefix to the postcodes which defines the regions of the U.K. referred to in the Consortium.

| | BD | CAD | CD | HT | RA | T1D | T2D |
|---|---|---|---|---|---|---|---|
| No covariates | 1.11 | 1.07 | 1.11 | 1.06 | 1.03 | 1.05 | 1.08 |
| PCA covariates | 1.09 | 1.06 | 1.07 | 1.07 | 1.03 | 1.05 | 1.06 |

**Supplementary Table 6 | Estimated over-dispersion of tests for association.** Values greater than one indicate that the distribution of the test statistic is shifted towards larger values relative to the expected Chi-squared distribution. Values are given for the trend test (equivalent to a score test in an additive logistic regression model with no covariates), and for a test based on an additive logistic regression model in which the two ancestry informative principal components were included as covariates. Note that inclusion of the principal components does reduce overdispersion, but only by a small amount. The SNPs used in making these estimates were those that passed the filter described in the legend for Figure 3.

## a) Bipolar Disorder

| Chromosome | Region / Position (Mb) | SNP | Type | Trend p-value | Genotypic p-value | $\log_{10}$ BF additive | $\log_{10}$ BF general | Trend p-value | Genotypic p-value |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Sex-differentiated | |
| 1 | 60.77 | rs2989476 | imputed | 1.61E-05 | 7.47E-06 | 3.09 | 3.42 | 6.74E-05 | 5.71E-05 |
| 2 | 11.94 - 12.00 | rs4027132 | chip | 1.31E-05 | 9.69E-06 | 3.07 | 3.27 | 5.15E-05 | 9.50E-05 |
| 2 | 104.41 - 104.58 | rs7570682 | chip | 3.11E-06 | 1.64E-05 | 3.68 | 3.23 | 3.35E-05 | 3.93E-05 |
| 2 | 115.63 - 116.11 | rs1375144 | chip | 2.43E-06 | 1.31E-05 | 3.80 | 3.34 | 1.17E-05 | 1.25E-04 |
| 2 | 181.18 - 181.34 | rs11888446 | imputed | 7.01E-07 | 2.96E-06 | 4.53 | 4.16 | 2.14E-06 | 1.56E-05 |
| 2 | 200.99 | rs4673905 | imputed | 9.72E-06 | 5.44E-05 | 2.86 | 2.37 | 2.98E-05 | 3.07E-04 |
| 2 | 241.23 - 241.28 | rs2953145 | chip | 1.11E-05 | 6.57E-06 | 3.22 | 3.50 | 7.32E-05 | 1.39E-05 |
| 3 | 32.26 – 32.33 | rs4276227 | chip | 4.57E-06 | 2.62E-05 | 3.52 | 3.04 | 3.39E-05 | 3.38E-04 |
| 3 | 36.83 | rs9834970 | imputed | 1.21E-06 | 7.00E-06 | 4.18 | 3.72 | 6.39E-06 | 6.02E-05 |
| 3 | 184.29 - 184.40 | rs683395 | chip | 2.30E-06 | 5.11E-06 | 3.87 | 3.73 | 4.26E-06 | 2.10E-05 |
| 6 | 42.82 - 42.86 | rs6458307 | chip | 3.43E-01 | 4.35E-06 | -0.80 | 2.84 | 5.14E-01 | 4.42E-05 |
| 6 | 123.82 | rs6901299 | imputed | 3.13E-06 | 1.08E-05 | 4.08 | 3.81 | 1.72E-05 | 1.08E-04 |
| 7 | 11.48 | rs1405318 | imputed | 4.54E-06 | 2.72E-05 | 3.37 | 3.06 | 1.11E-05 | 5.24E-05 |
| 8 | 34.22 - 34.61 | rs2609653 | chip | 6.86E-06 | 2.31E-05 | 3.44 | 3.21 | 2.97E-05 | 9.51E-05 |
| 9 | 114.31 - 114.39 | rs10982256 | chip | 8.80E-06 | 4.41E-05 | 3.23 | 2.78 | 6.76E-06 | 7.92E-05 |
| 14 | 57.17 - 57.24 | rs10134944 | chip | 3.21E-06 | 6.89E-06 | 3.73 | 3.59 | 2.63E-05 | 9.90E-05 |
| 14 | 103.43 - 103.62 | rs11622475 | chip | 2.10E-06 | 8.14E-06 | 3.87 | 3.24 | 9.15E-06 | 8.01E-05 |
| 16 | 23.3 – 23.62 | rs420259 | chip | 2.19E-04 | **6.29E-08** | 1.96 | **4.78** | 1.16E-03 | 6.56E-07 |
| 16 | 51.36 - 51.50 | rs1344484 | chip | 1.65E-06 | 1.03E-05 | 3.94 | 3.41 | 8.30E-06 | 3.69E-05 |
| 20 | 3.70 - 3.73 | rs3761218 | chip | 4.43E-05 | 6.71E-06 | 2.58 | 3.18 | 1.51E-04 | 3.44E-05 |

**Strong or moderate association (autosomes)** (title above table)

**Strong or moderate association (X chromsome)**

| Chromosome | Region / Position (Mb) | SNP | Type | Trend p-value | Genotypic p-value |
|---|---|---|---|---|---|
| X | 110.32 | Rs975687 | chip | 2.09E-06 | 9.99E-06 |

**$1 \times 10^{-5} <$ p-value $< 1 \times 10^{-4}$**

| Chromosome | Region / Position (Mb) | SNP | Type | Trend p-value | Genotypic p-value |
|---|---|---|---|---|---|
| 1 | 54.96 | rs10888879 | chip | 1.35E-05 | 1.00E-00 |
| 1 | 60.74 | rs10889189 | chip | 5.51E-05 | 2.09E-04 |
| 1 | 65.39 | rs4916031 | chip | 3.40E-02 | 9.80E-05 |
| 1 | 70.01 | rs6691577 | chip | 9.23E-05 | 2.37E-04 |
| 1 | 101.66 | rs1776905 | chip | 5.70E-05 | 3.03E-04 |
| 1 | 213.31 | rs10779279 | chip | 3.98E-05 | 2.15E-04 |
| 1 | 224.13 | rs12070036 | chip | 9.89E-05 | 2.85E-04 |
| 2 | 62.70 | rs2049674 | chip | 7.48E-05 | 1.00E-00 |
| 2 | 104.44 | rs17029753 | chip | 8.10E-05 | 4.17E-04 |
| 2 | 115.74 | rs13386690 | chip | 5.14E-05 | 2.43E-04 |
| 2 | 181.18 | rs4407218 | chip | 8.35E-05 | 3.73E-04 |
| 2 | 200.99 | rs4673905 | chip | 2.35E-05 | 1.30E-04 |
| 3 | 7.63 | rs1485171 | chip | 1.31E-01 | 9.73E-05 |

| | | | | | |
|---|---|---|---|---|---|
| 3 | 21.67 | rs6762678 | chip | 7.59E-05 | 2.31E-04 |
| 3 | 22.99 | rs711715 | chip | 1.99E-02 | 5.25E-05 |
| 3 | 24.25 | rs4858594 | chip | 4.02E-05 | 2.16E-04 |
| 3 | 42.38 | rs33460 | chip | 9.56E-05 | 1.00E-00 |
| 3 | 61.56 | rs13074575 | chip | 3.49E-05 | 5.43E-05 |
| 4 | 46.99 | rs7680321 | chip | 6.23E-05 | 1.55E-04 |
| 4 | 54.65 | rs1996755 | chip | 9.28E-05 | 3.01E-04 |
| 5 | 23.40 | rs5009031 | chip | 5.17E-05 | 2.76E-04 |
| 5 | 116.21 | rs1428006 | chip | 4.02E-05 | 2.17E-04 |
| 5 | 135.30 | rs17701996 | chip | 7.15E-05 | 9.91E-05 |
| 5 | 162.73 | rs999580 | chip | 9.70E-05 | 4.78E-04 |
| 6 | 18.29 | rs365237 | chip | 1.73E-04 | 8.59E-05 |
| 6 | 33.96 | rs6926599 | chip | 7.45E-05 | 1.00E-00 |
| 6 | 123.86 | rs17739564 | chip | 4.28E-05 | 2.22E-04 |
| 6 | 132.77 | rs6906574 | chip | 1.75E-04 | 8.76E-05 |
| 6 | 152.62 | rs2763025 | chip | 5.10E-05 | 1.92E-05 |
| 7 | 22.76 | rs2286492 | chip | 5.06E-01 | 2.04E-05 |
| 8 | 58.48 | rs2875734 | chip | 1.20E-03 | 3.13E-05 |
| 8 | 83.20 | rs16919670 | chip | 6.02E-05 | 1.58E-04 |
| 8 | 83.83 | rs9643449 | chip | 9.75E-05 | 1.76E-04 |
| 8 | 102.35 | rs10097578 | chip | 3.72E-05 | 1.46E-04 |
| 8 | 118.68 | rs1993980 | chip | 9.12E-05 | 2.13E-04 |
| 9 | 11.21 | rs7030123 | chip | 6.04E-05 | 3.11E-04 |
| 9 | 36.89 | rs1573257 | chip | 3.62E-04 | 7.45E-05 |
| 9 | 90.66 | rs10993698 | chip | 7.71E-05 | 3.56E-04 |
| 9 | 110.28 | rs4978927 | chip | 9.92E-05 | 5.12E-04 |
| 9 | 114.33 | rs10982246 | chip | 2.58E-05 | 1.27E-04 |
| 10 | 42.76 | rs788261 | chip | 4.93E-05 | 9.13E-05 |
| 10 | 60.39 | rs10826258 | chip | 7.26E-05 | 2.70E-04 |
| 10 | 79.20 | rs1866437 | chip | 4.72E-02 | 4.94E-05 |
| 10 | 94.54 | rs7896131 | chip | 1.56E-04 | 4.65E-05 |
| 10 | 129.77 | rs2096285 | chip | 4.64E-05 | 2.47E-04 |
| 11 | 81.99 | (no rsID) | chip | 6.50E-05 | 1.00E-00 |
| 11 | 129.67 | rs858719 | chip | 1.11E-03 | 2.87E-05 |
| 12 | 23.95 | rs7136898 | chip | 1.32E-05 | 2.97E-05 |
| 12 | 93.57 | rs17309820 | chip | 8.71E-05 | 1.00E-00 |
| 13 | 22.59 | rs4770394 | chip | 1.20E-05 | 1.00E-00 |
| 13 | 45.42 | rs2806922 | chip | 7.90E-03 | 9.45E-05 |
| 13 | 67.96 | rs12584910 | chip | 5.94E-05 | 3.14E-04 |
| 14 | 23.20 | rs221703 | chip | 4.49E-05 | 1.00E-00 |
| 14 | 38.38 | rs17108400 | chip | 3.02E-05 | 2.39E-05 |
| 14 | 42.67 | rs17113911 | chip | 5.89E-05 | 1.00E-00 |
| 14 | 49.23 | rs10146912 | chip | 6.80E-05 | 3.29E-04 |
| 14 | 75.15 | rs3784005 | chip | 3.57E-05 | 1.00E-00 |
| 14 | 103.42 | rs10438244 | chip | 7.94E-05 | 1.71E-04 |
| 15 | 71.95 | rs7163502 | chip | 8.72E-05 | 3.40E-04 |
| 16 | 51.43 | rs1420239 | chip | 4.47E-05 | 2.28E-04 |
| 16 | 53.86 | rs4567706 | chip | 1.55E-05 | 6.62E-05 |

| 16 | 72.66 | rs12149894 | chip | 8.99E-05 | 2.60E-04 |
|---|---|---|---|---|---|
| 16 | 81.17 | rs7184080 | chip | 6.73E-01 | 3.67E-05 |
| 16 | 85.85 | rs10220973 | chip | 9.18E-05 | 1.00E-00 |
| 17 | 19.75 | rs203466 | chip | 4.02E-05 | 9.23E-05 |
| 18 | 8.45 | rs7243929 | chip | 2.86E-05 | 1.00E-00 |
| 18 | 8.98 | rs1893146 | chip | 8.13E-05 | 4.14E-04 |
| 19 | 12.58 | rs12979795 | chip | 4.12E-05 | 2.03E-04 |
| 19 | 48.49 | rs7408169 | chip | 6.09E-05 | 3.13E-04 |
| 19 | 49.31 | rs2061332 | chip | 8.72E-05 | 4.44E-04 |
| 19 | 63.40 | rs7248493 | chip | 3.07E-05 | 1.48E-04 |
| 20 | 3.72 | rs4815603 | chip | 7.50E-05 | 1.77E-05 |
| 20 | 43.16 | rs6031991 | chip | 6.18E-05 | 2.66E-04 |
| 21 | 31.31 | rs2833193 | chip | 5.74E-05 | 1.00E-00 |
| 22 | 31.69 | rs11089599 | chip | 7.16E-05 | 1.67E-04 |
| 22 | 35.66 | rs16997510 | chip | 3.70E-05 | 1.00E-00 |

## b) Coronary Artery Disease

### Strong or moderate association

| Chromosome | Region / Position (Mb) | SNP | Type | Trend p-value | Genotypic p-value | $\log_{10}$ BF additive | $\log_{10}$ BF general | Trend p-value | Genotypic p-value |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Sex-differentiated | |
| 1 | 236.77 - 236.85 | rs17672135 | chip | 1.04E-04 | 2.35E-06 | 2.36 | 3.88 | 2.50E-04 | 8.37E-05 |
| 5 | 99.98 - 100.11 | rs383830 | chip | 5.71E-06 | 1.34E-05 | 3.49 | 3.26 | 1.56E-04 | 1.38E-04 |
| 6 | 151.34 - 151.42 | rs6922269 | chip | 6.33E-06 | 1.50E-05 | 3.38 | 3.14 | 2.32E-05 | 2.04E-04 |
| 9 | 21.93 - 22.12 | rs1333049 | chip | **1.79E-14** | **1.16E-13** | **11.66** | **11.03** | **8.86E-12** | **3.67E-11** |
| 15 | 76.64 | rs7173512 | imputed | 4.58E-06 | 1.57E-05 | 3.02 | 2.69 | 2.53E-04 | 1.10E-03 |
| 16 | 81.72 - 81.79 | rs8055236 | chip | 9.73E-06 | 5.60E-06 | 3.28 | 3.59 | 6.91E-05 | 5.20E-05 |
| 19 | 34.74 - 34.78 | rs7250581 | chip | 9.12E-06 | 2.50E-05 | 3.30 | 2.87 | 4.56E-04 | 1.65E-03 |
| 22 | 25.01 - 25.06 | rs688034 | chip | 6.90E-06 | 3.75E-06 | 3.33 | 3.15 | 1.05E-04 | 9.34E-05 |

### $1\times10^{-5}$ < p-value < $1\times10^{-4}$

| 1 | 45.10 | rs11211059 | chip | 2.28E-02 | 7.16E-05 |
|---|---|---|---|---|---|
| 1 | 55.64 | rs12068336 | chip | 6.51E-05 | 2.39E-04 |
| 1 | 176.88 | rs16855395 | chip | 9.63E-02 | 9.46E-05 |
| 1 | 227.56 | rs2883720 | chip | 5.07E-05 | 2.71E-04 |
| 2 | 3.78 | rs17018897 | chip | 3.11E-05 | 1.71E-04 |
| 2 | 145.76 | rs2044369 | chip | 4.86E-01 | 6.70E-05 |
| 2 | 159.07 | rs13391688 | chip | 2.93E-05 | 1.00E-00 |
| 2 | 226.89 | rs2943634 | chip | 1.19E-05 | 6.86E-05 |
| 3 | 39.42 | rs4464383 | chip | 7.86E-05 | 3.09E-04 |
| 3 | 82.23 | rs17728526 | chip | 1.61E-04 | 3.16E-05 |
| 3 | 82.74 | rs834858 | chip | 6.52E-05 | 8.19E-05 |

| | | | | | |
|---|---|---|---|---|---|
| 3 | 108.65 | rs7627215 | chip | 4.29E-01 | 1.73E-05 |
| 3 | 140.70 | rs295470 | chip | 1.87E-01 | 5.47E-05 |
| 3 | 149.31 | rs16860117 | chip | 2.18E-05 | 1.00E-00 |
| 3 | 152.29 | rs906766 | chip | 1.44E-05 | 1.00E-00 |
| 3 | 195.18 | rs7649230 | chip | 3.82E-03 | 9.55E-05 |
| 4 | 44.87 | rs4456994 | chip | 7.55E-05 | 2.86E-04 |
| 4 | 132.32 | rs17051141 | chip | 2.72E-05 | 1.34E-04 |
| 4 | 138.29 | rs6841127 | chip | 1.50E-02 | 2.95E-05 |
| 4 | 161.70 | rs6536520 | chip | 1.81E-02 | 9.97E-05 |
| 5 | 36.56 | rs2562544 | chip | 1.18E-05 | 1.00E-00 |
| 5 | 66.00 | rs4374700 | chip | 2.46E-01 | 7.54E-05 |
| 5 | 99.97 | rs247951 | chip | 6.73E-05 | 3.12E-04 |
| 5 | 103.15 | rs635331 | chip | 1.81E-01 | 6.22E-05 |
| 5 | 109.07 | rs6897334 | chip | 4.94E-05 | 2.63E-04 |
| 7 | 80.13 | rs17154557 | chip | 8.65E-05 | 4.00E-04 |
| 7 | 129.26 | rs11556924 | chip | 2.35E-05 | 1.26E-04 |
| 8 | 106.33 | rs12543827 | chip | 9.26E-05 | 4.75E-04 |
| 8 | 127.41 | rs2471935 | chip | 5.82E-04 | 3.17E-05 |
| 8 | 143.23 | rs10099944 | chip | 2.21E-05 | 8.03E-05 |
| 9 | 16.89 | rs10810661 | chip | 5.03E-05 | 2.55E-04 |
| 10 | 5.09 | rs7099555 | chip | 6.69E-01 | 3.06E-05 |
| 10 | 11.44 | rs7917066 | chip | 9.84E-05 | 6.28E-05 |
| 10 | 83.75 | rs10884019 | chip | 7.33E-03 | 8.01E-05 |
| 10 | 85.10 | rs11198250 | chip | 1.70E-05 | 1.00E-00 |
| 11 | 133.55 | rs11606866 | chip | 6.98E-05 | 1.76E-04 |
| 12 | 54.93 | rs808919 | chip | 7.03E-05 | 2.67E-04 |
| 12 | 106.28 | rs1426466 | chip | 1.46E-02 | 9.49E-05 |
| 12 | 128.80 | rs2398486 | chip | 5.48E-05 | 2.92E-04 |
| 13 | 51.32 | rs9535772 | chip | 7.23E-05 | 3.47E-04 |
| 13 | 75.72 | rs9544230 | chip | 7.83E-05 | 3.55E-04 |
| 13 | 109.13 | rs9521469 | chip | 7.00E-05 | 3.46E-04 |
| 14 | 57.21 | rs10431700 | chip | 2.21E-05 | 1.09E-04 |
| 14 | 61.88 | rs4644784 | chip | 2.36E-03 | 2.74E-05 |
| 15 | 38.23 | rs4924428 | chip | 2.71E-01 | 6.97E-05 |
| 15 | 76.67 | rs514743 | chip | 3.18E-05 | 1.15E-04 |
| 16 | 7.05 | rs11647415 | chip | 4.37E-05 | 2.17E-04 |
| 16 | 79.38 | rs17761499 | chip | 7.01E-01 | 8.50E-05 |
| 16 | 85.07 | rs7199903 | chip | 1.52E-05 | 7.14E-05 |
| 17 | 5.51 | rs6502872 | chip | 5.02E-05 | 2.69E-04 |
| 17 | 12.64 | rs16946601 | chip | 6.56E-05 | 3.37E-04 |
| 17 | 71.45 | rs2608881 | chip | 8.03E-05 | 4.16E-04 |
| 18 | 61.00 | rs9954012 | chip | 7.26E-05 | 3.34E-04 |
| 20 | 59.07 | rs6071467 | chip | 5.10E-05 | 2.72E-04 |
| 21 | 45.28 | rs2838756 | chip | 2.47E-05 | 1.29E-04 |
| 22 | 27.46 | rs5762763 | chip | 8.28E-01 | 8.33E-05 |

## c) Crohn's Disease

| | | | | | | | | Sex-differentiated | |
|---|---|---|---|---|---|---|---|---|---|
| Chromosome | Region / Position (Mb) | SNP | Type | Trend p-value | Genotypic p-value | $\log_{10}$ BF additive | $\log_{10}$ BF general | Trend p-value | Genotypic p-value |
| | | | | **Strong or moderate association** | | | | | |
| 1 | 67.3 – 67.48 | rs11805303 | chip | **6.45E-13** | **5.85E-12** | **10.07** | **9.19** | **6.79E-12** | **1.36E-10** |
| 1 | 169.53 - 169.67 | rs12037606 | chip | 1.79E-06 | 1.08E-05 | 3.89 | 3.35 | 8.71E-06 | 1.00E-04 |
| 2 | 27.64 - 28.55 | rs7606480 | imputed | 6.41E-06 | 2.62E-05 | 3.02 | 2.69 | 7.68E-05 | 5.05E-04 |
| 2 | 105.36 | rs3792048 | chip | 1.58E-02 | 2.77E-02 | 0.47 | 0.34 | 3.80E-02 | **2.13E-07** |
| 2 | 233.92 – 234 | rs10210302 | chip | **7.10E-14** | **5.26E-14** | **11.11** | **11.07** | **2.36E-14** | **5.27E-14** |
| 3 | 49.3 – 49.87 | rs9858542 | chip | **7.71E-07** | **3.58E-08** | **4.24** | **5.22** | 1.76E-06 | **3.25E-07** |
| 5 | 40.32 – 40.66 | rs17234657 | chip | **2.13E-13** | **1.99E-12** | **10.41** | **9.89** | **4.16E-12** | **5.66E-11** |
| 5 | 131.40 - 131.90 | rs6596075 | chip | 5.40E-07 | 3.19E-06 | **4.54** | **4.01** | 1.65E-06 | 2.15E-05 |
| 5 | 150.15 – 150.31 | rs1000113 | chip | **5.10E-08** | **3.15E-07** | 5.36 | 5.01 | 2.35E-07 | 1.87E-06 |
| | | rs11747270 | chip | 4.26E-08 | 2.60E-07 | **5.43** | **5.07** | **2.26E-07** | 3.12E-06 |
| 6 | 20.83 - 20.85 | rs6908425 | chip | 5.13E-06 | 1.10E-05 | 3.55 | 3.38 | 2.54E-05 | 6.48E-06 |
| 6 | 32.79 - 32.91 | rs9469220 | chip | 8.65E-07 | 2.28E-06 | **4.19** | 3.92 | 3.28E-06 | 2.26E-05 |
| 6 | 138.06 - 138.17 | rs7753394 | chip | 4.42E-06 | 2.59E-05 | 3.52 | 2.99 | 5.43E-05 | 1.98E-04 |
| 7 | 147.62 - 147.70 | rs7807268 | chip | 6.89E-06 | 4.43E-06 | 3.33 | 3.58 | 2.96E-05 | 4.17E-05 |
| 9 | 114.66 | rs7869487 | imputed | 3.25E-05 | 4.72E-06 | 3.12 | 3.78 | 1.63E-04 | 2.05E-05 |
| 10 | 38.52 - 38.57 | rs6601764 | chip | 2.56E-06 | 8.95E-06 | 3.74 | 3.01 | 1.53E-05 | 1.29E-04 |
| 10 | 64.06 – 64.31 | rs10761659 | chip | **2.68E-07** | 1.75E-06 | **4.69** | 3.80 | 8.70E-07 | 1.13E-05 |
| 10 | 101.26 – 101.32 | rs10883365 | chip | **1.41E-08** | **5.82E-08** | **5.91** | 5.13 | **7.29E-08** | **4.09E-07** |
| 12 | 30.08 | rs11610584 | imputed | 8.06E-06 | 3.70E-05 | 3.55 | 3.14 | 4.37E-05 | 1.94E-04 |
| 16 | 49.02 – 49.4 | rs17221417 | chip | **9.36E-12** | **3.98E-11** | 8.93 | 8.47 | 1.40E-10 | 1.21E-09 |
| | | rs2066843 | chip | 1.16E-12 | 1.79E-12 | **9.79** | **9.67** | **1.48E-11** | **7.29E-11** |
| 17 | 37.77 | rs744166 | imputed | 7.19E-06 | 3.85E-05 | 2.97 | 2.52 | 3.03E-05 | 2.90E-04 |
| 17 | 73.55 | rs4362447 | imputed | 6.46E-06 | 3.69E-05 | 3.18 | 2.69 | 4.74E-05 | 4.69E-04 |
| 18 | 12.76 – 12.91 | rs2542151 | chip | **4.56E-08** | **2.03E-07** | **5.42** | **5.00** | **2.28E-07** | 1.73E-06 |
| 19 | 50.89 - 51.07 | rs8111071 | chip | 6.13E-06 | 1.75E-05 | 3.48 | 3.29 | 5.20E-05 | 2.89E-04 |
| 21 | 39.21 | rs2836753 | imputed | 8.28E-06 | 4.74E-05 | 3.15 | 2.65 | 1.33E-05 | 5.33E-05 |
| | | | | $1\times10^{-5} <$ p-value $< 1\times10^{-4}$ | | | | | |
| 1 | 17.84 | rs7547331 | chip | 5.86E-05 | 2.79E-04 | | | | |
| 1 | 50.89 | rs11205760 | chip | 1.67E-05 | 8.86E-05 | | | | |
| 1 | 54.16 | rs7515322 | chip | 7.26E-05 | 1.00E-00 | | | | |
| 1 | 63.81 | rs2269252 | chip | 2.64E-05 | 1.05E-04 | | | | |
| 1 | 169.58 | rs12037853 | chip | 9.46E-05 | 4.86E-04 | | | | |
| 1 | 188.29 | rs10801047 | chip | 8.15E-05 | 3.40E-04 | | | | |
| 1 | 215.98 | rs2791559 | chip | 4.13E-05 | 2.10E-04 | | | | |
| 1 | 221.01 | rs7550648 | chip | 3.15E-05 | 6.13E-05 | | | | |
| 1 | 226.24 | rs541010 | chip | 2.36E-04 | 5.94E-05 | | | | |

| | | | | | |
|---|---|---|---|---|---|
| 1 | 227.18 | rs16852515 | chip | 1.50E-05 | 8.52E-05 |
| 2 | 27.65 | rs780094 | chip | 1.88E-05 | 1.04E-04 |
| 2 | 28.52 | rs906805 | chip | 9.35E-05 | 4.13E-04 |
| 2 | 45.58 | rs3755076 | chip | 4.96E-01 | 8.71E-05 |
| 2 | 51.43 | rs723713 | chip | 5.68E-05 | 1.24E-04 |
| 2 | 101.75 | *(no rsID)* | chip | 6.61E-04 | 2.72E-05 |
| 2 | 188.49 | rs6434236 | chip | 6.25E-05 | 2.76E-04 |
| 2 | 192.22 | rs17351803 | chip | 6.47E-05 | 2.53E-04 |
| 2 | 230.92 | rs13397985 | chip | 7.40E-05 | 3.15E-04 |
| 3 | 29.78 | rs9821929 | chip | 1.91E-04 | 7.62E-05 |
| 3 | 49.30 | rs2304442 | chip | 5.07E-05 | 1.05E-04 |
| 3 | 56.45 | rs9855289 | chip | 9.33E-05 | 4.62E-04 |
| 3 | 57.50 | rs9870678 | chip | 3.67E-05 | 1.97E-04 |
| 3 | 141.19 | rs1426036 | chip | 2.66E-04 | 7.83E-05 |
| 3 | 149.23 | rs16860030 | chip | 3.34E-05 | 1.66E-04 |
| 3 | 152.12 | rs936189 | chip | 8.61E-05 | 2.89E-04 |
| 3 | 162.94 | rs498051 | chip | 9.58E-01 | 3.60E-05 |
| 4 | 11.12 | rs425002 | chip | 1.01E-02 | 9.11E-05 |
| 4 | 25.81 | rs4692386 | chip | 2.31E-05 | 1.22E-04 |
| 4 | 38.70 | rs2130296 | chip | 3.06E-01 | 5.10E-05 |
| 4 | 57.87 | rs4315858 | chip | 9.50E-05 | 4.91E-04 |
| 4 | 89.51 | rs2046132 | chip | 7.20E-05 | 3.52E-04 |
| 4 | 127.57 | rs10011584 | chip | 2.56E-01 | 3.00E-05 |
| 5 | 40.32 | rs348621 | chip | 2.10E-05 | 4.23E-05 |
| 5 | 57.95 | rs2279980 | chip | 5.97E-05 | 8.50E-05 |
| 5 | 82.19 | rs12517180 | chip | 9.13E-05 | 1.61E-04 |
| 5 | 119.00 | rs17145587 | chip | 1.42E-02 | 5.34E-05 |
| 5 | 131.37 | rs7714191 | chip | 7.20E-05 | 3.74E-04 |
| 5 | 131.68 | rs3792884 | chip | 8.92E-05 | 4.48E-04 |
| 5 | 158.72 | rs1363670 | chip | 3.19E-05 | 1.62E-04 |
| 6 | 3.36 | rs9405639 | chip | 5.30E-05 | 2.72E-04 |
| 6 | 29.54 | rs2107192 | chip | 8.62E-05 | 4.10E-04 |
| 6 | 29.91 | rs2253981 | chip | 2.31E-05 | 9.10E-05 |
| 6 | 30.23 | rs2517646 | chip | 3.39E-05 | 4.73E-05 |
| 6 | 30.44 | rs3094055 | chip | 7.07E-05 | 6.76E-05 |
| 6 | 33.92 | rs9469615 | chip | 1.40E-05 | 5.62E-05 |
| 7 | 19.77 | rs10486379 | chip | 5.70E-01 | 8.63E-05 |
| 7 | 90.36 | rs3779585 | chip | 5.97E-05 | 1.00E-00 |
| 7 | 130.91 | rs1477226 | chip | 7.01E-05 | 3.51E-04 |
| 7 | 135.31 | rs834771 | chip | 9.05E-04 | 9.87E-05 |
| 7 | 147.69 | rs887822 | chip | 9.48E-05 | 2.29E-04 |
| 8 | 9.51 | rs4240626 | chip | 8.61E-05 | 4.11E-04 |
| 8 | 77.90 | rs10957818 | chip | 1.87E-05 | 1.00E-00 |
| 8 | 83.70 | rs10958116 | chip | 5.21E-03 | 4.14E-05 |
| 8 | 126.60 | rs2168131 | chip | 8.20E-05 | 3.67E-04 |
| 9 | 71.83 | rs2147240 | chip | 7.75E-05 | 1.00E-00 |
| 9 | 109.15 | rs3763640 | chip | 7.80E-04 | 7.43E-05 |
| 9 | 114.64 | rs6478108 | chip | 9.00E-05 | 2.46E-05 |

|  | 1035.33 | rs17582416 | chip | 3.12E-05 | 1.44E-04 |
|---|---|---|---|---|---|
| 10 | 104.31 | rs10786682 | chip | 3.85E-02 | 9.82E-05 |
| 11 | 115.93 | rs12362410 | chip | 1.45E-03 | 2.46E-05 |
| 12 | 30.08 | rs11609984 | chip | 7.00E-05 | 2.23E-04 |
| 12 | 111.83 | rs7134391 | chip | 6.63E-01 | 5.92E-05 |
| 13 | 43.36 | rs3764147 | chip | 3.97E-05 | 4.11E-05 |
| 13 | 70.48 | rs17620171 | chip | 7.72E-05 | 3.98E-04 |
| 14 | 51.37 | rs4898718 | chip | 6.65E-05 | 3.47E-04 |
| 14 | 53.06 | rs2251589 | chip | 8.73E-05 | 4.54E-04 |
| 14 | 75.07 | rs7161377 | chip | 4.13E-05 | 1.87E-04 |
| 14 | 77.10 | rs4903604 | chip | 2.59E-03 | 2.65E-05 |
| 14 | 95.70 | rs10149792 | chip | 2.35E-04 | 5.64E-05 |
| 15 | 30.95 | rs1451890 | chip | 9.69E-05 | 4.21E-04 |
| 15 | 93.06 | rs4984405 | chip | 4.42E-05 | 1.84E-04 |
| 17 | 31.42 | rs2015070 | chip | 9.38E-05 | 4.86E-04 |
| 17 | 37.75 | rs3816769 | chip | 3.10E-05 | 1.69E-04 |
| 17 | 42.18 | rs13341140 | chip | 6.80E-05 | 3.30E-04 |
| 17 | 73.52 | rs4789523 | chip | 6.95E-05 | 3.50E-04 |
| 18 | 48.70 | rs16955848 | chip | 3.40E-02 | 4.69E-05 |
| 18 | 54.29 | rs7235137 | chip | 6.27E-05 | 3.26E-04 |
| 19 | 1.07 | rs4807569 | chip | 2.81E-05 | 1.03E-04 |
| 19 | 49.16 | rs413061 | chip | 8.40E-05 | 4.09E-04 |
| 20 | 18.75 | *(no rsID)* | chip | 9.38E-05 | 4.42E-04 |
| 20 | 49.49 | rs880324 | chip | 1.68E-05 | 9.48E-05 |
| 20 | 57.35 | rs6128541 | chip | 3.32E-05 | 1.81E-04 |
| 20 | 61.81 | rs6011040 | chip | 8.92E-05 | 3.92E-04 |
| 21 | 26.39 | rs2830050 | chip | 8.60E-05 | 4.47E-04 |
| 21 | 39.21 | rs2836753 | chip | 1.29E-05 | 7.28E-05 |

## d) Hypertension

**Strong or moderate association**

| Chromosome | Region / Position (Mb) | SNP | Type | Trend p-value | Genotypic p-value | $\log_{10}$ BF additive | $\log_{10}$ BF general | Trend p-value | Genotypic p-value |
|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  |  |  | Sex-differentiated | |
| 1 | 71.81 – 71.82 | rs1577396 | imputed | 1.24E-01 | 5.11E-06 | -0.51 | 2.85 | 2.50E-01 | 6.12E-05 |
| 1 | 235.67 - 235.79 | rs2820037 | chip | 5.76E-05 | 7.66E-07 | 2.54 | 3.99 | 1.18E-04 | 1.62E-06 |
| 8 | 140.17 - 140.35 | rs6997709 | chip | 7.88E-06 | 4.36E-05 | 3.32 | 2.60 | 3.35E-05 | 3.42E-04 |
| 10 | 49.93 – 49.96 | rs7897289 | imputed | 3.31E-06 | 1.82E-05 | 3.71 | 3.24 | 1.51E-05 | 1.50E-04 |
| 12 | 24.86 - 24.95 | rs7961152 | chip | 7.39E-06 | 3.03E-05 | 3.29 | 2.87 | 3.63E-05 | 2.40E-04 |
| 12 | 100.52 - 100.58 | rs11110912 | chip | 9.18E-06 | 1.94E-05 | 3.27 | 3.11 | 2.64E-05 | 1.18E-04 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 13 | 66.90 - 67.04 | rs1937506 | chip | 9.23E-06 | 4.53E-05 | 3.25 | 2.85 | 2.17E-05 | 1.26E-04 |
| 15 | 94.60 - 94.67 | rs2398162 | chip | 7.85E-06 | 5.67E-06 | 3.33 | 3.40 | 4.84E-05 | 6.64E-05 |
| 19 | 48.99 | rs10426528 | imputed | 3.80E-06 | 2.23E-05 | 3.76 | 3.24 | 2.07E-05 | 1.14E-04 |

$$1\times10^{-5} < \text{p-value} < 1\times10^{-4}$$

| | | | | | |
|---|---|---|---|---|---|
| 1 | 71.81 | rs10889923 | chip | 2.14E-01 | 1.91E-05 |
| 1 | 226.22 | rs557208 | chip | 6.56E-05 | 2.89E-04 |
| 2 | 12.68 | rs4668771 | chip | 4.84E-05 | 1.18E-04 |
| 2 | 22.96 | rs13421717 | chip | 6.37E-05 | 2.57E-04 |
| 2 | 25.90 | rs17680828 | chip | 9.56E-05 | 4.36E-04 |
| 2 | 79.68 | rs17017233 | chip | 8.64E-05 | 1.52E-04 |
| 2 | 96.44 | rs17633463 | chip | 6.25E-05 | 1.55E-04 |
| 2 | 212.20 | rs6435632 | chip | 3.14E-02 | 2.82E-05 |
| 2 | 240.14 | rs11894982 | chip | 8.40E-05 | 4.32E-04 |
| 3 | 6.46 | rs17234606 | chip | 4.33E-05 | 1.21E-04 |
| 3 | 28.68 | rs4399848 | chip | 9.94E-05 | 4.44E-04 |
| 3 | 65.45 | rs11710619 | chip | 9.47E-05 | 1.20E-04 |
| 4 | 15.57 | rs2191003 | chip | 6.75E-02 | 1.23E-05 |
| 4 | 54.56 | rs6824846 | chip | 9.22E-05 | 4.71E-04 |
| 4 | 144.63 | rs300917 | chip | 9.29E-05 | 4.44E-04 |
| 4 | 145.63 | rs17709487 | chip | 1.52E-03 | 9.65E-05 |
| 5 | 10.25 | rs9312724 | chip | 1.53E-05 | 1.00E-00 |
| 5 | 100.02 | rs4702982 | chip | 5.75E-05 | 2.17E-04 |
| 6 | 0.46 | rs2493013 | chip | 2.53E-03 | 2.92E-05 |
| 6 | 76.51 | rs276699 | chip | 9.37E-05 | 1.00E-00 |
| 6 | 99.62 | rs1884184 | chip | 3.53E-04 | 7.51E-05 |
| 6 | 134.78 | rs4896044 | chip | 8.97E-04 | 7.21E-05 |
| 6 | 151.34 | rs12201472 | chip | 3.06E-05 | 8.30E-05 |
| 7 | 46.02 | rs6964415 | chip | 5.49E-05 | 2.71E-04 |
| 7 | 68.56 | rs2851504 | chip | 9.18E-01 | 6.29E-05 |
| 7 | 85.62 | rs7804971 | chip | 3.87E-05 | 2.07E-04 |
| 7 | 147.03 | rs2710107 | chip | 2.67E-05 | 1.41E-04 |
| 8 | 3.80 | rs17068216 | chip | 1.84E-04 | 4.20E-05 |
| 8 | 123.90 | rs10095188 | chip | 3.30E-02 | 7.52E-05 |
| 8 | 133.28 | rs17654436 | chip | 7.57E-05 | 1.51E-04 |
| 8 | 140.23 | rs4074554 | chip | 1.39E-05 | 6.75E-05 |
| 10 | 10.32 | rs2151595 | chip | 2.64E-05 | 1.00E-00 |
| 10 | 16.32 | rs2991895 | chip | 5.68E-05 | 3.72E-05 |
| 10 | 21.36 | rs604251 | chip | 3.72E-05 | 1.57E-04 |
| 10 | 27.72 | rs567829 | chip | 1.21E-04 | 6.58E-05 |
| 10 | 49.96 | rs12269023 | chip | 1.80E-05 | 8.37E-05 |
| 11 | 16.29 | rs297367 | chip | 8.70E-05 | 4.25E-04 |
| 11 | 21.38 | rs10833525 | chip | 2.39E-05 | 8.62E-05 |
| 11 | 30.38 | rs12575085 | chip | 8.14E-05 | 4.25E-04 |
| 11 | 73.80 | rs633568 | chip | 1.04E-02 | 4.29E-05 |
| 12 | 63.02 | rs10784404 | chip | 1.75E-04 | 8.87E-05 |
| 12 | 83.68 | rs7300456 | chip | 1.16E-05 | 4.85E-05 |
| 12 | 100.53 | rs1727091 | chip | 2.21E-05 | 1.20E-04 |

| 13 | 28.05 | rs3812868 | chip | 7.90E-05 | 4.06E-04 |
| 13 | 30.03 | rs1556428 | chip | 5.09E-04 | 5.86E-05 |
| 13 | 37.72 | rs610642 | chip | 1.11E-04 | 8.79E-05 |
| 13 | 42.82 | rs9316014 | chip | 9.74E-05 | 1.36E-04 |
| 13 | 60.33 | rs167272 | chip | 1.81E-01 | 3.66E-05 |
| 14 | 54.32 | rs709939 | chip | 1.85E-05 | 7.76E-05 |
| 14 | 60.77 | rs4902035 | chip | 4.83E-01 | 1.11E-05 |
| 16 | 77.21 | rs2548876 | chip | 8.37E-01 | 6.23E-05 |
| 18 | 63.55 | rs1373365 | chip | 2.45E-04 | 9.81E-05 |
| 19 | 43.87 | rs973009 | chip | 3.51E-01 | 3.14E-05 |
| 19 | 48.99 | rs349045 | chip | 6.59E-05 | 2.68E-04 |
| 20 | 22.25 | rs2424430 | chip | 2.85E-05 | 1.41E-04 |
| 20 | 59.07 | rs6129032 | chip | 4.37E-05 | 2.25E-04 |

## e) Rheumatoid Arthritis

| Chromosome | Region / Position (Mb) | SNP | Type | Trend p-value | Genotypic p-value | $\log_{10}$ BF additive | $\log_{10}$ BF general | Trend p-value | Genotypic p-value |
|---|---|---|---|---|---|---|---|---|---|
| | | | | **Strong or moderate association** | | | | | |
| | | | | | | | | Sex-differentiated | |
| 1 | 2.44 - 2.77 | rs6684865 | chip | 5.37E-06 | 3.14E-05 | 3.47 | 2.97 | 2.14E-05 | 1.71E-04 |
| 1 | 80.16 - 80.36 | rs11162922 | chip | 1.80E-06 | 1.03E-05 | **4.11** | 3.80 | 2.17E-05 | 2.39E-04 |
| 1 | 113.54 – 114.16 | rs6679677 | chip | **4.90E-26** | **5.55E-25** | **22.36** | **21.99** | **3.85E-24** | **1.57E-22** |
| 4 | 24.99 - 25.13 | rs3816587 | chip | 7.65E-03 | 9.25E-06 | 0.50 | 2.64 | 4.38E-02 | 5.64E-05 |
| 6 | MHC | rs6457617 | chip | **3.44E-76** | **5.18E-75** | 74.84 | 73.1754 | 5.65E-70 | 5.22E-68 |
| 6 | 138.00 - 138.06 | rs6920220 | chip | 4.99E-06 | 1.58E-05 | 3.49 | 3.17 | 1.76E-05 | 1.13E-04 |
| 7 | 130.80 - 130.84 | rs11761231 | chip | 1.74E-06 | 2.65E-06 | 3.92 | 3.42 | **3.91E-07** | 1.37E-06 |
| 10 | 6.07 - 6.16 | rs2104286 | chip | 7.03E-06 | 2.52E-05 | 3.37 | 2.57 | 9.82E-05 | 7.64E-04 |
| 12 | 56.26 – 56.29 | rs775251 | imputed | 3.44E-06 | 2.03E-05 | 3.91 | 3.24 | 3.74E-05 | 3.52E-04 |
| 13 | 19.845 - 19.855 | rs9550642 | chip | 8.44E-06 | 3.90E-05 | 3.35 | 3.02 | 5.03E-05 | 3.22E-04 |
| 21 | 41.430 - 41.465 | rs2837960 | chip | 3.45E-02 | 1.68E-06 | 0.05 | 2.70 | 2.97E-01 | 4.30E-05 |
| 22 | 35.870 - 35.885 | rs743777 | chip | 7.92E-06 | 1.15E-06 | 3.29 | 3.52 | 8.93E-06 | 6.33E-07 |
| | | | | **$1x10^{-5}$ < p-value < $1x10^{-4}$** | | | | | |
| 1 | 3.61 | rs12027041 | chip | 1.08E-05 | 6.21E-05 | | | | |
| 1 | 62.61 | rs626787 | chip | 8.48E-04 | 8.51E-05 | | | | |
| 1 | 113.60 | rs12723859 | chip | 2.98E-05 | 1.21E-04 | | | | |
| 2 | 40.03 | rs7601303 | chip | 9.36E-05 | 1.55E-04 | | | | |
| 2 | 241.24 | rs2953175 | chip | 3.77E-05 | 1.48E-04 | | | | |
| 3 | 65.79 | rs17073902 | chip | 9.33E-05 | 1.00E-00 | | | | |
| 3 | 150.56 | rs11718592 | chip | 3.03E-05 | 1.00E-00 | | | | |
| 3 | 195.97 | rs4677742 | chip | 9.42E-04 | 9.94E-05 | | | | |
| 4 | 182.12 | rs6831911 | chip | 4.87E-04 | 9.01E-05 | | | | |

| | | | | | |
|---|---|---|---|---|---|
| 5 | 79.13 | rs7343 | chip | 8.29E-05 | 1.35E-04 |
| 5 | 95.20 | rs17085170 | chip | 2.17E-05 | 1.00E-00 |
| 6 | 29.65 | rs1233400 | chip | 8.64E-05 | 3.71E-04 |
| 6 | 30.77 | rs1075496 | chip | 2.44E-05 | 2.90E-05 |
| 6 | 33.72 | rs12205634 | chip | 5.86E-05 | 2.20E-04 |
| 6 | 46.07 | rs3777612 | chip | 5.41E-03 | 7.37E-05 |
| 6 | 46.97 | rs220704 | chip | 4.06E-05 | 1.76E-04 |
| 6 | 93.61 | rs6909753 | chip | 4.29E-01 | 5.67E-05 |
| 7 | 83.74 | rs2715038 | chip | 8.63E-05 | 1.05E-04 |
| 7 | 109.19 | rs3114834 | chip | 1.21E-05 | 2.59E-05 |
| 7 | 128.17 | rs3807306 | chip | 3.03E-05 | 1.27E-04 |
| 7 | 134.46 | rs17236136 | chip | 8.08E-05 | 1.28E-04 |
| 8 | 21.05 | rs12549890 | chip | 2.32E-05 | 6.31E-05 |
| 8 | 34.25 | rs16881910 | chip | 2.32E-04 | 9.46E-05 |
| 8 | 85.02 | rs7009279 | chip | 8.41E-05 | 2.32E-04 |
| 9 | 18.13 | rs983230 | chip | 4.62E-05 | 1.18E-04 |
| 9 | 36.14 | rs10814339 | chip | 2.07E-03 | 6.77E-05 |
| 10 | 6.43 | rs4750316 | chip | 5.55E-05 | 1.96E-04 |
| 10 | 102.83 | rs10786617 | chip | 3.56E-03 | 4.71E-05 |
| 11 | 15.43 | rs7949682 | chip | 6.33E-05 | 2.67E-04 |
| 11 | 57.70 | rs2514189 | chip | 2.59E-05 | 1.44E-04 |
| 11 | 122.70 | rs7119209 | chip | 9.36E-05 | 3.93E-04 |
| 12 | 10.05 | rs1447888 | chip | 5.96E-05 | 9.39E-05 |
| 12 | 56.25 | rs1678542 | chip | 3.51E-05 | 1.32E-04 |
| 12 | 116.49 | rs6490130 | chip | 3.47E-03 | 1.18E-05 |
| 12 | 129.43 | rs11060878 | chip | 7.80E-03 | 8.55E-05 |
| 13 | 60.38 | rs17223208 | chip | 4.49E-05 | 2.13E-04 |
| 13 | 74.11 | rs9318297 | chip | 1.38E-02 | 8.57E-05 |
| 14 | 24.32 | rs854350 | chip | 8.11E-05 | 1.65E-04 |
| 14 | 102.75 | rs2771369 | chip | 3.84E-01 | 7.57E-05 |
| 16 | 26.78 | rs2188776 | chip | 1.35E-02 | 9.71E-05 |
| 16 | 82.60 | rs17724230 | chip | 4.62E-05 | 1.63E-04 |
| 17 | 28.98 | rs17836884 | chip | 2.84E-01 | 9.52E-05 |
| 17 | 29.95 | rs11080287 | chip | 2.15E-02 | 9.53E-05 |
| 17 | 35.90 | rs896136 | chip | 9.01E-05 | 3.05E-04 |
| 18 | 69.43 | rs4892117 | chip | 8.57E-03 | 3.21E-05 |
| 18 | 70.31 | rs11876710 | chip | 7.33E-01 | 4.13E-05 |
| 19 | 24.00 | rs7257520 | chip | 2.99E-05 | 1.00E-00 |
| 22 | 35.87 | rs3218253 | chip | 1.53E-04 | 6.98E-05 |
| 22 | 43.52 | rs1076933 | chip | 3.04E-02 | 4.21E-05 |

## f) Type 1 Diabetes

| | | | | Trend p-value | Genotypic p-value | $\log_{10}$ BF additive | $\log_{10}$ BF general | Trend p-value | Genotypic p-value |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Sex-differentiated | |
| Chromosome | Region / Position (Mb) | SNP | Type | | | | | | |
| | **Strong or moderate association** | | | | | | | | |
| 1 | 113.54 – 114.16 | rs6679677 | chip | **1.17E-26** | **5.43E-26** | **23.07** | **22.83** | **1.27E-25** | **2.13E-24** |
| 1 | 221.92 - 222.17 | rs2639703 | chip | 8.46E-06 | 1.74E-05 | 3.25 | 3.06 | 4.81E-05 | 1.65E-04 |
| 2 | 100.29 – 100.30 | rs2309837 | imputed | 3.57E-06 | 1.90E-05 | 3.58 | 3.09 | 9.21E-06 | 8.16E-05 |
| 4 | 123.02 - 123.92 | rs6534347 | imputed | **4.48E-07** | 1.83E-06 | 5.15 | 4.69 | 2.26E-06 | 2.47E-06 |
| 4 | 123.02 - 123.92 | rs17388568 | chip | 5.00E-07 | 3.27E-06 | **4.42** | 3.89 | 9.38E-07 | 7.67E-06 |
| 5 | 86.20 - 86.50 | rs2544677 | chip | 8.23E-06 | 4.43E-05 | 3.32 | 2.70 | 4.63E-05 | 4.21E-04 |
| 5 | 132.64 - 132.67 | rs17166496 | chip | 6.06E-01 | 5.20E-06 | -0.97 | 3.25 | 7.05E-01 | 1.02E-05 |
| 6 | MHC | rs9272346 | chip | **2.42E-134** | **5.47E-134** | 141.93 | 139.77 | 9.88E-133 | 1.63E-131 |
| 10 | 6.07 - 6.18 | rs2104286 | chip | 7.97E-06 | 4.32E-05 | 3.31 | 2.88 | 1.01E-05 | 1.15E-04 |
| 10 | 33.47 | rs2383983 | imputed | 2.72E-06 | 8.10E-06 | 3.74 | 3.47 | 7.64E-06 | 4.74E-05 |
| 12 | 9.71 - 9.80 | rs3764021 | imputed | 7.19E-05 | **5.08E-08** | 2.12 | 4.60 | 2.86E-04 | 7.36E-07 |
| 12 | 9.71 - 9.80 | rs11052552 | chip | 1.02E-04 | 7.24E-07 | 2.22 | 3.80 | 4.24E-04 | 7.85E-06 |
| 12 | 54.64 – 55.09 | rs11171739 | chip | **1.14E-11** | **9.71E-11** | **8.89** | **8.24** | **5.91E-11** | **1.42E-09** |
| 12 | 109.82 – 111.49 | rs17696736 | chip | **2.17E-15** | **1.51E-14** | **12.53** | **11.56** | **2.13E-14** | **2.90E-13** |
| 16 | 10.93 – 11.37 | rs12708716 | chip | **9.24E-08** | **4.92E-07** | 5.15 | 4.71 | 5.33E-07 | 4.10E-06 |
| 16 | 10.93 – 11.37 | rs9746695 | chip | 8.19E-09 | 4.85E-08 | **6.19** | **5.71** | **4.45E-08** | 6.17E-07 |
| 18 | 12.76 - 12.91 | rs2542151 | chip | 1.89E-06 | 1.16E-05 | 3.91 | 3.52 | 1.12E-05 | 3.29E-05 |
| | **$1\times10^{-5}$ < p-value < $1\times10^{-4}$** | | | | | | | | |
| 1 | 19.44 | rs214321 | chip | 5.71E-05 | 2.12E-04 | | | | |
| 1 | 63.82 | rs2269241 | chip | 1.23E-05 | 6.69E-05 | | | | |
| 1 | 111.15 | rs2070748 | chip | 1.93E-02 | 6.54E-05 | | | | |
| 1 | 120.00 | rs17258425 | chip | 5.51E-05 | 1.31E-04 | | | | |
| 1 | 201.12 | rs12061474 | chip | 1.27E-05 | 2.66E-05 | | | | |
| 1 | 218.40 | rs4579763 | chip | 7.53E-05 | 3.11E-04 | | | | |
| 1 | 221.98 | rs9804142 | chip | 8.43E-05 | 6.57E-05 | | | | |
| 1 | 226.22 | rs640333 | chip | 7.47E-05 | 3.40E-04 | | | | |
| 1 | 227.44 | rs10864649 | chip | 6.30E-05 | 1.52E-04 | | | | |
| 1 | 233.13 | rs577193 | chip | 8.91E-05 | 3.87E-04 | | | | |
| 2 | 43.50 | rs6732426 | chip | 7.96E-05 | 3.76E-04 | | | | |
| 2 | 74.60 | rs1063588 | chip | 6.93E-05 | 2.21E-04 | | | | |
| 2 | 100.28 | rs9653442 | chip | 3.19E-05 | 1.75E-04 | | | | |
| 2 | 175.01 | rs13035792 | chip | 3.98E-01 | 4.19E-05 | | | | |
| 2 | 184.60 | rs826140 | chip | 5.85E-05 | 2.56E-04 | | | | |
| 2 | 204.53 | rs11571304 | chip | 4.35E-05 | 1.61E-04 | | | | |
| 2 | 215.45 | rs10221582 | chip | 2.36E-05 | 9.63E-05 | | | | |
| 3 | 12.49 | rs709165 | chip | 4.97E-05 | 2.47E-04 | | | | |

| | | | | | |
|---|---|---|---|---|---|
| 3 | 22.48 | rs1450349 | chip | 9.11E-05 | 1.81E-04 |
| 3 | 46.26 | rs13096142 | chip | 2.35E-05 | 2.46E-05 |
| 3 | 55.44 | rs1520703 | chip | 1.08E-05 | 6.16E-05 |
| 3 | 97.03 | rs1368515 | chip | 8.85E-05 | 2.12E-04 |
| 3 | 179.98 | rs11924694 | chip | 4.89E-01 | 1.96E-05 |
| 4 | 57.69 | rs1718886 | chip | 8.24E-05 | 4.07E-04 |
| 5 | 7.04 | rs6873965 | chip | 5.45E-05 | 2.90E-04 |
| 5 | 35.94 | rs1025039 | chip | 1.57E-05 | 8.90E-05 |
| 5 | 86.33 | rs7722135 | chip | 1.70E-05 | 7.89E-05 |
| 5 | 167.89 | rs244895 | chip | 9.63E-05 | 3.34E-04 |
| 6 | 18.29 | rs365237 | chip | 1.44E-04 | 8.75E-05 |
| 6 | 25.53 | rs9295657 | chip | 2.63E-05 | 2.71E-05 |
| 6 | 92.88 | rs2452941 | chip | 9.98E-05 | 4.98E-04 |
| 7 | 29.10 | rs2214570 | chip | 5.79E-02 | 8.61E-05 |
| 8 | 134.27 | rs3739262 | chip | 3.84E-05 | 1.75E-04 |
| 9 | 22.01 | rs1292136 | chip | 3.71E-05 | 1.88E-04 |
| 9 | 124.09 | rs4838140 | chip | 6.86E-04 | 4.93E-05 |
| 10 | 33.46 | rs2666236 | chip | 2.13E-05 | 6.78E-05 |
| 10 | 130.27 | rs12358786 | chip | 5.31E-05 | 2.15E-04 |
| 11 | 2.23 | rs6578252 | chip | 5.87E-05 | 2.82E-04 |
| 11 | 6.64 | rs10500664 | chip | 5.93E-01 | 9.96E-05 |
| 11 | 7.55 | rs7120154 | chip | 8.52E-05 | 1.00E-00 |
| 11 | 116.86 | rs4938390 | chip | 9.41E-05 | 3.72E-05 |
| 12 | 9.71 | rs2114870 | chip | 2.04E-04 | 1.84E-05 |
| 12 | 54.65 | rs2069408 | chip | 1.45E-04 | 6.53E-05 |
| 12 | 67.98 | rs11177587 | chip | 4.88E-01 | 7.63E-05 |
| 13 | 22.54 | rs9634385 | chip | 1.56E-03 | 8.17E-05 |
| 13 | 23.20 | rs4238171 | chip | 3.39E-03 | 6.58E-05 |
| 13 | 29.05 | rs9579410 | chip | 7.57E-05 | 3.64E-04 |
| 15 | 84.95 | rs2346733 | chip | 1.30E-04 | 8.83E-05 |
| 15 | 91.02 | rs285753 | chip | 2.96E-04 | 8.33E-05 |
| 16 | 10.98 | rs12708713 | chip | 5.66E-05 | 1.33E-04 |
| 16 | 88.12 | rs3803676 | chip | 1.83E-03 | 9.38E-05 |
| 17 | 36.02 | rs7221109 | chip | 2.20E-05 | 9.78E-05 |
| 18 | 40.56 | rs12958322 | chip | 1.27E-04 | 5.14E-05 |
| 20 | 6.11 | rs6133296 | chip | 4.91E-01 | 2.34E-05 |
| 22 | 35.87 | rs3218253 | chip | 6.79E-05 | 3.19E-04 |

## g) Type 2 Diabetes

| | | | | | | | | | Sex-differentiated | |
|---|---|---|---|---|---|---|---|---|---|---|
| Chromosome | Region / Position (Mb) | SNP | Type | Trend p-value | Genotypic p-value | $\log_{10}$ BF additive | $\log_{10}$ BF general | Trend p-value | Genotypic p-value |

**Strong or moderate association**

| Chromosome | Region / Position (Mb) | SNP | Type | Trend p-value | Genotypic p-value | $\log_{10}$ BF additive | $\log_{10}$ BF general | Trend p-value | Genotypic p-value |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 66.04 - 66.36 | rs4655595 | chip | 2.68E-06 | 1.33E-05 | 3.81 | 3.47 | 8.91E-06 | 7.41E-05 |
| 2 | 160.90 - 161.17 | rs6718526 | chip | 2.40E-06 | 1.15E-05 | 3.86 | 3.35 | 2.14E-05 | 7.68E-05 |
| 2 | 205.87 | rs7587983 | imputed | 9.98E-06 | 5.68E-05 | 3.39 | 2.91 | 5.76E-05 | 5.29E-04 |
| 3 | 55.24 - 55.32 | rs358806 | chip | 4.77E-01 | 3.05E-06 | -0.83 | 2.72 | 7.22E-01 | 3.30E-05 |
| 4 | 122.92 - 123.02 | rs7659604 | chip | 2.10E-02 | 9.42E-06 | 0.13 | 2.74 | 5.70E-02 | 9.64E-05 |
| 5 | 65.87 | rs4583845 | imputed | 8.87E-06 | 4.73E-05 | 3.20 | 2.77 | 4.14E-05 | 4.30E-04 |
| 6 | 20.63 – 20.84 | rs9465871 | chip | 1.02E-06 | **3.34E-07** | **4.15** | 3.98 | 2.90E-06 | 3.08E-06 |
| 10 | 43.43 - 43.63 | rs9326506 | chip | 7.78E-06 | 2.99E-05 | 3.27 | 2.92 | 4.95E-05 | 3.91E-04 |
| 10 | 81.90 – 81.91 | rs2789686 | imputed | 8.47E-07 | 2.64E-06 | 4.35 | 4.09 | 1.61E-06 | 5.95E-06 |
| 10 | 114.71 – 114.81 | rs4506565 | chip | **5.68E-13** | **5.05E-12** | **10.14** | **9.43** | **7.92E-12** | **1.53E-10** |
| 12 | 49.50 - 49.87 | rs12304921 | chip | 5.37E-02 | 7.07E-06 | -0.09 | 2.68 | 1.09E-01 | 4.28E-06 |
| 12 | 69.58 - 69.96 | rs1495377 | chip | 1.31E-06 | 6.52E-06 | **4.01** | 3.15 | 4.56E-06 | 4.15E-05 |
| 15 | 72.24 - 72.50 | rs2930291 | chip | 7.72E-06 | 4.40E-05 | 3.30 | 2.42 | 2.03E-05 | 1.23E-04 |
| 15 | 78.12 - 78.36 | rs2903265 | chip | 9.57E-06 | 4.98E-05 | 3.24 | 2.53 | 3.57E-05 | 2.42E-04 |
| 16 | 9.29 | rs2099106 | imputed | 8.08E-06 | 1.52E-05 | 3.26 | 3.17 | 3.95E-05 | 2.58E-05 |
| 16 | 52.36 – 52.41 | rs7193144 | chip | 1.44E-08 | 4.78E-08 | **5.89** | **5.64** | **8.52E-08** | **6.90E-07** |
| | | rs9939609 | chip | **5.24E-08** | **1.91E-07** | 5.35 | 5.05 | 2.98E-07 | 2.39E-06 |

**$1x10^{-5}$ < p-value < $1x10^{-4}$**

| Chromosome | Region / Position (Mb) | SNP | Type | Trend p-value | Genotypic p-value |
|---|---|---|---|---|---|
| 1 | 48.93 | rs12086219 | chip | 6.95E-05 | 1.00E-00 |
| 1 | 73.98 | rs1340430 | chip | 6.68E-05 | 2.70E-04 |
| 1 | 205.98 | rs6691406 | chip | 3.36E-05 | 1.83E-04 |
| 1 | 219.68 | rs1341987 | chip | 1.45E-04 | 4.34E-05 |
| 2 | 30.78 | rs7583600 | chip | 8.83E-05 | 3.38E-04 |
| 2 | 60.46 | rs9309324 | chip | 1.52E-04 | 1.93E-05 |
| 2 | 160.97 | rs1020731 | chip | 9.42E-05 | 3.57E-04 |
| 2 | 189.00 | rs11688935 | chip | 2.13E-05 | 8.35E-05 |
| 2 | 205.86 | rs17248501 | chip | 1.37E-05 | 7.62E-05 |
| 3 | 11.27 | rs440646 | chip | 4.42E-05 | 2.23E-04 |
| 3 | 134.46 | rs769097 | chip | 7.31E-05 | 3.11E-04 |
| 3 | 150.03 | rs16861027 | chip | 2.71E-05 | 1.00E-00 |
| 3 | 154.52 | rs10513440 | chip | 6.23E-04 | 9.01E-05 |
| 4 | 17.12 | rs1852749 | chip | 9.84E-05 | 1.00E-00 |
| 4 | 123.02 | rs6815973 | chip | 1.81E-01 | 1.61E-05 |
| 4 | 161.74 | rs1371251 | chip | 9.72E-01 | 7.59E-05 |
| 4 | 178.39 | rs6846031 | chip | 5.64E-05 | 9.84E-05 |
| 5 | 72.74 | rs4292434 | chip | 2.75E-05 | 1.00E-00 |

| 5  | 122.49 | rs6872465  | chip | 3.42E-05 | 1.00E-00 |
|----|--------|------------|------|----------|----------|
| 5  | 153.56 | rs4958711  | chip | 8.85E-05 | 2.34E-04 |
| 6  | 2.40   | rs9391949  | chip | 6.34E-05 | 2.46E-04 |
| 6  | 55.33  | rs7452656  | chip | 1.35E-04 | 3.15E-05 |
| 6  | 107.54 | rs1665901  | chip | 2.46E-05 | 1.37E-04 |
| 8  | 15.75  | rs2736010  | chip | 5.42E-02 | 5.83E-05 |
| 8  | 98.43  | rs2679765  | chip | 2.27E-03 | 3.37E-05 |
| 9  | 88.03  | rs7019589  | chip | 4.73E-01 | 7.49E-05 |
| 9  | 114.58 | rs2185935  | chip | 9.63E-05 | 1.51E-04 |
| 9  | 135.59 | rs2590504  | chip | 1.17E-03 | 8.84E-05 |
| 10 | 7.78   | rs7474871  | chip | 2.34E-01 | 6.59E-05 |
| 10 | 53.47  | rs11000542 | chip | 7.04E-05 | 9.72E-05 |
| 10 | 104.07 | rs17780667 | chip | 4.90E-05 | 2.08E-04 |
| 10 | 130.48 | rs10829494 | chip | 1.02E-04 | 3.37E-05 |
| 11 | 94.53  | rs11021059 | chip | 1.35E-03 | 2.22E-05 |
| 11 | 119.32 | rs657317   | chip | 3.80E-05 | 1.00E-00 |
| 12 | 12.55  | rs16908188 | chip | 9.48E-05 | 4.45E-04 |
| 12 | 18.47  | rs12581163 | chip | 1.16E-01 | 6.07E-05 |
| 12 | 49.61  | rs17125088 | chip | 3.60E-02 | 4.90E-05 |
| 12 | 69.69  | rs11178531 | chip | 1.01E-05 | 3.75E-05 |
| 13 | 71.99  | rs4053550  | chip | 3.91E-05 | 1.00E-00 |
| 14 | 83.09  | rs1007383  | chip | 3.31E-01 | 7.59E-05 |
| 14 | 98.08  | rs8012854  | chip | 3.98E-05 | 2.13E-04 |
| 14 | 98.29  | rs4343209  | chip | 9.40E-05 | 1.45E-04 |
| 16 | 9.29   | Rs2099106  | chip | 1.74E-05 | 2.98E-05 |
| 18 | 62.34  | Rs508987   | chip | 1.50E-03 | 6.28E-05 |
| 18 | 75.56  | Rs70198    | chip | 6.91E-03 | 9.84E-05 |
| 20 | 40.25  | Rs7262414  | chip | 9.94E-05 | 1.58E-04 |
| 22 | 45.01  | Rs739164   | chip | 7.12E-05 | 3.58E-04 |

**Supplementary Table 7 | Association results by disease.** Regions with at least one SNP with either a strong or moderate association (from Tables 3 & 4 and Supplementary Tables 8, 9 & 10) or a p-value in the range $1\times10^{-5}$ to $1\times10^{-4}$ and within 200 Kb of at least one other SNP with a p-value less than $1\times10^{-3}$. Numbers in bold represent strong associations that were displayed in a previous table. Positions are in NCBI build 35 coordinates

| Collection | Gene | Chromosome | SNP | Add vs. Gen p-value | Dom/Rec vs. Gen p-value |
|---|---|---|---|---|---|
| **BD** | *PALB2* | 16p2 | rs420259 | $5.41 \cdot 10^{-6}$ | 0.958 (rec) |
| **CAD** | | 9p21 | rs1333049 | 0.273 | |
| **CD** | | 1p31 | rs11805303 | 0.750 | |
| **CD** | | 2q37 | rs10210302 | 0.039 | 0.028 (dom) |
| **CD** | *BSN* | 3p21 | rs9858542 | 0.003 | 0.148 (dom) |
| **CD** | | 5p13 | rs17234657 | 0.930 | |
| **CD** | *IRGM* | 5q33 | rs1000113 | 0.591 | |
| **CD** | | 10q21 | rs10761659 | 0.924 | |
| **CD** | | 10q24 | rs10883365 | 0.344 | |
| **CD** | | 16q12 | rs17221417 | 0.296 | |
| **CD** | | 18p11 | rs2542151 | 0.389 | |
| **RA** | *PTPN22* | 1p13 | rs6679677 | 0.928 | |
| **T1D** | *PTPN22* | 1p13 | rs6679677 | 0.117 | |
| **T1D** | | 12q13 | rs11171739 | 0.745 | |
| **T1D** | | 12q24 | rs17696736 | 0.490 | |
| **T1D** | | 16p13 | rs12708716 | 0.522 | |
| **T2D** | *CDKAL1* | 6p22 | rs9465871 | 0.019 | 0.008 (dom) |
| **T2D** | *TCF7L2* | 10q25 | rs4506565 | 0.896 | |
| **T2D** | *FTO* | 16q12 | rs9939609 | 0.219 | |

**Supplementary Table 8 | Comparision of disease models**. For each of the 19 SNPs outside the MHC region that are listed in Main Table 3 we tested for departures from an additive model on the log-odds scale (a model with multiplicative odds ratios). We compared a 1-df additive model with a 2-df general model, the unadjusted p-values are reported in the column "Add vs. Gen p-value". Two of the 19 SNPs show strong evidence for departure from additivity. At the SNP rs420259 associated with BD the best fitting model is a recessive model and at the SNP rs9858542 associated with CD a dominant model fits best. Another two SNPs showed moderate evidence for departure from additivity, rs10210302 associated with CD and rs9465871 associated with T2D. The best fitting model for both of these is a general 2-df model.

| Collection | Chromosome | SNP | Position | Trend p-value | Genotypic p-value | Trend p-value | Genotypic p-value | Exp. ref. group frequency | Case frequency |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Expanded reference group | | 58C+UKBS controls | | | |
| BD | 1p31 | rs2989476 | 60771280 | 1.71E-07 | 2.60E-07 | 2.27E-05 | 1.24E-05 | 0.425 | 0.470 |
| BD | 2q31 | rs12465451 | 176719036 | 1.18E-03 | 3.30E-07 | 5.06E-03 | 3.50E-04 | 0.130 | 0.149 |
| BD | 12q21 | rs1526805 | 73670904 | 6.80E-02 | 2.18E-07 | 3.37E-02 | 1.26E-04 | 0.050 | 0.057 |
| BD | 22q12 | rs8138016 | 35026649 | 6.41E-02 | 1.61E-07 | 5.04E-02 | 2.20E-02 | 0.012 | 0.016 |
| CAD | 9p21 | rs6475606 | 22071850 | 1.64E-17 | 1.75E-16 | 4.39E-14 | 2.67E-13 | 0.480 | 0.554 |
| CAD | 15q25 | rs1994016 | 76867289 | 4.93E-07 | 2.68E-06 | 1.06E-04 | 3.94E-04 | 0.422 | 0.379 |
| CD | 1p31 | rs11805303 | 67387537 | 3.03E-23 | 2.90E-22 | 6.45E-13 | 5.85E-12 | 0.306 | 0.391 |
| CD | 1q24 | rs12037606 | 169630059 | 3.37E-07 | 2.15E-06 | 1.79E-06 | 1.08E-05 | 0.392 | 0.438 |
| CD | 2p23 | rs906805 | 28516530 | 5.98E-08 | 3.57E-07 | 9.34E-05 | 4.13E-04 | 0.468 | 0.419 |
| CD | 2q37 | rs6431654 | 233943769 | 1.39E-16 | 5.98E-16 | 8.68E-14 | 9.06E-14 | 0.476 | 0.401 |
| CD | 3p21 | rs9858542 | 49676987 | 8.55E-08 | 1.20E-08 | 7.71E-07 | 3.58E-08 | 0.286 | 0.331 |
| CD | 5p13 | rs17234657 | 40437266 | 1.04E-16 | 4.00E-16 | 2.13E-13 | 1.99E-12 | 0.128 | 0.181 |
| CD | 5q23 | rs10077785 | 131829057 | 2.25E-09 | 1.55E-08 | 1.81E-06 | 1.11E-05 | 0.238 | 0.192 |
| CD | 5q33 | rs1000113 | 150220269 | 4.31E-07 | 1.68E-06 | 5.10E-08 | 3.15E-07 | 0.073 | 0.098 |
| CD | 10q21 | rs10761659 | 64115570 | 2.36E-08 | 1.55E-07 | 2.68E-07 | 1.75E-06 | 0.457 | 0.406 |
| CD | 10q24 | rs10883371 | 101282445 | 1.23E-09 | 4.20E-09 | 1.43E-08 | 4.93E-08 | 0.482 | 0.537 |
| CD | 14q13 | rs17496932 | 33007950 | 8.49E-06 | 3.14E-07 | 5.28E-04 | 2.90E-04 | 0.037 | 0.053 |
| CD | 16q12 | rs17221417 | 49297083 | 2.90E-14 | 1.46E-14 | 9.36E-12 | 3.98E-11 | 0.292 | 0.356 |
| CD | 18p11 | rs2542151 | 12769947 | 1.04E-10 | 8.46E-11 | 4.56E-08 | 2.03E-07 | 0.164 | 0.208 |
| CD | 21q22 | rs2836754 | 39213610 | 1.07E-07 | 5.94E-07 | 1.07E-05 | 6.11E-05 | 0.353 | 0.399 |
| HT | 14q11 | rs11158632 | 23839503 | 1.93E-08 | 1.16E-07 | 2.57E-04 | 1.20E-03 | 0.208 | 0.247 |
| RA | 1p13 | rs6679677 | 114015850 | 1.33E-37 | 2.00E-36 | 4.90E-26 | 5.55E-25 | 0.098 | 0.168 |
| RA | 6q23 | rs5029939 | 138237416 | 1.21E-08 | 3.24E-08 | 5.42E-06 | 2.09E-05 | 0.036 | 0.055 |
| RA | 10p15 | rs10795791 | 6148346 | 5.17E-08 | 1.40E-07 | 2.62E-05 | 6.74E-06 | 0.407 | 0.455 |
| RA | 11p15 | rs10500889 | 20994596 | 7.87E-13 | 1.00E-00 | 1.63E-04 | 1.63E-04 | 0.000 | 0.002 |
| T1D | 1p13 | rs6679677 | 114015850 | 3.98E-40 | 1.40E-41 | 1.17E-26 | 5.43E-26 | 0.098 | 0.169 |
| T1D | 2q33 | rs3087243 | 204564425 | 2.07E-07 | 1.14E-06 | 3.27E-05 | 1.41E-04 | 0.448 | 0.404 |
| T1D | 3p21 | rs6441961 | 46327388 | 4.50E-07 | 5.58E-07 | 1.17E-05 | 2.20E-05 | 0.295 | 0.335 |
| T1D | 10p15 | rs10795791 | 6148346 | 1.26E-08 | 6.95E-08 | 1.36E-05 | 5.94E-05 | 0.407 | 0.456 |
| T1D | 12p13 | rs10772079 | 9765661 | 4.14E-08 | 1.79E-07 | 1.70E-04 | 2.29E-04 | 0.354 | 0.308 |
| T1D | 12q13 | rs11171739 | 54756892 | 2.04E-14 | 1.98E-13 | 1.14E-11 | 9.71E-11 | 0.426 | 0.493 |
| T1D | 12q24 | rs17696736 | 110949538 | 2.62E-15 | 2.23E-14 | 2.17E-15 | 1.51E-14 | 0.437 | 0.506 |
| T1D | 16p13 | rs12708716 | 11087374 | 3.73E-11 | 1.91E-10 | 9.24E-08 | 4.92E-07 | 0.352 | 0.297 |
| T1D | 17q21 | rs7221109 | 36023812 | 2.00E-07 | 1.27E-06 | 2.20E-05 | 9.78E-05 | 0.355 | 0.311 |
| T1D | 18p11 | rs2542151 | 12769947 | 1.67E-08 | 1.04E-07 | 1.89E-06 | 1.16E-05 | 0.164 | 0.201 |
| T1D | 22q13 | rs229541 | 35915818 | 3.39E-07 | 2.18E-06 | 7.68E-04 | 1.29E-03 | 0.423 | 0.466 |
| T2D | 2q24 | rs7593730 | 160996961 | 2.02E-07 | 1.24E-06 | 3.58E-06 | 1.87E-05 | 0.225 | 0.188 |
| T2D | 5q14 | rs6865544 | 82933140 | 1.38E-07 | 1.01E-07 | 7.09E-06 | 3.91E-05 | 0.008 | 0.016 |
| T2D | 10q25 | rs4506565 | 114746031 | 2.72E-24 | 3.30E-23 | 5.68E-13 | 5.05E-12 | 0.313 | 0.395 |
| T2D | 12q15 | rs7132840 | 69697828 | 1.93E-08 | 9.42E-08 | 8.29E-06 | 2.97E-05 | 0.454 | 0.502 |
| T2D | 16q12 | rs8050136 | 52373776 | 6.46E-11 | 4.20E-10 | 2.00E-08 | 7.04E-08 | 0.400 | 0.455 |

**Supplementary Table 9 | Regions of the genome exhibiting strong signals using expanded reference group analysis.** Regions containing p-values less than $5 \times 10^{-7}$ on trend and/or genotypic tests of association for analyses that used an expanded reference group. For each of BD, CAD, HT and T2D, the expanded reference group comprised the 58BC and UKBS controls supplemented by the other six disease sample sets (See Main text). For CD, RA, and T1D, the expanded reference group included 58BC and UKBS controls augmented with the 7670 cases from the non-autoimmune disease sets. For result on the X chromosome see Table 16. Allele frequencies are shown for the allele that is minor in the expanded reference group. Positions are in NCBI build 35 coordinates.

| Collection | Gene | Chromosome | Strongest signal of association in region | | | | | Evidence at previously reported SNPs | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | SNP | Trend p-value | Genotypic p-value | $\log_{10}$ BF additive | $\log_{10}$ BF general | Reported SNP | WTCCC SNP | $r^2$ | Trend p-value | Genotypic p-value |
| **BD** | *BDNF* | 11p14 | rs4923460 | 9.82E-02 | 1.80E-01 | -0.36 | -0.55 | rs6265 | rs6265 | - | - | 0.17 |
| **BD** | *DAOA* | 13q33 | rs1981272 | 3.15E-02 | 2.71E-02 | -0.04 | -0.32 | - | - | - | - | - |
| **BD** | *DTNBP1* | 6p22 | rs742206 | 1.14E-03 | 1.48E-03 | 1.41 | 1.31 | - | - | - | - | - |
| **BD** | *DISC1* | 1q42 | rs1407601 | 3.22E-02 | 9.33E-02 | 0.09 | -0.23 | - | - | - | - | - |
| **BD** | *NRG1* | 8p12 | rs1487152 | 3.48E-03 | 1.34E-02 | 0.81 | -1.59 | - | - | - | - | - |
| **CAD** | *ALOX5AP* | 13q12 | rs4075131 | 1.82E-01 | 1.78E-01 | -0.59 | -0.72 | - | - | - | - | - |
| **CAD** | *KIAA0992* | 4q32 | rs17054463 | 6.55E-02 | 1.81E-01 | -0.08 | -0.35 | rs12510359 | rs1039386 | - | 0.49 | 0.37 |
| **CAD** | *ROS1* | 6q22 | rs9320600 | 6.07E-03 | 2.14E-02 | 0.75 | 0.49 | rs619203 | rs501109 | 0.07 | 0.92 | 0.97 |
| **CAD** | *TAS2R50* | 12p13 | rs10772414 | 4.74E-02 | 8.09E-02 | -0.07 | -0.23 | rs1376251 | - | - | - | - |
| **CAD** | *OR13G1* | 1q44 | rs1144812 | 5.72E-02 | 9.72E-03 | -0.24 | 0.28 | rs1151640 | rs880143 | - | 0.83 | 0.98 |
| **CAD** | *PCSK9* | 1p32 | rs594226 | 1.56E-01 | 3.65E-01 | -0.53 | -0.67 | - | - | - | - | - |
| **CAD** | *FactorV* | 1q24 | rs7474070 | 1.57E-01 | 3.68E-01 | -0.30 | -0.31 | rs6025 | rs6020 | - | 0.68 | 1 |
| **CAD** | *Prothrombin* | 11p11 | rs3136439 | 1.40E-01 | 3.34E-01 | -0.31 | -0.43 | - | - | - | - | - |
| **CAD** | *PAI-1* | 7q22 | rs3807513 | 8.50E-02 | 1.35E-01 | -0.32 | -0.49 | - | - | - | - | - |
| **CD** | *CARD15* | 16q12 | rs17221417 | 9.36E-12 | 3.98E-11 | 8.93 | 8.47 | rs2066844 | rs17221417 | 0.23 | 9.40E-12 | 4.00E-11 |
| **CD** | *IL23R* | 1p31 | rs11805303 | 6.45E-13 | 5.85E-12 | 10.07 | 9.19 | rs11805303 | rs11805303 | - | 6.50E-13 | 5.90E-12 |
| **CD** | *ATG16L1* | 2q37 | rs10210302 | 7.10E-14 | 5.26E-14 | 11.11 | 11.07 | rs2241880 | rs10210302 | 0.97 | 7.10E-14 | 5.30E-14 |
| **HT** | *ADD1* | 4p16 | rs7665452 | 2.84E-02 | 7.04E-02 | 0.27 | 0.29 | rs4961 | rs2239728 | 0.95 | 0.39 | 0.69 |
| **HT** | *GNB3* | 12p13 | rs11064432 | 3.35E-01 | 1.62E-01 | -0.45 | -0.40 | rs5443 | rs10849538 | 0.77 | 0.66 | 0.91 |
| **HT** | *ADRB2* | 5q32 | rs11959615 | 1.58E-02 | 3.69E-02 | 0.22 | -0.36 | rs1042713 | rs17778257 | 0.96 | 0.089 | 0.23 |
| **HT** | | | | | | | | rs1042714 | rs2400707 | 0.97 | 0.034 | 0.05 |
| **HT** | *AGT* | 1q42 | rs2479131 | 1.82E-02 | 6.01E-02 | 0.17 | -0.12 | rs4762 | rs2479131 | 0.52 | 0.019 | 0.06 |
| **HT** | | | | | | | | rs699 | rs11122577 | 0.69 | 0.16 | 0.26 |
| **HT** | *WNK1* | 12p13 | rs11611246 | 5.06E-02 | 1.41E-01 | -0.13 | -0.33 | - | - | - | - | - |
| **RA** | *PADI4* | 1p36 | rs1748041 | 1.56E-01 | 3.59E-01 | -0.56 | -0.70 | - | - | - | - | - |
| **RA** | *MHC2TA* | 16p13 | rs7201430 | 2.71E-01 | 3.70E-01 | -0.59 | -0.66 | - | - | - | - | - |
| **RA** | *FCRL3* | 1q23 | rs17676026 | 5.86E-01 | 2.76E-01 | -0.88 | -0.84 | - | - | - | - | - |
| **RA** | *SLC22A4* | 5q23 | rs4705938 | 4.56E-01 | 1.12E-01 | -0.91 | -0.67 | - | - | - | - | - |
| **RA** | *CTLA4* | 2q33 | rs11571300 | 3.38E-02 | 5.16E-03 | 0.08 | 0.34 | rs3087243 | rs3087243 | - | 0.085 | 0.22 |

**Supplementary Table 10 | Evidence for signal of association at other genes of previous interest.** For all genomic regions of prior interest we scanned the data for signals of association in the relevant collection of the WTCCC. Two approaches were taken. First we looked at the reported putative disease gene and surrounding 20kb, reporting the lowest p-value for the trend and genotypic test, the highest $\log_{10}$ Bayes factor for the additive and general models, and the rsID of the SNP (columns 4-8). Second, where information on the strength of association at a particular SNP had been previously published we tabulated the p-value of both the trend and genotype test at the same SNP (if in our study), or the best tag SNP (defined to be the SNP with highest $r^2$ with the reported SNP, calculated in the CEU population of the HapMap project). This information is given in columns 9-13. Positions are in NCBI build 35 coordinates.

| Combination of Collections | Chromosome | SNP | Position | Trend p-value | Genotypic p-value | In Main Table 3 | In Main Table 4 |
|---|---|---|---|---|---|---|---|
| T1D+RA | 1p13 | rs6679677 | 114015850 | 2.54E-34 | 3.90E-33 | y | |
| T1D+RA | 6 | MHC | | | | y | |
| T1D+RA | 10p15 | rs2104286 | 6139051 | 5.92E-08 | 2.53E-07 | y | y |
| T1D+RA | 12q24 | rs17696736 | 110949538 | 5.72E-11 | 3.29E-10 | y | |
| T1D+RA+CD | 1p13 | rs6679677 | 114015850 | 2.96E-16 | 2.55E-15 | y | |
| T1D+RA+CD | 6 | MHC | | | | y | |
| T1D+RA+CD | 12q24 | rs17696736 | 110949538 | 9.33E-10 | 2.62E-09 | y | |
| T1D+RA+CD | 18p11 | rs2542151 | 12769947 | 9.29E-08 | 6.17E-07 | y | |

**Supplementary Table 11 | Strongest association signals in combinations of diseases with putatively similar aetiology.** Regions with at least one SNP giving a p-value of less than $5 \times 10^{-7}$ in either the trend or the genotypic test when the given cases are pooled together, with a representative SNP for each (chosen to have the smallest p-value and a good cluster plot). Also included are whether these regions showed a strong or moderate association in a previous analysis. Positions are in NCBI build 35 coordinates.

| Collection | Chromosome | SNP | Position | Trend p-value | Genotypic p-value |
|---|---|---|---|---|---|
| | | | p-value < $5 \times 10^{-7}$ | | |
| T1D | 4q27 | rs6534347 | 123556040 | 4.48E-07 | 1.83E-06 |
| T1D | 12p13 | rs3764021 | 9724895 | 7.19E-05 | 5.08E-08 |
| | | | $5 \times 10^{-7}$ < p-value < $1 \times 10^{-5}$ | | |
| BD | 1p31 | rs2989476 | 60771280 | 1.61E-05 | 7.47E-06 |
| BD | 2q31 | rs11888446 | 181196401 | 7.01E-07 | 2.96E-06 |
| BD | 2q33 | rs4673905 | 200989289 | 9.72E-06 | 5.44E-05 |
| BD | 3p22 | rs9834970 | 36831034 | 1.21E-06 | 7.00E-06 |
| BD | 6q22 | rs6901299 | 123817025 | 3.13E-06 | 1.08E-05 |
| BD | 7p21 | rs1405318 | 11484132 | 4.54E-06 | 2.72E-05 |
| CAD | 15q25 | rs7173512 | 76636969 | 4.58E-06 | 1.57E-05 |
| CD | 9q32 | rs7869487 | 114660468 | 3.25E-05 | 4.72E-06 |
| CD | 12p11 | rs11610584 | 30076780 | 8.06E-06 | 3.70E-05 |
| CD | 17q21 | rs744166 | 37767727 | 7.19E-06 | 3.85E-05 |
| CD | 17q25 | rs4362447 | 73545157 | 6.46E-06 | 3.69E-05 |
| CD | 21q22 | rs2836753 | 39213057 | 8.28E-06 | 4.74E-05 |
| HT | 1p31 | rs1577396 | 71813438 | 0.124169 | 5.11E-06 |

| | | | | | |
|---|---|---|---|---|---|
| **HT** | 10q11 | rs7897289 | 49938769 | 3.31E-06 | 1.82E-05 |
| **HT** | 19q13 | rs10426528 | 48991138 | 3.80E-06 | 2.23E-05 |
| **T1D** | 2q11 | rs2309837 | 100296085 | 3.57E-06 | 1.90E-05 |
| **T1D** | 10p11 | rs2383983 | 33466820 | 2.72E-06 | 8.10E-06 |
| **T2D** | 2q33 | rs7587983 | 205865210 | 9.98E-06 | 5.68E-05 |
| **T2D** | 5q12 | rs4583845 | 65866380 | 8.87E-06 | 4.73E-05 |
| **T2D** | 16p13 | rs2099106 | 9288209 | 8.08E-06 | 1.52E-05 |

**Supplementary Table 12 | Regions of strong and moderate association identified by imputing HapMap SNPs, but not near regions already found.** This table gives SNPs that represent possible regions of association found through imputation. These are separated into two classes: the top of the table shows strong signals of association (p-value $< 5 \times 10^{-7}$) and the bottom of the table shows moderate signals of association ($5 \times 10^{-7} <$ p-value $< 1 \times 10^{-5}$). Note that regions with strong association are reported only when there is no strong signal at a SNP directly typed in the study within 500kb (the results are robust to this figure), and SNPs showing moderate association are reported only if there is no moderate or stronger association at SNPs directly typed in the study within 500kb. This is to identify regions of association not found in the single SNP analyses. See Methods for details of QC for these analyses. Positions are in NCBI build 35 coordinates.

| | Number of samples | Proportion missing |
|---|---|---|
| **58C** | 1480 | 0.0030 |
| **UKBS** | 1458 | 0.0037 |
| **BD** | 1868 | 0.0039 |
| **CAD** | 1926 | 0.0034 |
| **CD** | 1748 | 0.0033 |
| **HT** | 1952 | 0.0036 |
| **RA** | 1860 | 0.0035 |
| **T1D** | 1963 | 0.0034 |
| **T2D** | 1924 | 0.0038 |
| **Total** | **16179** | **0.0035** |

**Supplementary Table 13 | Missing data rates by collection.** For each collection, the number of non-excluded samples and the proportion of missing data in the clean dataset (after excluding bad samples and bad SNPs).

| Collection | Chromosome | SNP | Position | Trend p-value | Genotypic p-value | $\log_{10}$ BF additive | $\log_{10}$ BF general | In Main Table 3 | In Main Table 4 |
|---|---|---|---|---|---|---|---|---|---|
| **BD** | 16p12 | rs420259 | 23541527 | 2.19E-04 | 6.29E-08 | 1.96 | 4.78 | y | |
| **CAD** | 9p21 | rs1333049 | 22115503 | 1.79E-14 | 1.16E-13 | 11.66 | 11.03 | y | |
| **CD** | 1p31 | rs11805303 | 67387537 | 6.45E-13 | 5.85E-12 | 10.07 | 9.19 | y | |
| **CD** | 2q37 | rs10210302 | 233940839 | 7.10E-14 | 5.26E-14 | 11.11 | 11.07 | y | |
| **CD** | 3p21 | rs9858542 | 49676987 | 7.71E-07 | 3.58E-08 | 4.24 | 5.22 | y | |
| **CD** | 5p13 | rs17234657 | 40437266 | 2.13E-13 | 1.99E-12 | 10.41 | 9.89 | y | |
| **CD** | 5q23 | rs6596075 | 131770127 | 5.40E-07 | 3.19E-06 | 4.54 | 4.01 | | y |
| **CD** | 5q33 | rs11747270 | 150239060 | 4.26E-08 | 2.03E-07 | 5.43 | 5.07 | y | |
| **CD** | 6p21 | rs9469220 | 32766288 | 8.65E-07 | 2.28E-06 | 4.19 | 3.92 | | y |
| **CD** | 10q21 | rs10761659 | 64115570 | 2.68E-07 | 1.75E-06 | 4.69 | 3.80 | y | |
| **CD** | 10q24 | rs10883365 | 101277754 | 1.41E-08 | 5.82E-08 | 5.91 | 5.13 | y | |
| **CD** | 16q12 | rs2066843 | 49302700 | 1.16E-12 | 1.79E-12 | 9.79 | 9.67 | y | |
| **CD** | 18p11 | rs2542151 | 12769947 | 4.56E-08 | 2.03E-07 | 5.42 | 5.00 | y | |
| **RA** | 1p31 | rs11162922 | 80284079 | 1.80E-06 | 3.60E-06 | 4.11 | 3.80 | | y |
| **RA** | 1p13 | rs6679677 | 114015850 | 4.90E-26 | 5.55E-25 | 22.36 | 21.99 | y | |
| **RA** | 6 | MHC | | | | | | y | |
| **T1D** | 1p13 | rs6679677 | 114015850 | 1.17E-26 | 5.43E-26 | 23.07 | 22.83 | y | |
| **T1D** | 4q27 | rs17388568 | 123686967 | 5.00E-07 | 3.27E-06 | 4.42 | 3.89 | | y |
| **T1D** | 6 | MHC | | | | | | y | |
| **T1D** | 12q13 | rs11171739 | 54756892 | 1.14E-11 | 9.71E-11 | 8.89 | 8.24 | y | |
| **T1D** | 12q24 | rs17696736 | 110949538 | 2.17E-15 | 1.51E-14 | 12.53 | 11.56 | y | |
| **T1D** | 16p13 | rs9746695 | 11115395 | 8.19E-09 | 4.85E-08 | 6.19 | 5.71 | y | |
| **T2D** | 6p22 | rs9465871 | 20825234 | 1.02E-06 | 3.34E-07 | 4.15 | 3.98 | y | |
| **T2D** | 10q25 | rs4506565 | 114746031 | 5.68E-13 | 5.05E-12 | 10.14 | 9.43 | y | |
| **T2D** | 12q15 | rs1495377 | 69863368 | 1.31E-06 | 6.52E-06 | 4.01 | 3.15 | | y |
| **T2D** | 16q12 | rs7193144 | 52368187 | 1.44E-08 | 4.78E-08 | 5.89 | 5.64 | y | |

**Supplementary Table 14 | Strongest association signals using Bayesian Analysis.** Regions with at least one SNP with a -$\log_{10}$ Bayes factor of greater than 4. Also included are the p-values for the frequentist tests and whether these SNPs feature in Main Tables 3 & 4. Positions are in NCBI build 35 coordinates.

| Combination | Chromosome | SNP | Position | Trend p-value | Genotypic p-value | In Main Table 3 | In Main Table 4 |
|---|---|---|---|---|---|---|---|
| | | | | Sex as effect modifier | | | |
| CAD | 9p21 | rs1333049 | 22115503 | 8.86E-12 | 3.67E-11 | Y | |
| CD | 1p31 | rs11805303 | 67387537 | 6.79E-12 | 1.36E-10 | Y | |
| CD | 2q12 | rs3792048 | 105360191 | 3.80E-02 | 2.13E-07 | | |
| CD | 2q37 | rs10210302 | 233940839 | 2.36E-14 | 5.27E-14 | Y | |
| CD | 3p21 | rs9858542 | 49676987 | 1.76E-06 | 3.25E-07 | Y | |
| CD | 5p13 | rs17234657 | 40437266 | 4.16E-12 | 5.66E-11 | Y | |
| CD | 5q33 | rs11747270 | 150239060 | 2.26E-07 | 3.12E-06 | Y | |
| CD | 10q24 | rs10883365 | 101277754 | 7.29E-08 | 4.09E-07 | Y | |
| CD | 16q12 | rs2066843 | 49302700 | 1.48E-11 | 7.29E-11 | Y | |
| CD | 18p11 | rs2542151 | 12769947 | 2.28E-07 | 1.73E-06 | Y | |
| RA | 1p13 | rs6679677 | 114015850 | 3.85E-24 | 1.57E-22 | Y | |
| RA | 6 | MHC | | | | Y | |
| RA | 7q32 | rs11761231 | 130827294 | 3.91E-07 | 1.37E-06 | Y | y |
| T1D | 1p13 | rs6679677 | 114015850 | 1.27E-25 | 2.13E-24 | Y | |
| T1D | 6 | MHC | | | | Y | |
| T1D | 12q13 | rs11171739 | 54756892 | 5.91E-11 | 1.42E-09 | Y | |
| T1D | 12q24 | rs17696736 | 110949538 | 2.13E-14 | 2.90E-13 | Y | |
| T1D | 16p13 | rs9746695 | 11115395 | 4.45E-08 | 6.17E-07 | Y | |
| T2D | 10q25 | rs4506565 | 114746031 | 7.92E-12 | 1.53E-10 | Y | |
| T2D | 16q12 | rs7193144 | 52368187 | 8.52E-08 | 6.90E-07 | Y | |

**Supplementary Table 15 | Strong association at SNPs using a sex differentiated test.** Regions with at least one SNP giving a p-value of less than $5 \times 10^{-7}$ in either the trend or the genotypic test using a sex differentiated test (see Methods), with a representative SNP for each (chosen to have the smallest p-value and a good cluster plot). Also included are whether these regions showed a strong or moderate evidence of association in a previous analysis. As noted in the main text, this test is still sensitive to SNPs whose effects are the same in both sexes, but with some loss of power compared to the earlier analyses. Positions are in NCBI build 35 coordinates.

| Collection | SNP | Position | Trend p-value | Genotypic p-value |
|---|---|---|---|---|
| **BD** | rs975687 | 110318150 | 2.09E-06 | 9.99E-06 |
| Expanded reference group | | | | |
| **CD** | rs2807261 | 135387319 | 1.32E-07 | 3.95E-07 |
| **HT** | rs5938070 | 74450099 | 1.36E-08 | 8.60E-08 |
| **HT** | rs5932296 | 126859352 | 8.49E-06 | 4.48E-05 |

**Supplementary Table 16 | Regions with strong or moderate association on the X Chromosome**.  SNPs showing strong signal of association on the X chromosome. We used a modified version of the trend and genotypic test which controls for the hemizygosity of males (see Methods). Expanded references groups explained above. Positions are in NCBI build 35 coordinates.