doi:10.1038/nature14618

Supplementary Table Legends

Supplementary Table 1 | Intra-sex phenotypic standard deviations. The intra-sex trait standard deviations are given for each of the 16 study traits. * indicates phenotype was natural log transformed; + indicates the phenotype was rank transformed; BMI is body mass index; BP is blood pressure; FEV1 is forced expiratory lung volume in one second; FEV1/FVC is the ratio of FEV1 to forced vital capacity, another measure of lung function; FPGlucose is fasting plasma glucose; Cognitiveg is the general cognitive factor; HBA1c is haemoglobin A1c; HDL and LDL are high and low density lipoprotein cholesterol, respectively.

Supplementary Table 2 | Cohort-trait beta F_{ROH} outliers against meta-analytical beta F_{ROH}. The cohort-specific effect size estimates (beta F_{ROH}) are given for a small subset of cohorts and traits where the cohort estimates are outliers (which fail the hypothesis, cohort (β_{FROH}) = pre-QC meta-analysis (β_{FROH}), with a t-test statistic >3). Beta is the cohort-specific effect size estimate, se_beta, the standard error, beta_meta, the meta-analytical effect size, t_stat, the t-test statistic. bp_dia is diastolic blood pressure; bp_sys is systolic blood pressure; edu is educational attainment; ln_fast_ins is natural logarithm of fasting insulin; hba1c is haemoglobin A1c; lntriglyc is natural logarithm of triglycerides; rn_bmi_resids is rank normalised residuals of body mass index. Cohorts are described further in Supplementary Table 6.

Supplementary Table 3 | Estimated beta F_{ROH} stratified in various ways. Effect sizes (beta F_{ROH}) are given for educational attainment (edu), height, rank normalised forced expiratory lung volume in one second residuals (rn_fev1_resids) and rank normalised general cognitive factor residuals (rn_g_resids) under different stratified models (a). Further details are given in panel (b), n is number, beta is the effect size, and se_beta, the standard error of the effect size. Pop indicates population category on the basis of geography and demographic history – E Asian is East Asian, Eur_Isolate is European isolate population, SC_Asian is South and Central Asian. Poten_conf_edu means that educational attainment is being tested a potential confounder, with edu indicating that educational attainment is included in the model as a covariate whereas none means it is not. SROH_level indicates a stratified analysis by the sum of runs of homozygosity (SROH) in the population, into low and high. For each trait the cohorts are divided into statistically equally powered halves, and the mean SROH of the high and low strata are given in the first column of panel (b) after High and Low, respectively. These differ by trait according to which cohorts had each trait measured – the lower mean SROH for the high stratum for cognitive g (compared to the other three traits) means that fewer of the more homozygous cohorts had this trait measured. NA means not applicable as missing or too few data points.

Supplementary Table 4 | Estimated beta F_{ROH} under different models. Data are only presented for cohorts with all results, in summary (a) and with further detail (b). Effect sizes (beta F_{ROH}) are given for educational attainment (edu), height, rank normalised forced expiratory lung volume in one second residuals (rn_fev1_resids) and rank normalised general cognitive factor residuals (rn_g_resids) under different models. Fixed indicates no mixed modelling was used, gr_res indicates the GRAMMAR+ residuals were fitted and hglm indicates the full hierarchical generalised linear mixed model was used. N is number, beta is the effect size, and se_beta, the standard error of the effect size. Pheno means phenotype, , type indicates the model type is being varied (e.g. mixed modelling or not).

Supplementary Table 5 | Comparison of fixed and random effects meta-analyses for key phenotypes. The sample size, effect sizes (beta) and standard errors (se_beta), p value for association (p) and for heterogeneity (p_het) are given for each trait for both the fixed- and random-effects meta-analysis. + indicates phenotype was rank transformed; edu is educational attainment; FEV1 is forced expiratory lung volume in one second; Cognitiveg is the general cognitive factor.

Supplementary Table 6 | Cohort information. Information on cohort recruitment, genotyping, quality control, acknowledgements and funding are presented. PMID, PubMed ID; MAF, minor allele frequency; HWE, Hardy-Weinberg equilibrium P value threshold; SNP, single nucleotide polymorphism.

Supplementary Table 7 | SNP counts on different genotyping arrays. SNP counts are given for three different commonly used genotyping arrays both pre- and post-quality control, including using a minor allele frequency (MAF) threshold of >5% and SNP genotyping call rate threshold (Geno) of <3%; 1kG, 1000 Genomes Project; LD, linkage disequilibrium.

Supplementary Table 8 | Effects of inbreeding on 16 traits, with and without outlier removal. The effect sizes (beta) and standard errors (se_beta), p value for association (p) and for heterogeneity (p_het) are given for each trait in the fixed effects meta-analysis before and after removal of sub-cohorts with outlying effect sizes. * indicates phenotype was natural log transformed; + indicates phenotype was rank transformed; BMI is body mass index, DBP is diastolic blood pressure; SBP is systolic blood pressure; edu is educational attainment; FI is fasting insulin; FEV1 is forced expiratory lung volume in one second; FEV1/FVC is the ratio of FEV1 to forced vital capacity, another measure of lung function; FPG is fasting plasma glucose; g is the general cognitive factor; HBA1c is haemoglobin A1c; HDL and LDL are high and low density lipoprotein cholesterol, respectively; Tot Chol is total cholesterol; WHR is waist to hip ratio.

Supplementary Table 9 | Trait means and standard deviations by sub-cohort. The count of subjects, mean and standard deviation (sd) are given for each trait by sub-cohort. Logd indicates whether the trait was natural log transformed. + indicates phenotype was rank transformed. bmi is body mass index, bp_dia is diastolic blood pressure; bp_sys is systolic blood pressure; edu is educational attainment; fast_ins is fasting insulin; fev1 is forced expiratory lung volume in one second; fev1perfvc is the ratio of FEV1 to forced vital capacity, another measure of lung function; fpg is fasting plasma glucose; g is the general cognitive factor; hba1c is haemoglobin A1c; hdl and ldl are high and low density lipoprotein cholesterol, respectively; tot_chol is total cholesterol; triglyc is triglycerides; whr is waist to hip ratio. Sub-cohorts are differentiated with suffixes not given in Supplementary Table 6 (where further information is available), as follows: black, AA, AFR, AFA indicates African heritage; CEU, CAU, EA indicates European-heritage; CHN indicates Chinese heritage; HIS and HA indicate Hispanic heritage; AJ indicates Ashkenazi Jewish heritage; nAJ indicates non-Ashkenazi Jewish heritage; IE indicates collection in Ireland, NL in the Netherlands and SC in Scotland; CA, case or cases indicates case status and CT, ctrl, cntl or controls indicates control status; diabetics or T2D indicates type-2-diabetes subjects; CVD indicates cardiovascular disease subjects; non-diabetics indicates subjects without type-2-diabetes; OTH indicates subjects without cardiovascular disease or type-2-diabetes.

Supplementary Table 10 | Age and gender information by sub-cohort. The number, mean age and proportion male are given for each sub-cohort. Sub-cohorts are differentiated with suffixes not given in Supplementary Table 6 (where further information is available), as follows: black, AA, AFR, AFA indicates African heritage; CEU, CAU, EA indicates European-heritage; CHN indicates Chinese heritage; HIS and HA indicate Hispanic heritage; AJ indicates Ashkenazi Jewish heritage; nAJ indicates non-Ashkenazi Jewish

heritage; IE indicates collection in Ireland, NL in the Netherlands and SC in Scotland; CA, case or cases indicates case status and CT, ctrl, cntl or controls indicates control status; diabetics or T2D indicates type-2-diabetes subjects; CVD indicates cardiovascular disease subjects; non-diabetics indicates subjects without type-2-diabetes; OTH indicates subjects without cardiovascular disease or type-2-diabetes.

Supplementary Table 11 | ROH summary statistics by sub-cohort. The mean and standard deviation for the sum and number of runs of homozygosity (SROH and NROH, respectively) are given for each sub-cohort, as well as the count of subjects included. Sub-cohorts are differentiated with suffixes not given in Supplementary Table 6 (where further information is available), as follows: black, AA, AFR, AFA indicates African heritage; CEU, CAU, EA indicates European-heritage; CHN indicates Chinese heritage; HIS and HA indicate Hispanic heritage; AJ indicates Ashkenazi Jewish heritage; nAJ indicates non-Ashkenazi Jewish heritage; IE indicates collection in Ireland, NL in the Netherlands and SC in Scotland; CA, case or cases indicates case status and CT, ctrl, cntl or controls indicates control status; diabetics or T2D indicates type-2-diabetes subjects; CVD indicates cardiovascular disease subjects; non-diabetics indicates subjects without type-2-diabetes; OTH indicates subjects without cardiovascular disease or type-2-diabetes.