

Association of Body Mass Index and Parkinson Disease: A Bidirectional Mendelian Randomization Study

Author

Domenighetti, C, Sugier, PE, Sreelatha, AAK, Schulte, C, Grover, S, Portugal, B, Lee, PC, May, P, Bobbili, D, Blagojevic, MR, Lichtner, P, Singleton, AB, Hernandez, D, Edsall, C, Mellick, GD, et al.

Published

2024

Journal Title

Neurology

Version

Accepted Manuscript (AM)

DOI

[10.1212/WNL.0000000000209620](https://doi.org/10.1212/WNL.0000000000209620)

Rights statement

This work is covered by copyright. You must assume that re-use is limited to personal use and that permission from the copyright owner must be obtained for all other uses. If the document is available under a specified licence, refer to the licence for details of permitted re-use. If you believe that this work infringes copyright please make a copyright takedown request using the form at <https://www.griffith.edu.au/copyright-matters>.

Downloaded from

<https://hdl.handle.net/10072/432656>

Griffith Research Online

<https://research-repository.griffith.edu.au>

Association of body mass index and Parkinson disease: A bidirectional Mendelian randomization study

Cloé Domenighetti, Pierre-Emmanuel Sugier, Ashwin Ashok Kumar Sreelatha, Claudia Schulte, Sandeep Grover, Berta Portugal, Pei-Chen Lee, Patrick May, Dheeraj Bobbili, Milena Radivojkov Blagojevic, Peter Lichtner, Andrew B Singleton, Dena Hernandez, Connor Edsall, George D Mellick, Alexander A Zimprich, Walter Pirker, Ekaterina A Rogaeva, Anthony E Lang, Sulev Koks, Pille Taba, Suzanne Lesage, Alexis Brice, Jean-Christophe Corvol, Marie-Christine Chartier-Harlin, Eugénie Mutez, Kathrin Brockmann, Angela B Deutschlander, Georgios M Hadjigeorgiou, Efthimios Dardiotis, Leonidas Stefanis, Athina Maria Simitsi, Enza Maria Valente, Simona Petrucci, Letizia Straniero, Anna L Zecchinelli, Gianni Pezzoli, Laura Brighina, Carlo Ferrarese, Grazia Annesi, Andrea Quattrone, Monica Gagliardi, Hirotaka Matsuo, Akiyoshi Nakayama, Nobutaka Hattori, Kenya Nishioka, Sun Ju Chung, Yun Joong Kim, Pierre Kolber, Bart P C Van De Warrenburg, Bastiaan R Bloem, Mathias Toft, Lasse Pihlstrøm, Leonor Correia Guedes, Joaquim J Ferreira, Soraya Barden, Jonathan Carr, Eduardo Tolosa, Mario Ezquerra, Pau Pastor, Monica Diez-Fairen, Karin Wirdefeldt, Nancy L Pedersen, Caroline Ran, Andrea C Belin, Andreas Puschmann, Clara Hellberg, Carl E Clarke, Karen E Morrison, Manuela M Tan, Dimitri Krainc, Lena F Burbulla, Matthew Farrer, Rejko Kruger, Thomas Gasser, Manu Sharma, Alexis Elbaz ; Comprehensive Unbiased Risk Factor Assessment for Genetics and Environment in Parkinson's Disease (COURAGE-PD) Consortium

From the Université Paris-Saclay (C.D., P.-E.S., B.P., A.E.), UVSQ, Inserm, Gustave Roussy, CESP, Villejuif, France; Centre for Genetic Epidemiology (A.A.K.S., M.S.), Institute for Clinical Epidemiology and Applied Biometry, and Department for Neurodegenerative Diseases (C.S., K.B., T.G.), Hertie Institute for Clinical Brain Research, University of Tübingen; German Center for Neurodegenerative Diseases (DZNE) (C.S., K.B., T.G.), Tübingen; Center for Human Genetics (S.G.), Universitätsklinikum Gießen und Marburg, Germany; Department of Public Health (P.-C.L.), National Cheng Kung University, Tainan, Taiwan; Translational Neuroscience (P.M., D.B., R.K.), Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Esch-Belval; Institute of Human Genetics (M.R.B., P.L.), Helmholtz Zentrum München, Neuherberg, Germany; Molecular Genetics Section (A.B.S., D.H., C.E.), Laboratory of Neurogenetics, and Center for Alzheimer's and Related Dementias (A.B.S.), NIA, NIH, Bethesda, MD; Griffith Institute for Drug Discovery (G.D.M.), Griffith University, Nathan, Australia; Department of Neurology (A.A.Z.), Medical University of Vienna; Department of Neurology (W.P.), Wilhelminenspital, Austria; Tanz Centre for Research in Neurodegenerative Diseases (E.A.R., A.E.L.), University of Toronto; Edmond J. Safra Program in Parkinson's Disease (A.E.L.), Morton and Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital, UHN; Division of Neurology (A.E.L.), University of Toronto; Krembil Brain Institute (A.E.L.), Toronto, Ontario, Canada; Centre for Molecular Medicine and Innovative Therapeutics (S.K.), Murdoch University; Perron Institute for Neurological and Translational Science (S.K.), Nedlands, Australia; Department of Neurology and Neurosurgery (P.T.), University of Tartu; Neurology Clinic (P.T.), Tartu University Hospital, Estonia; Department of Neurologie (S.L., A.B., J.-C.C.), Institut du Cerveau-Paris Brain Institute-ICM, INSERM, CNRS, Assistance Publique Hôpitaux de Paris, Sorbonne Université; Assistance Publique Hôpitaux de Paris (J.-C.C.), Department of Neurology, CIC Neurosciences; Univ. Lille (M.-C.C.-H., E.M.), Inserm, CHU Lille, UMR-S 1172-LilNCog-Centre de Recherche Lille Neurosciences & Cognition, France; Department of Neurology (A.B.D.), Ludwig Maximilians University of Munich; Department of Neurology (A.B.D.), Max Planck Institute of Psychiatry, Munich, Germany; Department of Neurology and Department of Clinical Genomics (A.B.D.), Mayo Clinic Florida, Jacksonville; Department of Neurology (G.M.H., E.D.), Laboratory of Neurogenetics, University of Thessaly, University Hospital of Larissa, Greece; Department of Neurology (G.M.H.), Medical School, University of Cyprus, Nicosia; 1st Department of Neurology (L. Stefanis, A.M.S.), Eginition Hospital, Medical School, National and Kapodistrian University of Athens; Center of Clinical Research, Experimental Surgery

and Translational Research (L. Stefanis), Biomedical Research Foundation of the Academy of Athens, Greece; Department of Molecular Medicine (E.M.V.), University of Pavia; Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Mondino Foundation (E.M.V.), Pavia; UOC Medical Genetics and Advanced Cell Diagnostics (S.P.), S. Andrea University Hospital, Rome; Department of Clinical and Molecular Medicine (S.P.), University of Rome; Department of Biomedical Sciences (L. Straniero), Humanitas University, Milan; Parkinson Institute (A.L.Z.), Azienda Socio Sanitaria Territoriale (ASST) Gaetano Pini/CTO, Milano; Parkinson Institute (G.P.), Fontazione Grigioni-Via Zuretti, Milan; Department of Neurology (L.B., C.F.), San Gerardo Hospital, Monza; Department of Medicine and Surgery and Milan Center for Neuroscience (L.B., C.F.), University of Milano Bicocca, Milano; Institute for Biomedical Research and Innovation (G.A.), National Research Council, Cosenza; Institute of Neurology (A.Q.), Magna Graecia University; Institute of Molecular Bioimaging and Physiology National Research Council (M.G.), Catanzaro, Italy; Department of Integrative Physiology and Bio-Nano Medicine (H.M., A.N.), National Defense Medical College, Saitama; Department of Neurology (N.H., K.N.), Juntendo University School of Medicine, Bunkyo-ku, Tokyo, Japan; Department of Neurology (S.J.C.), Asan Medical Center, University of Ulsan College of Medicine; Department of Neurology (Y.J.K.), Yonsei University College of Medicine, Seoul, South Korea; Neurology (P.K., R.K.), Centre Hospitalier de Luxembourg; Department of Neurology (B.P.C.V.D.W., B.R.B.), Donders Institute for Brain, Cognition and Behaviour, Nijmegen, Radboud University Medical Centre, the Netherlands; Department of Neurology (M.T., L.P.), Oslo University Hospital, Norway; Instituto de Medicina Molecular João Lobo Antunes (L.C.G., J.J.F.), Faculdade de Medicina, Universidade de Lisboa; Department of Neurosciences and Mental Health (L.C.G.), Neurology, Hospital de Santa Maria, Centro Hospitalar Universitario Lisboa Norte (CHULN); Laboratory of Clinical Pharmacology and Therapeutics (J.J.F.), Faculdade de Medicina, Universidade de Lisboa, Portugal; Division of Molecular Biology and Human Genetics (S.B.), Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa; Division of Neurology (J.C.), Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa; Parkinson's disease & Movement Disorders Unit (E.T.), Neurology Service, Hospital Clínic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona; Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED: CB06/05/0018-ISCIII) (E.T.); Lab of Parkinson Disease and Other Neurodegenerative Movement Disorders (M.E.), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Institut de Neurociències, Universitat de Barcelona; Fundació per la Recerca Biomèdica i Social Mútua Terrassa (P.P., M.D.-F.), Terrassa; Movement Disorders Unit (P.P., M.D.-F.), Department of Neurology, Hospital Universitari Mutua de Terrassa, Barcelona, Spain; Department of Clinical Neuroscience (K.W.), Department of Medical Epidemiology and Biostatistics (K.W., N.L.P.), and Department of Neuroscience (C.R., A.C.B.), Karolinska Institutet, Stockholm; Department of Clinical Sciences Lund (A.P., C.H.), Neurology, Skåne University Hospital, Lund University, Sweden; University of Birmingham and Sandwell and West Birmingham Hospitals NHS Trust (C.E.C.); Faculty of Medicine (K.E.M.), Health and Life Sciences, Queens University, Belfast; Department of Clinical and Movement Neurosciences (M.M.T.), UCL Queen Square Institute of Neurology, University College London, United Kingdom; Department of Neurology (D.K., L.F.B.), Northwestern University Feinberg School of Medicine, Chicago, IL; Metabolic Biochemistry (L.F.B.), Biomedical Center (BMC), Faculty of Medicine, Ludwig-Maximilians-Universität München; Munich Cluster for Systems Neurology (SyNergy) (L.F.B.); German Center for Neurodegenerative Diseases (DZNE) (L.F.B.), Munich, Germany; Department of Neurology (M.F.), McKnight Brain Institute, University of Florida, Gainesville; Parkinson's Research Clinic (R.K.), Centre Hospitalier de Luxembourg; and Transversal Translational Medicine (R.K.), Luxembourg Institute of Health (LIH), Strassen.

Corresponding author: Alexis Elbaz, INSERM U1018 CESP, Hôpital Paul Brousse, Bâtiment 15/16, 16 avenue Paul Vaillant Couturier, 94807 Villejuif Cedex, France.
Phone number: +33 1 45595370. E-mail: alexis.elbaz@inserm.fr

Abstract

Background: The role of body mass index (BMI) in Parkinson's disease (PD) is unclear. Based on the Courage-PD consortium, we used two-sample Mendelian randomisation (MR) to replicate a previously reported inverse association of genetically-predicted BMI with PD, and investigated whether findings were robust in analyses addressing the potential for survival and incidence-prevalence biases. We also examined whether the BMI-PD relation is bidirectional by performing a reverse MR.

Methods: We used summary statistics from a genome-wide association study (GWAS) to extract the association of 501 polymorphisms with BMI, and from the Courage-PD and iPDGC consortia to estimate their association with PD. Analyses are based on participants of European ancestry. We used the inverse-weighted method to compute odds ratios (OR_{IVW} per 4.8kg/m² [95% confidence interval, CI]) of PD and additional pleiotropy-robust methods. We performed analyses stratified by age, disease duration, and sex. For reverse MR, we used SNPs associated with PD from two iPDGC GWAS to assess the effect of genetic liability toward PD on BMI.

Results: Summary statistics for BMI are based on 806,834 participants (54% women). Summary statistics for PD are based on 8919 (40% women) cases and 7600 (55% women) controls from Courage-PD, and 19,438 (38% women) cases and 24,388 (51% women) controls from iPDGC. In Courage-PD, we found an inverse association between genetically-predicted BMI and PD ($OR_{IVW}=0.82$ [0.70-0.97], $P=0.012$) without evidence for pleiotropy. This association tended to be stronger in younger participants (≤ 67 years, $OR_{IVW}=0.71$ [0.55-0.92]) and cases with shorter disease duration (≤ 7 years, $OR_{IVW}=0.75$ [0.62-0.91]). In pooled Courage-PD+iPDGC analyses, the association was stronger in women ($OR_{IVW}=0.85$ [0.74-0.99], $P=0.032$) than men ($OR_{IVW}=0.92$ [0.80-1.04], $P=0.18$), but the interaction was not statistically significant (P -interaction=0.48). In reverse MR, there was evidence for pleiotropy, but pleiotropy-robust methods showed a significant inverse association.

Conclusion: Using an independent dataset (Courage-PD), we replicate an inverse association of genetically-predicted BMI with PD, not explained by survival or incidence-prevalence biases. Moreover, reverse MR analyses support an inverse association between genetic liability toward PD and BMI, in favour of a bidirectional relation.

Keywords: Body mass index, Parkinson's disease, Bidirectional Mendelian randomisation, Epidemiology, protective factor.

INTRODUCTION

Previous epidemiological studies on the relation between body mass index (BMI) and PD provided inconsistent results.^{1,2} Associations between BMI and PD may be affected by reverse causation because PD is characterized by a long prodromal phase;³ cohort studies showed that weight loss begins 2-10 years before PD diagnosis.⁴⁻⁶ Moreover, weight loss is common in PD patients. On average, PD patients have lower weight than controls, with a difference that increases with disease duration.⁷ These observations raise the questions whether BMI has a causal effect on PD and whether the BMI-PD relation is bidirectional.

Mendelian randomisation (MR) uses genetic variants associated with exposures as instrumental variables (IV) to estimate their causal association with diseases.⁸ Under several assumptions, this method provides findings not biased by confounding or reverse causation. Bidirectional MR allows examining whether diseases also has an effect on exposures.⁹ In MR studies of age-related diseases, survival bias may distort MR estimates for exposures associated with mortality, because study participants are a non-random subset of the population who survived long enough to be included into the study.¹⁰ Incident-prevalent bias may also occur in studies including prevalent cases, if genetic instruments are associated with survival after disease onset.¹¹

A previous MR study examined the association of BMI with PD using data from the international Parkinson Disease Genomics Consortium (iPDGC) and 77 polymorphisms associated with BMI. That study reported an inverse association (OR per 5kg/m²=0.82, 95% confidence interval [CI]=0.69-0.98).¹² Another study that used data from 23andMe and ~700 BMI-associated SNPs also showed an inverse association (OR per 1kg/m²=0.99, 95% CI=0.98-1.00),¹³ thus suggesting that higher BMI is associated with decreased PD risk. A follow-up iPDGC study reported an inverse association between other traits related to increasing adiposity and PD.¹⁴

As part of the COMprehensive Unbiased Risk factor Assessment for Genetics and Environment in PD (Courage-PD) consortium, we used two-sample MR to replicate the causal association of genetically-predicted BMI with PD, and investigated whether findings were robust in analyses addressing the potential for survival and incidence-prevalence biases. In addition, we used reverse MR to examine whether genetic liability towards PD also has a causal influence on BMI in favour of a bidirectional association.

METHODS

Two-sample Mendelian Randomisation

MR estimates the causal association between an exposure and an outcome by using single nucleotide polymorphisms (SNPs) associated with the exposure. These SNPs must verify three assumptions: they must be associated with the exposure (IV1), and not associated with the outcome (except through the exposure, IV2) or with unmeasured confounders of the exposure-outcome association (*i.e.*, no horizontal pleiotropy, IV3).⁸ In two-sample MR, effect size and standard errors (SE) of the SNP-exposure and SNP-outcome association come from independent samples.

Parkinson's disease GWAS

Courage-PD

SNP-PD associations come from a GWAS using the NeuroChip¹⁵ in 23 out of 35 studies from the Courage-PD consortium (eMethods). We excluded (i) samples overlapping with iPDGC, (ii) Asian studies, so that both SNP-exposure and SNP-PD association estimates come from populations of European ancestry, (iii) studies with cases only, and (iv) studies including less than 50 cases and 50 controls.

We compared the frequency of SNPs in cases and controls in each study under an additive model using logistic regression adjusted for sex and the first four principal components. We performed a meta-analysis of the 23 GWAS using a fixed ($I^2 \leq 25\%$) or random ($I^2 > 25\%$) effects model (eMethods). We estimated and compared the mean (95% CI) pooled age of cases and controls using random effects meta-analysis.

iPDGC

We used data from the iPDGC consortium (non-overlapping with Courage-PD) that performed a sex-stratified GWAS in order to study sex-specific genetic factors associated with PD

(European ancestry).¹⁶ We used sex-specific summary statistics that did not include UK Biobank participants to avoid overlap with the summary statistics for BMI.⁸ We also pooled summary statistics from women and men to obtain summary statistics that combined both sexes.

GWAS of exposures

Body mass index

We selected SNPs associated with BMI at a genome-wide significant threshold ($P < 5 \times 10^{-8}$) and with a minor allele frequency (MAF) $\geq 1\%$ using summary statistics (betas, SEs) provided by a GWAS in participants of European ancestry (GIANT consortium and UK Biobank).¹⁷ We retained independent SNPs after clumping based on European ancestry reference data (1000 Genomes Project; $r^2 > 0.001$; genomic region = 10,000 kb). For SNPs not available in Courage-PD, we used proxies in high linkage disequilibrium with the index SNP ($r^2 > 0.8$) according to LDlink¹⁸ or SNIPA.¹⁹ We harmonized summary statistics on alleles positively associated with exposures; ambiguous palindromic SNPs (*i.e.*, A/T or C/G with MAF > 0.42) were discarded.⁸

We selected 543 SNPs from the BMI GWAS (eMethods), of which five were not available in Courage-PD and 37 were excluded (ambiguous palindromic SNPs, MAF < 0.01 , available in less than 17 studies in Courage-PD), leaving 501 SNPs for the analysis (F-statistic = 85.4).⁸

For sex-stratified, we used SNPs associated with BMI in women (299 SNPs used in the analysis) and men (248 SNPs used in the analysis) and corresponding sex-specific summary statistics.¹⁷

Parkinson's disease (reverse Mendelian randomisation)

We used two iPDGC GWASs to identify SNPs associated with PD; the associations of these SNPs with BMI come from the GWAS of BMI described above:

- Using the same approach as described above for BMI, we selected SNPs associated with PD at a genome-wide significant threshold ($P < 5 \times 10^{-8}$) and with a minor allele (MAF) $\geq 1\%$ from an iPDGC GWAS.²⁰ After clumping (1000 Genomes Project; $r^2 > 0.001$; genomic region, 10,000 kb), we selected 38 SNPs; we excluded one SNP that was not available in the BMI GWAS, one ambiguous SNP, and three SNPs associated with BMI at a genome-wide significant level ($P < 5 \times 10^{-8}$),⁹ leaving 33 SNPs for the analysis.

- We did not use the most recent iPDGC GWAS,²¹ as it included UK Biobank participants and overlapped with the BMI GWAS, which can induce bias in two-sample MR studies.⁸ However, a sex-stratified analysis of a subset of this GWAS made available sex-specific summary statistics without UK Biobank participants.¹⁶ Therefore, we pooled summary statistics from men and women to obtain pooled estimates, and retained 24 SNPs associated with PD at GWAS significance level in analyses of men and women combined.

Statistical analyses

We performed statistical analyses using *TwoSampleMR*, *MendelianRandomisation*, *MRPRESSO*, *simex*, and *phenoscanner* R packages (R Foundation for Statistical Computing, Austria). *P*-values are two-sided.

Mendelian randomisation

Wald ratio estimates (exponentiated ratio of SNP-outcome to SNP-exposure association estimates) and R^2 (proportion of BMI variance explained) were computed for each SNP.⁸

For our main analyses, we used the random-effects inverse-variance weighted (IVW) method that provides valid estimates for SNPs that verify IV assumptions. We tested heterogeneity across SNPs with the Cochran's Q-statistic.⁸

We also used additional methods that relax some IV assumptions to examine the robustness of our findings. The *MR-Egger method* provides an estimate corrected for directional

pleiotropy.²² However, this method has lower power than IVW. To be valid, the strength of the gene-exposure association should not correlate with the strength of bias due to potential pleiotropy if IVs correlate with confounders of the exposure-outcome association (InSIDE assumption).²² The I^2_{GX} statistics quantifies the strength of regression dilution bias of SNP-exposure associations. Values <90% indicate a violation of the No Measurement Error (NOME) assumption. In this case, we used the *SIMEX* method, which corrects MR-Egger estimates.²³ The *weighted median method* provides consistent estimates if $\geq 50\%$ of IVs are valid.²⁴ The *weighted mode-based method* calculates the modal estimate using the causal estimate from each SNP, so that the largest group of variants with the same causal estimate in the asymptotic limit contains valid IVs.²⁵ *MR-PRESSO* allows testing for horizontal pleiotropy and to identify outliers (p-global test), to compute corrected estimates by removing outliers (when p-global test < 0.05), and to test whether the difference between uncorrected and corrected estimates is statistically significant (distortion test).²⁶ The contamination mixture approach involves two steps: first, it identifies groups of genetic variants with similar causal estimates; second, it performs MR robustly and efficiently in the presence of invalid IVs.²⁷ Finally, we performed leave-one-out analyses, by removing one by one each SNP from the analysis and re-estimating the causal effect, to assess whether MR findings were explained by specific variants.⁸

We computed the proportion of variance explained by IVs, the F-statistic (as a measure of instrument strength),⁸ and statistical power for a type-I error rate of 5%.²⁸

LD Score Regression

We investigated the genetic correlation between BMI and PD using cross-trait LD score regression²⁹ using the same filters as in previous studies.³⁰ Genetic correlations were estimated separately for Courage-PD and iPDGC and were then meta-analyzed using an inverse-variance weighted model.

Sensitivity analyses

- There is some evidence of sex dimorphism in genetic susceptibility of BMI,¹⁷ and male sex is associated with increased PD risk. We performed sex-stratified analyses in Courage-PD based on sex-specific summary statistics, both for BMI and PD, and compared MR estimates from both strata (interaction test). As sex-stratified analyses in Courage-PD had insufficient power to detect weak associations (eTable 1), we leveraged publicly available sex-specific summary statistics from iPDGC¹⁶ to increase the sample size by performing a pooled analysis of Courage-PD and iPDGC.
- As PD is a disease of old age, selection by survival may distort MR estimates when exposures (such as BMI) are associated with survival into old age (eFigure 1).¹⁰ Bias may be in any direction, increases with age, and is expected to be more pronounced in two-sample compared to one-sample MR. We performed analyses stratified by median-age at study of cases and controls (67 years) and examined whether MR estimates observed overall were consistent with those seen in younger participants with lower mortality rates and in whom survival bias is therefore unlikely.^{31,32}
- The consortium included prevalent and incident patients. Genetic associations may be biased if genetic variants have a different effect on survival in PD patients and controls.¹¹ We assessed whether MR estimates in cases with shorter disease duration (median ≤ 7 years) were consistent with those obtained overall.
- As the role of environmental factors may be different in carriers of Mendelian PD mutations, we repeated the analyses after excluding participants with *GBA/LRRK2* mutations or with positive PD family history among first degree relatives.
- To examine the influence of pleiotropy, we used the PhenoScanner database-V2³³ to identify SNPs associated with PD or environmental exposures that are associated with PD (physical activity, lipid fractions, uric acid, vitamin D, cigarette smoking, alcohol drinking, coffee drinking), and repeated our analyses after excluding them; we also removed SNPs associated

with depression/anxiety/neuroticism to examine their influence if these exposures had a causal role on PD. Of the BMI-associated SNPs, one is associated with milk intake (rs4988235);³⁴ we also excluded this SNP as milk intake is associated with PD.^{35,36}

- We applied Steiger filtering to exclude SNPs that have a disproportionately large effect on the outcome compared with the exposure.⁸ We did not use this approach for our main analyses as it can produce erroneous results under some scenarios (differential measurement error, unmeasured confounding), and large differences in sample sizes between the exposure and outcome GWAS may also impact on the efficacy of this approach.⁹

Reverse Mendelian randomisation

Using the same approaches as described above, we estimated the causal effect of genetic liability toward PD on BMI in order to examine whether PD has a causal effect on BMI. Please note that several authors recommended that MR investigations based on a rare binary exposure (i.e., PD in reverse MR in this paper) should only test the causal null hypothesis, rather than attempt to calculate a causal estimate; therefore, for these analyses we will consider whether associations are significant but we do not discuss the value of the estimates.³⁷

Because there was high heterogeneity across SNPs and evidence for outliers in reverse MR analyses, we used an additional outlier-robust method, MR-Lasso, to examine the robustness of our findings.³⁸ An intercept term that represents the pleiotropic effect of SNPs on the outcome is added for each SNP. The causal estimate is obtained by the IVW method using the SNPs with a null intercept, while those with an intercept different from 0 are excluded. ORs are scaled to 1-unit increase in log odds of liability to PD.³⁷ We also performed leave-one-out analyses for reverse MR.

Standard protocol approvals, registrations, and patient consents

Individual studies that contributed data to Courage-PD received approval from an institutional review board from their country, and informed signed consent was obtained from the participants.

Data availability

All the results reported in the paper can be reproduced using the data available in eTables.

RESULTS

Summary statistics for BMI are based on 806,834 participants (54% women). Summary statistics for PD are based on 8919 (40% women) cases and 7600 (55% women) controls from Courage-PD, and 19,438 (38% women) cases and 24,388 (51% women) controls from iPDGC.

Causal effect of genetically-predicted body mass index on Parkinson's disease

Courage-PD participant's characteristics are shown in eTable 2. The pooled mean age (in years) of PD cases (68.5, 95% CI=64.4-72.6, $I^2=0\%$, P -heterogeneity=0.99) and controls (66.9, 95% CI=62.5-71.1, $I^2=0\%$, P -heterogeneity=0.99) were similar ($P=0.58$).

The proportion of the variance of BMI explained by all SNPs was 5.03%. In Courage-PD, the statistical power to detect an OR (per 4.8kg/m²) of 0.8 at a type-1 error of 5% was 90% overall (eTable 1).

SNPs-BMI and SNPs-PD (Courage-PD) associations are shown in eTable 3 (overall), eTable 4 (by sex), and eTable 5 (by median age and disease duration).

Genetically-predicted BMI was inversely associated with PD (OR_{IVW} per 1SD=0.82, 95% CI=0.70-0.97, $P=0.0120$; Table 1, Figure 1, eFigure 2) without heterogeneity across SNPs (P -heterogeneity=0.20). The weighted median approach also showed an inverse association although with a wider CI, while no association was observed using the weighted mode approach. The MR-Egger and MR-PRESSO methods did not show pleiotropy. Leave-one-out analyses showed consistent results after removing SNPs one-by-one (eTable 6).

The association tended to be stronger in younger individuals (OR_{IVW}=0.71, 95% CI=0.55-0.92, $P=0.009$) than in older ones (OR_{IVW}=0.89, 95% CI=0.69-1.15, $P=0.39$), but the difference was not statistically significant (P -interaction=0.22; Figure 1, eTable 7). The association also tended to be stronger in patients with shorter disease duration (OR_{IVW}=0.75, 95% CI=0.62-0.91, $P=0.003$) compared to those with longer disease duration (OR_{IVW}=0.92,

95% CI=0.75-1.13, $P=0.45$; Figure 1, eTable 7). The inverse association was confirmed in participants without a family history of PD ($OR_{IVW}=0.84$, 95% CI=0.71-1.00, $P=0.047$).

In analyses stratified by sex in Courage-PD (Figure 1, eTable 7), the inverse association was stronger in women ($OR_{IVW}=0.81$, 95% CI=0.64-1.03, $P=0.087$) than men ($OR_{IVW}=0.95$, 95% CI=0.75-1.21, $P=0.67$), but the sex-difference was not statistically significant (P -interaction=0.36). In iPDGC, the association was of a similar size in women ($OR_{IVW}=0.88$, 95% CI=0.73-1.05, $P=0.17$) and men ($OR_{IVW}=0.90$, 95% CI=0.77-1.05, $P=0.18$; P -interaction=0.86). In pooled sex-stratified analyses, the association was statistically significant in women ($OR_{IVW}=0.85$, 95% CI=0.74-0.99, $P=0.032$) but not in men ($OR_{IVW}=0.92$, 95% CI=0.80-1.04, $P=0.18$); however, the difference between the two ORs was not statistically significant (P -interaction=0.48).

Using PhenoScanner, we identified one SNP associated with PD, 13 SNPs with lipid fractions (eight for HDL-cholesterol, five for LDL-cholesterol, four for triglycerides), one with uric acid, three with smoking initiation, ten with alcohol drinking, one with coffee drinking, and four with neuroticism, depression, or anxiety (eTable 8). After excluding these SNPs and one SNP associated with milk intake, results were consistent with those seen overall ($OR_{IVW}=0.79$, 95% CI=0.67-0.94, $P=0.008$; Figure 2).

Steiger filtering did not identify significant outliers.

Causal effect of genetic liability toward Parkinson's disease on body mass index

eTable 9 shows SNPs retained for reverse MR analyses, associations with PD (in two iPDGC GWAS) and BMI, and corresponding Wald-ratio MR estimates.

Results of reverse MR analyses are shown in Table 2 and eFigure 2. Based on 33 SNPs from the Chang et al. GWAS,²⁰ the IVW method yielded an inverse association that was not statistically significant, but there was evidence of large heterogeneity (P -heterogeneity<0.001)

thus suggesting the potential for pleiotropy. The MR-Egger approach did not detect directional pleiotropy ($P=0.92$), but there was strong evidence for horizontal pleiotropy based on the MR-PRESSO approach ($P<0.001$) that detected seven outliers. After excluding outliers, there was an inverse association between genetic liability toward PD and BMI (OR=0.99, 95% CI=0.97-1.00, $P=0.013$). The MR-Lasso detected 21 valid and 12 invalid instruments, and there was an association based on valid instruments (OR=0.99, 95% CI=0.98-1.00, $P=0.038$). There was an association of the same magnitude using the weighted median and mode approaches ($P<0.002$). Leave-one-out analyses showed consistent results after removing SNPs one-by-one (eTable 10).

Similar findings were obtained based on 24 SNPs from the Blauwendraat et al. GWAS,¹⁶ except that MR-PRESSO did not show a significant association; however, other robust methods showed significant inverse associations (Table 2, eFigure 2).

Steiger filtering did not identify significant outliers.

Genetic correlation between BMI and PD

Analyses using LD score regression showed similar negative correlations in Courage-PD and iPDGC, with a pooled estimate of -0.087 (95% CI=-0.132; -0.042, $P<0.001$) without heterogeneity ($I^2=0.0\%$, $P=0.969$).

DISCUSSION

Using data from Courage-PD, after excluding samples overlapping with iPDGC, our results support an inverse causal association between genetically-predicted BMI and PD. In addition, although there was evidence for pleiotropy, our findings also suggest that genetic liability toward PD may be inversely associated with lower BMI.

A meta-analysis of 10 prospective studies showed no association between BMI and PD (RR per 5kg/m²=1.00, 95% CI=0.89-1.12), but there was significant heterogeneity across studies ($I^2=64.5\%$, p -heterogeneity=0.003).¹ In contrast, another meta-analysis of three prospective studies showed that persons with underweight (BMI<18.5kg/m²) had a ~20% increased risk of developing PD, while there was no association between obesity and PD based on four studies.² However, the association between BMI and PD may be biased by reverse causation, as previous studies showed that BMI starts declining a few years before diagnosis.^{5,39,40} Hence, large observational studies with very long follow-up and repeated BMI measures are needed to assess whether midlife BMI is associated with PD incidence in older age. In the E3N cohort study in 96,702 French women 40-65 years old at baseline and followed for ~29y with 11 BMI measures, the frequency of obesity started to decrease in PD cases 5-10y before diagnosis, showing the importance of analyses that include an exposure lag to address reverse causation; in addition, incidence was lower among women with obesity compared with those with normal BMI, even when BMI was assessed more than 20 years before diagnosis.⁶

Weight loss is also common in PD patients after diagnosis. On average, PD patients have lower weight than controls, with a difference that increases with disease duration and severity.⁷ A variety of factors are involved in weight loss in PD.⁴¹ Metabolic studies suggest that increased energy expenditure related to rigidity, tremor, and dyskinesias play a role. Appetite loss, nausea, vomiting, and gastrointestinal function impairment are also involved.

MR may contribute to better understand the association between BMI and PD. Based on data from iPDGC (13,708 PD cases, 95,282 controls), one MR study used 77 BMI-associated SNPs and reported an inverse association of genetically-predicted BMI with PD (OR per 5kg/m²=0.82, 95% CI=0.69-0.98).¹² A split-sample MR analysis of 23andMe data (19,924 cases, 2,413,087 controls), also showed an inverse association (OR per 1kg/m²=0.99, 95% CI=0.98-1.00) using 729 and 693 SNPs in subsamples 1 and 2; the OR scaled to an increase of 5kg/m², as in iPDGC, was 0.94, therefore suggesting a weaker association in this sample.¹³ However, cases and controls from both GWAS were not matched on age and BMI is strongly associated with age; for instance, in 23andMe, cases were 20 years older on average than controls, and this difference may lead to issues related to differential cohort effects on the exposure or residual confounding even after age adjustment. In iPDGC, the authors performed simulations to assess whether findings might have been explained by age-differences between cases and controls. They concluded that survivor bias could have contributed to the inverse association but did not explain all the effect. Another analysis of iPDGC (26,035 PD cases, 403,190 controls) showed an inverse association between several traits related to increasing adiposity and PD;¹⁴ there was also an inverse association between BMI and PD using the same genetic instrument as in the previous study (77 SNPs, OR per 5kg/m²=0.81; *P*=0.037) or another instrument (273 SNPs, OR per 4.8kg/m²=0.81, *P*=0.03).¹⁴ In contrast, there was no association between genetically-predicted BMI and PD among clinically-diagnosed cases from a smaller iPDGC GWAS (5851 cases, 5866 controls),¹⁴ and in an analysis of a Korean dataset (1,050 cases, 5,000 control; 9 SNPs).⁴² Finally, one study pooled results of two MR studies, one based on the FinnGen consortium (305 SNPs, 2162 cases, 21,6630 controls; OR=0.76, 95% CI=0.60-0.96) and the other using the smaller iPDGC study in clinically-diagnosed cases (300 SNPs, 5851 cases, 5866 controls; OR=0.96, 95% CI=0.83-1.12), and showed an inverse but non-significant association (OR per ~4.8kg/m²=0.90, 95% CI=0.83-1.02).⁴³

We used a large number of BMI-associated SNPs to replicate the inverse association of genetically-predicted BMI with PD, with an OR of the same size as reported by the iPDGC consortium.¹² In our study, cases and controls were of a similar age; therefore, age-differences between the two groups could not explain the observed association. However, more complex scenarios of selection by death could be involved.¹⁰ To address this issue, we performed analyses stratified by age and examined whether associations observed overall were replicated in younger subjects. The stronger inverse association in younger participants compared to older subjects is against the hypothesis that differential survival explains the inverse association between BMI and PD. Similarly, the stronger inverse association in cases with shorter disease duration suggests that incidence-prevalence bias does not explain our findings.

There is some evidence of sex dimorphism in genetic susceptibility of BMI,¹⁷ and sex is associated with PD risk. In pooled sex-stratified analysis of Courage-PD and iPDGC datasets, the association between genetically-predicted BMI and PD was significant in women only and tended to be stronger in women than men, although the difference was not statistically significant. It is possible that sex-stratified analyses lacked statistical power to detect weak associations and interactions, and larger studies will be needed to estimate more precisely the association in men.

The mechanisms underlying an inverse association between BMI and PD remain poorly understood. It is argued that neuroprotective benefits may arise in subjects with higher BMI, in particular for the preservation of cognitive function and neural networks.⁴⁴ In addition, BMI affects levels of circulating and central insulin that could play a beneficial role against neurodegeneration.⁴⁵ Insulin crosses the blood-brain-barrier and there is evidence to suggest that it influences a multitude of pathways in the brain including the promotion of neuronal survival and dopaminergic transmission.⁴⁶ The Insulin/IGF-1 signalling pathway contributes to the control of neuronal excitability, and growing evidence suggests that its dysfunction

contributes to the progressive loss of neurons in PD.⁴⁷ Further studies are needed to understand the mechanisms underlying the inverse association between BMI and PD.

Our reverse MR analysis supports an effect of genetic liability to PD on BMI, although the results are more difficult to interpret due to large heterogeneity across SNPs and evidence for horizontal pleiotropy. However, MR-PRESSO showed an inverse association after excluding outliers, and the weighted median and mode approaches also yielded inverse associations. Although they need to be replicated, these findings suggest that genetic susceptibility to PD may predispose to lower BMI. Bidirectional relations, where each of the variables causes the other, may reflect variation in causal effects of the variables across different periods of the lifespan;⁴⁸ the effect of BMI on PD may reflect the role of midlife BMI, while the effect of PD on BMI may reflect its role later in life. The mechanisms involved are likely to be multifactorial, including disruption of both peripheral and central regulatory mechanisms of body weight, increased energy expenditure, appetite loss, nausea, vomiting, and gastrointestinal function impairment.^{41,49} Alternatively, bidirectional relations may reflect a shared cause and a departure from the exclusion-restriction assumption underlying MR.⁵⁰ We found a negative genetic correlation between BMI and PD; although the correlation was weak, it was consistent in two large independent datasets. Additional analyses at a SNP, gene, or pathway level may help better understand the mechanisms underlying the association between BMI and PD.

Strengths of this study include its large size and careful clinical assessment by movement disorders specialists. Another strength relates to the MR design whose findings are not biased by reverse causation and confounding under three main validity assumptions.⁸ Our sample size was sufficient to detect an association of the size reported previously in iPDGC with a statistical power >80%.¹² Our findings are unlikely to be affected by weak instrument bias, because the F-statistic was >10 and weak genetic instruments are expected to lead to bias towards the null in two-sample MR studies.⁸ Pleiotropy is one of the main issues for MR analyses and, in order to

assess the robustness of their findings, researchers are advised to use multiple methods that rely on different assumptions.⁸ We used several approaches developed to address pleiotropy such as the weighted median and mode, MR-Egger, MR-PRESSO, contamination mixture, and MR-Lasso. Since we restricted analyses to individuals of European descent, our findings are unlikely to be affected by population stratification; in addition, cases were compared to controls from the same study site, and analyses were adjusted for principal components. Another strength of our approach is that we carried out analyses stratified by age and diseased duration. We compared our main findings to associations in younger participants and those with shorter disease duration. Selection by survival may lead to bias for PD genetic associations studies; however, bias is unlikely in younger persons with lower mortality rates.¹⁰

One limitation of our analysis is that two-sample MR assumes linear relations between exposure and disease, and do not allow examining non-linear relations. There are several examples of non-linear associations between BMI and health-related outcomes, although reverse causation probably accounts for some of the departures from linearity (*e.g.*, low BMI and increased mortality). In addition, our findings cannot be generalized to Asian populations because GWAS summary statistics were derived from populations of European origin.

In conclusion, using an independent dataset, our study replicates previous MR findings in favour of a causal protective effect of BMI on PD, and shows that this association is not explained by survival or incidence-prevalence bias. In addition, our reverse MR analysis supports an inverse association between genetic liability to PD and BMI. Additional studies are needed to elucidate the mechanisms underlying the bidirectional relation between BMI and PD.

Funding

- This work was supported by the EU Joint Program for Neurodegenerative Disease research (JPND; <https://www.neurodegenerationresearch.eu/initiatives/annual-calls-for-proposals/closed-calls/risk-factors-2012/risk-factor-call-results/courage-pd/>). This study used data from the Courage-PD consortium, conducted under a partnership agreement between 35 studies.
- C. Domenighetti is the recipient of a doctoral grant from Université Paris-Saclay, France.
- P. May was funded by the Fonds National de Recherche (FNR), Luxembourg as part of the National Centre of Excellence in Research on Parkinson's disease (NCER-PD, FNR11264123) and the DFG Research Units FOR2715 (INTER/DFG/17/11583046) and FOR2488 (INTER/DFG/19/14429377).
- A.B. Singleton, D.G. Hernandez, and C. Edsall are funded by the Intramural Research Program of the National Institute on Aging, National Institutes of Health, Department of Health and Human Services, project ZO1 AG000949.
- E. Rogaeva is funded by the Canadian Consortium on Neurodegeneration in Aging.
- S. Koks is funded by MSA.
- P. Taba is the recipient of an Estonian Research Council Grant PRG957.
- E.M. Valente is funded by the Italian Ministry of Health (Ricerca Corrente 2021).
- S. Bardien and J. Carr are supported by grants from the National Research Foundation of South Africa (Grant Number: 106052, 129249); the South African Medical Research Council (Self-Initiated Research Grant); and Stellenbosch University, South Africa; they also acknowledge the support of the NRF-DST Centre of Excellence for Biomedical Tuberculosis Research; South African Medical Research Council Centre for Tuberculosis Research; Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town.
- P. Pastor and M. Diez-Fairen have received funding from the Spanish Ministry of Science and Innovation (SAF2013-47939-R).
- K. Wirdefeldt and N.L. Pedersen are funded by the Swedish Research Council, grant numbers K2002-27X-14056-02B, 521-2010-2479, 521-2013-2488, 2017-02175.
- N.L. Pedersen is funded by the National Institutes of Health, grant numbers ES10758 and AG 08724.
- C. Ran is funded by the Märta Lundkvist Foundation, Swedish Brain Foundation, Karolinska Institutet Research Fund.
- A.C. Belin from the Swedish Brain Foundation, Swedish Research Council, Karolinska Institutet Research Funds.
- M. Sharma was supported by the grants from the German Research Council (DFG/SH 599/6-1), MSA Coalition, and Michael J Fox Foundation (USA Genetic Diversity in PD Program: GAP-India Grant ID: 17473).
- PG GEN sample collection was funded by the MRC and UK Medical Research Council (C.E. Clarke, K.E. Morrison).
- The sponsors had no role in the study design, data collection, data analysis, data interpretation, the writing of the report, or the decision to submit the paper for publication.

Conflict of interest

C. Domenighetti reports no disclosures relevant to the manuscript;

P.E. Sugier reports no disclosures relevant to the manuscript;

A. Ashok Kumar Sreelatha reports no disclosures relevant to the manuscript;

C. Schulte reports no disclosures relevant to the manuscript;

S. Grover reports no disclosures relevant to the manuscript;

B. Portugal reports no disclosures relevant to the manuscript;

P.C. Lee reports no disclosures relevant to the manuscript;

P. May reports no disclosures relevant to the manuscript;

D.R. Bobbili reports no disclosures relevant to the manuscript;

M. Radivojkov-Blagojevic reports no disclosures relevant to the manuscript;

P. Lichtner reports no disclosures relevant to the manuscript;

A.B. Singleton reports grants from Department of Defense, during the conduct of the study, grants from Michael J Fox Foundation, outside the submitted work. A.B. Singleton is an unpaid Scientific Advisory Board member for Cajal Neuroscience outside of the submitted work;

D.G. Hernandez reports no disclosures relevant to the manuscript;

C. Edsall reports no disclosures relevant to the manuscript;

G.D. Mellick reports no disclosures relevant to the manuscript;

A. Zimprich reports no disclosures relevant to the manuscript;

W. Pirker reports personal fees from Grünenthal, AbbVie, AOP Health Orphan, Zambon, Boehringer Ingelheim, Stada, Bial UCB Pharma, outside the submitted work;

E. Rogaeva reports no disclosures relevant to the manuscript;

A.E. Lang reports personal fees from AbbVie, AFFiRis, Janssen, Biogen, Merck, Sun Pharma, Corticobasal Solutions, Sunovion, Paladin, Lilly, Medtronic, Theravance, Lundbeck, Retrophin, Roche, PhotoPharmics, outside the submitted work;

S. Koks reports no disclosures relevant to the manuscript;

P. Taba reports no disclosures relevant to the manuscript;

S. Lesage reports no disclosures relevant to the manuscript;

A. Brice reports grants from France Parkinson, FRC, ANR - EPIG - Agence nationale de recherche, ANR - JPND - Agence nationale de recherche, RDS (Roger de Spoelberch Foundation), France Alzheimer, Institut de France, ANR - EPIG, FMR (maladies rares), outside the submitted work;

J.C. Corvol reports grants from the Michael J Fox Foundation, Sanofi, and served in advisory boards for Air Liquide, Biogen, Denali, Ever Pharma, Idorsia, Prevail Therapeutic, TheraNexus, UCB, outside the submitted work;

M.C. Chartier-Harlin reports no disclosures relevant to the manuscript;

E. Mutez reports no disclosures relevant to the manuscript;

K. Brockmann has received research funding from the Michael J. Fox Foundation for Parkinson's Research (MJFF-022343, MJFF-023275, MJFF-023365), the German Society for Parkinson DPG, the Health Forum Baden Wuerttemberg, the Else Kröner Fresenius Stiftung (ClinbrAIn), the University of Tuebingen, and from the German Research Foundation DFG (BR-655671-1. K. Brockmann is a consultant for F. Hoffmann-La Roche Ltd., Vanqua Bio, and

the Michael J. Fox Foundation for Parkinson's Research and has received speaker honoraria from Abbvie, Lundbeck, UCB and Zambon;

A.B. Deutschlander reports no disclosures relevant to the manuscript;

G.M. Hadjigeorgiou reports no disclosures relevant to the manuscript;

E. Dardiotis reports no disclosures relevant to the manuscript;

L. Stefanis reports the following grants: PPMI2 (supported by the Michael J. Fox Foundation), IMPRIND-IMI2 Number 116060 (EU, H2020), “Transferring autonomous and non-autonomous cell degeneration 3D models between EU and USA for development of effective therapies for neurodegenerative diseases (ND) - CROSS NEUROD” (H2020-EU 1.3.3., Grant Number778003), «Chaperone-Mediated Autophagy in Neurodegeneration» (Hellenic Foundation for Research and Innovation Grant HFRI-FM17-3013), and “CMA as a Means to Counteract alpha-Synuclein Pathology in Non-Human Primates” Grant by the Michael J. Fox Foundation (Collaborator), he is co-Head and PI at the NKUA of the General Secretariat of Research and Technology (GSRT)-funded Grant “National Network of Precision Medicine for Neurodegenerative Diseases”, he has served on an Advisory Board for Abbvie, ITF Hellas and Biogen and has received honoraria from Abbvie and Sanofi;

A.M. Simitsi reports no disclosures relevant to the manuscript;

E.M. Valente serves as Associate Editor of Journal of Medical Genetics, Section Editor of Pediatric Research, Member of the Editorial Board of Movement Disorders Clinical Practice; grants from the Italian Ministry of Health, CARIPLO Foundation, Pierfranco and Luisa Mariani Foundation, Telethon Foundation Italy;

S. Petrucci reports no disclosures relevant to the manuscript;

L. Straniero reports no disclosures relevant to the manuscript;

A. Zecchinelli reports no disclosures relevant to the manuscript;

G. Pezzoli reports no disclosures relevant to the manuscript;

L. Brighina reports no disclosures relevant to the manuscript;

C. Ferrarese reports no disclosures relevant to the manuscript;

G. Annesi reports no disclosures relevant to the manuscript;

A. Quattrone reports no disclosures relevant to the manuscript;

M. Gagliardi reports no disclosures relevant to the manuscript;

H. Matsuo reports no disclosures relevant to the manuscript;

A. Nakayama reports no disclosures relevant to the manuscript;

N. Hattori reports grants from Japan Agency for Medical Research and Development (AMED), Japan Society for the Promotion of Science (JSPS), Ministry of Education Culture,Sports,Science and Technology Japan, Grant-in-Aid for Scientific Research on Innovative Areas, Ono Pharmaceutical Co.,Ltd, Nihon Pharmaceutical Co., Ltd, Asahi Kasei Medical Co.,Ltd, Mitsubishi Tanabe Pharma Corporation, and personal fees from Dai-Nippon Sumitomo Pharma Co.,Ltd, from Takeda Pharmaceutical Co.,Ltd., Kyowa Kirin Co.,Ltd., GSK K.K, Nippon Boehringer Ingelheim,Co.,Ltd, FP Pharmaceutical Corporation, Eisai Co.,Ltd. , Kissei Pharmaceutical Company, Nihon Medi-physics Co.,Ltd, Novartis Pharma K.K, Biogen Idec Japan Ltd, AbbVie, Medtronic, Inc., Boston Scientific Japan, Astellas Pharma Inc., Daiichi Sankyo Co., OHARA Pharmaceutical Co.,Ltd, Meiji Seika Pharma, Sanofi K.K., Pfizer Japan Inc., Alexion Pharmaceuticals, Mylan N.V, MSD K.K, LundBeck Japan, Hisamitsu Pharmaceutical Co.,Inc, outside the submitted work;

K. Nishioka reports grants from Japan Society for the Promotion of Science (JSPS), outside the submitted work;

S.J. Chung reports no disclosures relevant to the manuscript;

Y.J. Kim reports no disclosures relevant to the manuscript;

P. Kolber reports other from Centre Hospitalier de Luxembourg, University of Luxembourg, grants from Fonds National de Recherche (FNR), from null, outside the submitted work;

B.P.C. van de Warrenburg reports grants from ZonMw, Hersenstichting, Gossweiler Fund, Radboud university medical centre, and Christina Foundation outside the submitted work, he has done paid consultancy for Biohaven Pharmaceuticals, Vico Therapeutics, and Servier, and receives royalties from BSL/Springer-Nature;

B.R. Bloem reports grants from Netherlands Organization for Health Research and Development, Michael J. Fox Foundation, Parkinson Vereniging, Parkinson Foundation, Gatsby Foundation, Verily Life Sciences, Horizon 2020, Topsector Life sciences and Health, Stichting Parkinson Fonds, UCB, Abbvie, during the conduct of the study, and personal fees from Biogen, Abbvie, Walk with Path, UCB, Abbvie, Zambon, Bial, Roche, outside the submitted work, and he serves as editor-in-chief of the Journal of Parkinson's Disease and serves on the editorial board of Practical Neurology and Digital Biomarkers;

M. Toft reports grants from Research Council of Norway, during the conduct of the study; grants from South-Eastern Norway Regional Health Authority, and Michael J. Fox Foundation, outside the submitted work;

L. Pihlstrøm reports grants from Norwegian Health Association and South-Eastern Norway Regional Health Authority, outside the submitted work;

L. Correia Guedes reports no disclosures relevant to the manuscript;

J.J. Ferreira reports grants from GlaxoSmithKline, Grunenthal, Fundação MSD (Portugal), TEVA, MSD, Allergan, Novartis, Medtronic, GlaxoSmithKline, Novartis, TEVA, Lundbeck, Solvay, BIAL, Merck-Serono, Merz, Ipsen, Biogen, Acadia, Allergan, Abbvie, Sunovion Pharmaceuticals, and personal fees from Faculdade de Medicina de Lisboa, CNS - Campus Neurológico Sénior, BIAL, Novartis, outside the submitted work;

S. Bardien reports no disclosures relevant to the manuscript;

J. Carr reports no disclosures relevant to the manuscript;

E. Tolosa received honoraria for consultancy from TEVA, Bial, Prevail Therapeutics, Boehringer Ingelheim, Roche and BIOGEN and has received funding for research from Spanish Network for Research on Neurodegenerative Disorders (CIBERNED)-Instituto Carlos III (ISCIII), and The Michael J. Fox Foundation for Parkinson's Research(MJFF) ;

M. Ezquerra reports no disclosures relevant to the manuscript;

P. Pastor reports no disclosures relevant to the manuscript;

M. Diez-Fairen reports no disclosures relevant to the manuscript;

K. Wirdefeldt reports no disclosures relevant to the manuscript;

N.L. Pedersen reports no disclosures relevant to the manuscript;

C. Ran reports no disclosures relevant to the manuscript;

A.C. Belin reports no disclosures relevant to the manuscript;

A. Puschmann reports grants from Parkinsonfonden (The Swedish Parkinson Foundation), ALF (Swedish Government), Region Skåne, Sweden, Skåne University Hospital, Hans-Gabriel och Trolle Wachtmeister Stiftelse för Medicinsk Forskning, Sweden, Multipark – a strategic research environment at Lund University, during the conduct of the study, personal fees from Elsevier, outside the submitted work;

C. Helberg reports no disclosures relevant to the manuscript;

C.E. Clarke reports no disclosures relevant to the manuscript;

K.E. Morrison reports no disclosures relevant to the manuscript;

M. Tan reports grants from Parkinson's UK, other from Michael J Fox Foundation, other from University College London, outside the submitted work;

D. Krainc reports no disclosures relevant to the manuscript;

L.F. Burbulla reports no disclosures relevant to the manuscript;

M. Farrer reports no disclosures relevant to the manuscript;

R. Kruger reports grants from Fonds National de Recherche Luxembourg (FNR), German Research Council (DFG), non-financial support from Abbvie, Zambon, Luxembourg/German Research Council (DFG), Fonds National de Recherche, Luxembourg (FNR), during the conduct of the study, and personal fees from University of Luxembourg, Luxembourg Institute of Health, Centre Hospitalier de Luxembourg, Desitin/Zambon, Abbvie GmbH, Medtronic GmbH, outside the submitted work;

T. Gasser reports personal fees from UCB Pharma, Novartis, Teva, MedUpdate, and grants from The Michael J Fox Foundation for Parkinson's Research, Bundesministerium für Bildung und Forschung (BMBF), Deutsche Forschungsgemeinschaft (DFG), other from "Joint Programming for Neurodegenerative Diseases"(JPND) program, funded by the European Commission, outside the submitted work, in addition, Dr. Gasser has a patent Patent Number: EP1802749 (A2) KASPP (LRRK2) gene, its production and use for the detection and treatment of neurodegenerative disorders issued;

M. Sharma reports no disclosures relevant to the manuscript;

A. Elbaz reports grants from Agence nationale de recherche (ANR), Michael J Fox foundation, Plan Ecophyto (French ministry of agriculture), and France Parkinson, outside the submitted work.

Acknowledgments

We thank iPDGC, the GIANT consortium, and the UK Biobank study for providing summary statistics for these analyses.

Additional Courage-PD contributors: Sophia N Pchelina (Saint Petersburg, Russia; collection of data), Thomas Brücke (Wien, Austria; collection of data), Marie-Anne Lorient (Paris, France; DNA banking), Claire Mulot (Paris, France; DNA banking), Georgia Xiromerisiou (Larissa, Greece; collection of data), Christos Koros (Athens, Greece; collection of data), Matina Maniati (Athens, Greece; collection of data), Maria Bozi (Athens, Greece; collection of data), Micol Avenali (Pavia, Italy; collection of data), Margherita Canesi (Milan, Italy; collection of data), Giorgio Sacilotto (Milan, Italy; collection of data), Michela Zini (Milan, Italy; collection of data), Roberto Cilia (Milan, Italy; collection of data), Francesca Del Sorbo (Milan, Italy; collection of data), Nicoletta Meucci (Milan, Italy; collection of data), Letizia Straniero (Milan, Italy; collection of data), Rosanna Asselta (Milan, Italy; collection of data), Radha Procopio (Catanzaro, Italy; collection of data), Aldo Quattrone (Catanzaro, Italy; collection of data), Manabu Funayama (Tokyo, Japan; collection of data), Aya Ikeda (Tokyo, Japan; collection of data), Takashi Matsushima (Tokyo, Japan; collection of data), Yuanzhe Li (Tokyo, Japan; collection of data), Hiroyo Yoshino (Tokyo, Japan; collection of data), Zied Landoulsi (Luxembourg, Luxembourg; collection of data), Rubén Fernández-Santiago (Barcelona, Spain; collection of data), Nicholas Wood (London, UK; site supervision), Huw R Morris (London, UK; site supervision).

References

1. Wang YL, Wang YT, Li JF, Zhang YZ, Yin HL, Han B. Body Mass Index and Risk of Parkinson's Disease: A Dose-Response Meta-Analysis of Prospective Studies. *PLoS One* 2015;10(6):e0131778;doi:10.1371/journal.pone.0131778.
2. Rahmani J, Roudsari AH, Bawadi H, et al. Body mass index and risk of Parkinson, Alzheimer, Dementia, and Dementia mortality: a systematic review and dose-response meta-analysis of cohort studies among 5 million participants. *Nutr Neurosci* 2020;1-9;doi:10.1080/1028415X.2020.1758888.
3. Savica R, Boeve BF, Mielke MM. When Do α -Synucleinopathies Start? An Epidemiological Timeline: A Review. *JAMA neurology* 2018;75(4):503-509;doi:10.1001/jamaneurol.2017.4243.
4. Chen H, Zhang SM, Hernán MA, Willett WC, Ascherio A. Weight loss in Parkinson's disease. *Ann Neurol* 2003;53(5):676-679;doi:10.1002/ana.10577.
5. Song S, Luo Z, Li C, et al. Changes in Body Composition Before and After Parkinson's Disease Diagnosis. *Mov Disord* 2021;36(7):1617-1623;doi:10.1002/mds.28536.
6. Portugal B, Artaud F, Domenighetti C, et al. Body Mass Index, Abdominal Adiposity, and Incidence of Parkinson Disease in French Women From the E3N Cohort Study. *Neurology* 2023;100(3):e324-e335;doi:10.1212/WNL.0000000000201468.
7. van der Marck MA, Dicke HC, Uc EY, et al. Body mass index in Parkinson's disease: a meta-analysis. *Parkinsonism Relat Disord* 2012;18(3):263-267;doi:10.1016/j.parkreldis.2011.10.016.
8. Burgess S, Davey Smith G, Davies NM, et al. Guidelines for performing Mendelian randomization investigations. *Wellcome Open Res* 2019;4:186;doi:10.12688/wellcomeopenres.15555.2.

9. Richmond RC, Davey Smith G. Commentary: Orienting causal relationships between two phenotypes using bidirectional Mendelian randomization. *Int J Epidemiol* 2019;48(3):907-911;doi:10.1093/ije/dyz149.
10. Smit RAJ, Trompet S, Dekkers OM, Jukema JW, le Cessie S. Survival Bias in Mendelian Randomization Studies: A Threat to Causal Inference. *Epidemiology* 2019;30(6):813-816;doi:10.1097/EDE.0000000000001072.
11. Ellenberg JH. Differential postmorbidity mortality in observational studies of risk factors for neurologic disorders. *Neuroepidemiology* 1994;13(5):187-194;doi:10.1159/000110378.
12. Noyce AJ, Kia DA, Hemani G, et al. Estimating the causal influence of body mass index on risk of Parkinson disease: A Mendelian randomisation study. *PLoS Med* 2017;14(6):e1002314;doi:10.1371/journal.pmed.1002314.
13. Heilbron K, Jensen MP, Bandres-Ciga S, et al. Unhealthy Behaviours and Risk of Parkinson's Disease: A Mendelian Randomisation Study. *J Parkinsons Dis* 2021;doi:10.3233/JPD-202487.
14. Noyce AJ, Bandres-Ciga S, Kim J, et al. The Parkinson's Disease Mendelian Randomization Research Portal. *Mov Disord* 2019;34(12):1864-1872;doi:10.1002/mds.27873.
15. Blauwendraat C, Faghri F, Pihlstrom L, et al. NeuroChip, an updated version of the NeuroX genotyping platform to rapidly screen for variants associated with neurological diseases. *Neurobiol Aging* 2017;57:247.e249-247.e213;doi:10.1016/j.neurobiolaging.2017.05.009.
16. Blauwendraat C, Iwaki H, Makarios MB, et al. Investigation of Autosomal Genetic Sex Differences in Parkinson's Disease. *Ann Neurol* 2021;90(1):35-42;doi:10.1002/ana.26090.

17. Pulit SL, Stoneman C, Morris AP, et al. Meta-analysis of genome-wide association studies for body fat distribution in 694 649 individuals of European ancestry. *Hum Mol Genet* 2019;28(1):166-174;doi:10.1093/hmg/ddy327.
18. Machiela MJ, Chanock SJ. LDlink: a web-based application for exploring population-specific haplotype structure and linking correlated alleles of possible functional variants. *Bioinformatics* 2015;31(21):3555-3557;doi:10.1093/bioinformatics/btv402.
19. Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmuller G. SNIIPA: an interactive, genetic variant-centered annotation browser. *Bioinformatics* 2015;31(8):1334-1336;doi:10.1093/bioinformatics/btu779.
20. Chang D, Nalls MA, Hallgrímsdóttir IB, et al. A meta-analysis of genome-wide association studies identifies 17 new Parkinson's disease risk loci. *Nat Genet* 2017;49(10):1511-1516;doi:10.1038/ng.3955.
21. Nalls MA, Blauwendraat C, Vallerga CL, et al. Identification of novel risk loci, causal insights, and heritable risk for Parkinson's disease: a meta-analysis of genome-wide association studies. *Lancet Neurol* 2019;18(12):1091-1102;doi:10.1016/S1474-4422(19)30320-5.
22. Burgess S, Thompson SG. Interpreting findings from Mendelian randomization using the MR-Egger method. *Eur J Epidemiol* 2017;32(5):377-389;doi:10.1007/s10654-017-0255-x.
23. Bowden J, Del Greco MF, Minelli C, Davey Smith G, Sheehan NA, Thompson JR. Assessing the suitability of summary data for two-sample Mendelian randomization analyses using MR-Egger regression: the role of the I² statistic. *Int J Epidemiol* 2016;45(6):1961-1974;doi:10.1093/ije/dyw220.
24. Bowden J, Davey SG, Haycock PC, Burgess S. Consistent Estimation in Mendelian Randomization with Some Invalid Instruments Using a Weighted Median Estimator. *Genet Epidemiol* 2016;40(4):304-314

25. Hartwig FP, Davey Smith G, Bowden J. Robust inference in summary data Mendelian randomization via the zero modal pleiotropy assumption. *Int J Epidemiol* 2017;46(6):1985-1998;doi:10.1093/ije/dyx102.
26. Verbanck M, Chen CY, Neale B, Do R. Detection of widespread horizontal pleiotropy in causal relationships inferred from Mendelian randomization between complex traits and diseases. *Nat Genet* 2018;50(5):693-698;doi:10.1038/s41588-018-0099-7.
27. Burgess S, Foley CN, Allara E, Staley JR, Howson JMM. A robust and efficient method for Mendelian randomization with hundreds of genetic variants. *Nat Commun* 2020;11(1):376;doi:10.1038/s41467-019-14156-4.
28. Brion MJ, Shakhbazov K, Visscher PM. Calculating statistical power in Mendelian randomization studies. *Int J Epidemiol* 2013;42(5):1497-1501;doi:dvt179 [pii];10.1093/ije/dvt179 [doi].
29. Bulik-Sullivan B, Finucane HK, Anttila V, et al. An atlas of genetic correlations across human diseases and traits. *Nat Genet* 2015;47(11):1236-1241;doi:10.1038/ng.3406.
30. Sugier PE, Lucotte EA, Domenighetti C, et al. Investigation of Shared Genetic Risk Factors Between Parkinson's Disease and Cancers. *Mov Disord* 2023;38(4):604-615;doi:10.1002/mds.29337.
31. Schooling CM. Selection bias in population-representative studies? A commentary on Deaton and Cartwright. *Soc Sci Med* 2018;210:70;doi:10.1016/j.socscimed.2018.04.047.
32. Schooling CM. Biases in GWAS – the dog that did not bark. *bioRxiv* 2019:709063;doi:10.1101/709063.
33. Kamat MA, Blackshaw JA, Young R, et al. PhenoScanner V2: an expanded tool for searching human genotype-phenotype associations. *Bioinformatics* 2019;35(22):4851-4853;doi:10.1093/bioinformatics/btz469.

34. Mendelian Randomization of Dairy Consumption Working G. Dairy Consumption and Body Mass Index Among Adults: Mendelian Randomization Analysis of 184802 Individuals from 25 Studies. *Clin Chem* 2018;64(1):183-191;doi:10.1373/clinchem.2017.280701.
35. Jiang W, Ju C, Jiang H, Zhang D. Dairy foods intake and risk of Parkinson's disease: a dose-response meta-analysis of prospective cohort studies. *Eur J Epidemiol* 2014;29(9):613-619;doi:10.1007/s10654-014-9921-4.
36. Domenighetti C, Sugier PE, Ashok Kumar Sreelatha A, et al. Dairy Intake and Parkinson's Disease: A Mendelian Randomization Study. *Mov Disord* 2022;37(4):857-864
37. Burgess S, Labrecque JA. Mendelian randomization with a binary exposure variable: interpretation and presentation of causal estimates. *Eur J Epidemiol* 2018;33(10):947-952;doi:10.1007/s10654-018-0424-6.
38. Rees JMB, Wood AM, Dudbridge F, Burgess S. Robust methods in Mendelian randomization via penalization of heterogeneous causal estimates. *PLoS One* 2019;14(9):e0222362;doi:10.1371/journal.pone.0222362.
39. Chen H, Zhang SM, Schwarzschild MA, Hernan MA, Willett WC, Ascherio A. Obesity and the risk of Parkinson's disease. *Am J Epidemiol* 2004;159(6):547-555;doi:10.1093/aje/kwh059.
40. Logroscino G, Sesso HD, Paffenbarger RS, Jr., Lee IM. Body mass index and risk of Parkinson's disease: a prospective cohort study. *Am J Epidemiol* 2007;166(10):1186-1190;doi:10.1093/aje/kwm211.
41. Kistner A, Lhommée E, Krack P. Mechanisms of body weight fluctuations in Parkinson's disease. *Front Neurol* 2014;5:84;doi:10.3389/fneur.2014.00084.
42. Park KW, Hwang YS, Lee SH, Jo S, Chung SJ. The Effect of Blood Lipids, Type 2 Diabetes, and Body Mass Index on Parkinson's Disease: A Korean Mendelian Randomization Study. *J Mov Disord* 2023;16(1):79-85;doi:10.14802/jmd.22175.

43. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. *BMC Med* 2021;19(1):320;doi:10.1186/s12916-021-02188-x.
44. Hsu CL, Voss MW, Best JR, et al. Elevated body mass index and maintenance of cognitive function in late life: exploring underlying neural mechanisms. *Front Aging Neurosci* 2015;7:155;doi:10.3389/fnagi.2015.00155.
45. Craft S, Watson GS. Insulin and neurodegenerative disease: shared and specific mechanisms. *Lancet Neurol* 2004;3(3):169-178;doi:10.1016/s1474-4422(04)00681-7.
46. Athauda D, Foltynie T. Insulin resistance and Parkinson's disease: A new target for disease modification? *Prog Neurobiol* 2016;145-146:98-120;doi:10.1016/j.pneurobio.2016.10.001.
47. Bassil F, Fernagut PO, Bezard E, Meissner WG. Insulin, IGF-1 and GLP-1 signaling in neurodegenerative disorders: targets for disease modification? *Prog Neurobiol* 2014;118:1-18;doi:10.1016/j.pneurobio.2014.02.005.
48. Burgess S, Daniel RM, Butterworth AS, Thompson SG. Network Mendelian randomization: using genetic variants as instrumental variables to investigate mediation in causal pathways. *Int J Epidemiol* 2015;44(2):484-495;doi:10.1093/ije/dyu176.
49. De Pablo-Fernández E, Breen DP, Bouloux PM, Barker RA, Foltynie T, Warner TT. Neuroendocrine abnormalities in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 2017;88(2):176-185;doi:10.1136/jnnp-2016-314601.
50. Farasat SM, Morrell CH, Scuteri A, et al. Pulse pressure is inversely related to aortic root diameter implications for the pathogenesis of systolic hypertension. *Hypertension* 2008;51(2):196-202;doi:10.1161/HYPERTENSIONAHA.107.099515.

Figures legends

Figure 1

Title Forest plot showing Mendelian randomisation estimates for the association between body mass index and Parkinson's disease, overall and after stratification by age at study, disease duration in cases, and sex.

OR = odds ratio per 4.8kg/m²; CI = confidence interval.

Figure 2

Title Forest plot showing Mendelian randomisation estimates for the association between body mass index and Parkinson's disease, after excluding SNPs associated with traits related to Parkinson's disease.

OR = odds ratio per 4.8kg/m²; CI = confidence interval.

Table 1: Causal effect of genetically-predicted body mass index on Parkinson's disease in Courage-PD.

Exposure	Odds ratio (95% CI)	<i>P</i>
BMI (501 SNPs, per 1SD=4.8kg/m²)		
IVW (<i>P</i> -heterogeneity=0.20)	0.82 (0.70-0.97)	0.012
Weighted median	0.87 (0.66-1.15)	0.34
Weighted mode	1.06 (0.59-1.94)	0.84
MR Egger (<i>P</i> -pleiotropy=0.84; I^2_{GX} =0.90)	0.79 (0.50-1.26)	0.32
MR-PRESSO (<i>P</i> -pleiotropy=0.15)	-	-
Contamination mixture (number of valid SNPs, 407)	0.83 (0.66-1.14)	0.21

CI, confidence interval; IVW, inverse variance weighted; SD, standard deviation.

Table 2: Reverse Mendelian randomisation using SNPs associated with PD from two GWAS from the iPDGC consortium.

Exposure	Odds ratio (95% CI)	P
Chang et al. 2017; 33 SNPs		
IVW (P -heterogeneity<0.001)	1.00 (0.98-1.01)	0.49
Weighted median	0.98 (0.97-0.99)	0.002
Weighted mode	0.98 (0.97-0.99)	<0.001
MR Egger (P -pleiotropy=0.92; I^2_{GX} =0.94)	0.99 (0.96-1.02)	0.69
MR-PRESSO (P -pleiotropy<0.001, P -distortion=0.53) ^a	0.99 (0.97-1.00)	0.013
Contamination mixture (number of valid SNPs, 18)	0.98 (0.98-0.99)	<0.001
MR-Lasso (number of valid SNPs, 21; lambda=0.44)	0.99 (0.98-1.00)	0.038
Blauwendraat et al. 2021; 24 SNPs		
IVW (P -heterogeneity<0.001)	1.00 (0.99-1.01)	0.91
Weighted median	0.99 (0.98-1.00)	0.031
Weighted mode	0.98 (0.97-0.99)	0.004
MR Egger (P -pleiotropy=0.47; I^2_{GX} =0.94)	0.99 (0.96-1.02)	0.48
MR-PRESSO (P -pleiotropy<0.001, P -distortion=0.12) ^b	1.00 (0.99-1.01)	0.87
Contamination mixture (number of valid SNPs, 11)	0.98 (0.98-0.99)	0.003
MR-Lasso (number of valid SNPs, 9; lambda=0.38)	0.99 (0.98-1.00)	0.014

CI, confidence interval; IVW, inverse variance weighted.

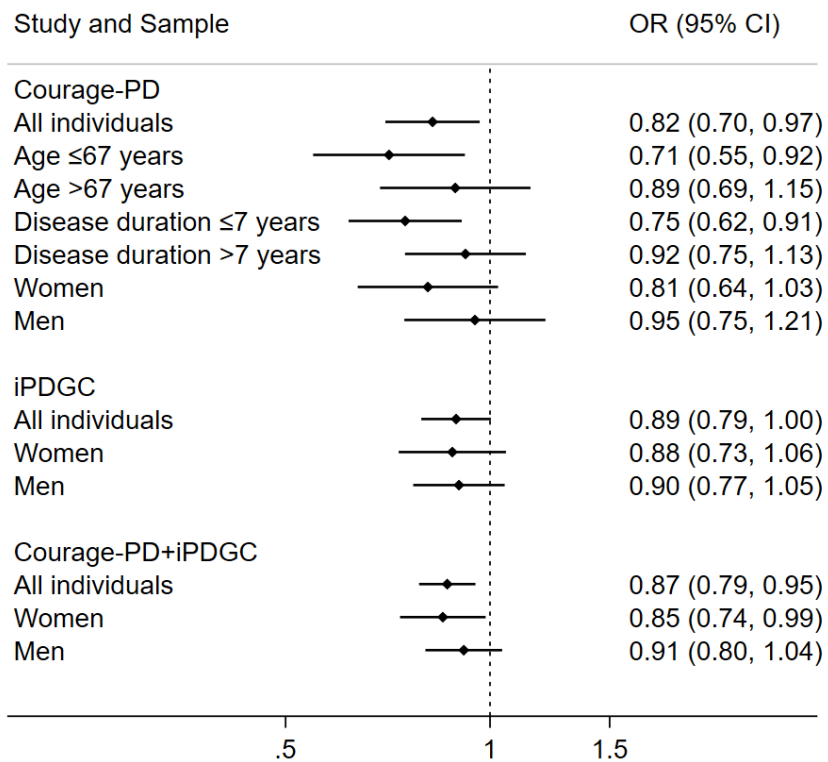
^a Outliers: rs11158026, rs11343, rs12456492, rs12637471, rs1474055, rs4073221, rs6430538.

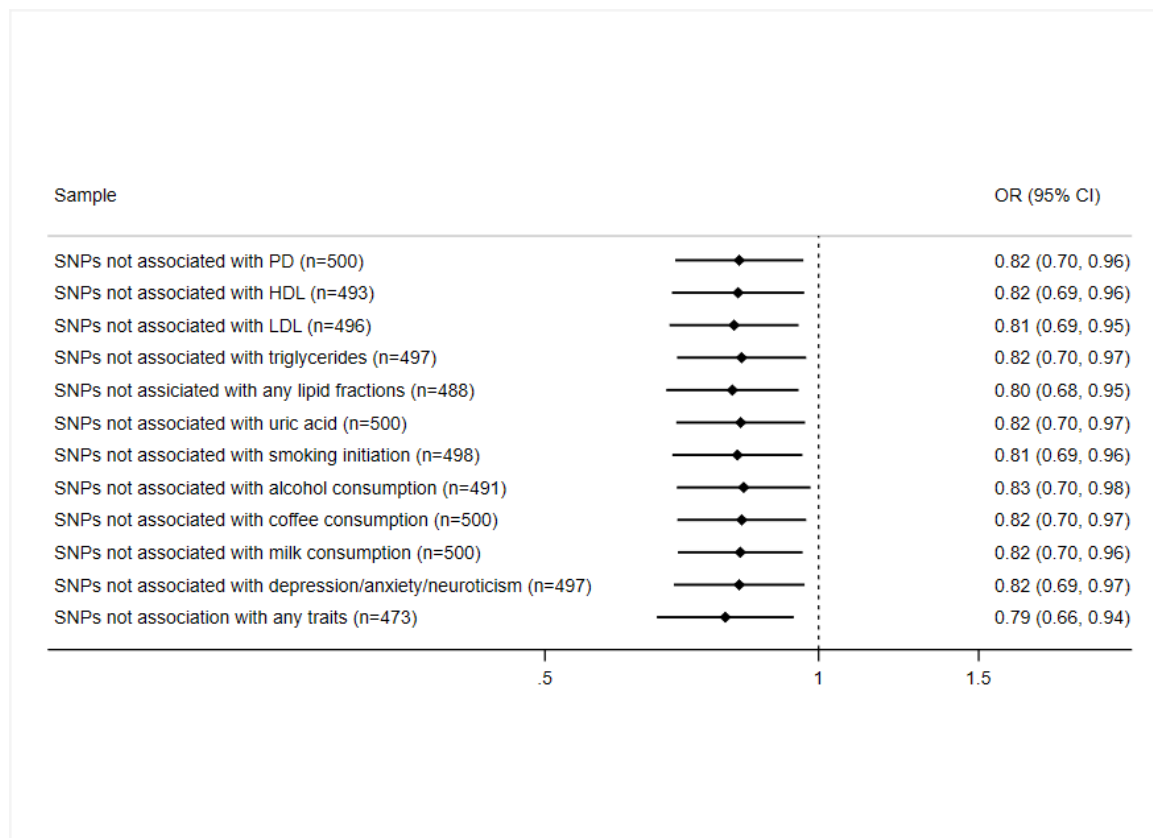
^b Outliers: rs10513789 rs1692821 rs356182 rs4588066 rs6741007 rs823116.

Table 3: Genetic correlations between BMI and Parkinson's disease.

Study	N SNPs	G_{corr}	95% CI	P	I²	P-het.
Courage-PD	1,051,136	-0.086	-0.157; -0.015	0.0178		
iPDGC	756,723	-0.088	-0.146; -0.030	0.0029		
Pooled	--	-0.087	-0.132; -0.042	<0.001	0.0%	0.969

G_{corr}, genetic correlation; CI, confidence interval; iPDGC, International Parkinson Disease Genomics Consortium; P-het., Cochran's Q test for heterogeneity across studies.





Supplementary material

eMethods.....	2
eTable 1: Power calculations for forward Mendelian randomisation analyses.	5
eTable 2: Characteristics of cases and controls from the Courage-PD consortium by study site (after quality control).	6
eTable 3: SNPs used for Mendelian randomisation analyses: individual associations with BMI and PD (Courage-PD), and R^2	8
eTable 4: SNPs used for Mendelian randomisation analyses: individual associations with PD (Courage-PD) and BMI stratified by sex.	20
eTable 5: SNPs used for Mendelian randomisation analyses: individual associations with PD (Courage-PD) stratified by age and disease duration.	35
eTable 6: Forward MR analysis: Leave-one-out analysis.....	47
eTable 7: Mendelian randomisation analyses stratified by age at study, disease duration, and sex.	51
eTable 8: Association between IVs used for BMI and other traits related to PD using the PhenoScanner V2 database at genome-wide significant threshold (5×10^{-8}).	52
eTable 9: SNPs used for reverse Mendelian randomisation analyses: individual associations with PD in iPDGC (Chang et al., 2017; Blauwendraat et al., 2021) and BMI.	53
eTable 10: Reverse MR analysis: Leave-one-out analysis.....	55
eFigure 1: Survival bias in Mendelian randomisation studies of diseases in elderly populations.	56
eFigure 2: Bidirectional MR analyses between BMI and PD: (A) Plots relating the effects sizes of the SNPs-exposure (x-axis) and SNP-outcome (y-axis, log OR) associations with standard error bars: the slope of the lines corresponds to causal estimates using different methods; (B) funnel plots of individual variant effects plotted against the inverse of their standard error. For reverse MR, SNP-PD associations come from two GWAS using the iPDGC dataset.....	57

eMethods

Courage-PD international consortium

The Courage-PD (COMprehensive Unbiased Risk Factor Assessment for Genetics and Environment in Parkinson's Disease) international consortium pooled individual-level data from 35 studies on Parkinson's disease (PD) from different populations worldwide and used the same array to genotype their participants.

The Geo-PD (Genetic Epidemiology Of Parkinson's disease; <https://geopd.biomedinfo.org/>) consortium represents one of the components of Courage-PD. This consortium aims at conducting collaborative studies on genetic susceptibility in PD; one of its main features is that participating sites are distributed in the five continents, therefore representing a highly diverse population. In addition, several other studies from Europe contributed to Courage-PD. PD was diagnosed using standard criteria (United Kingdom Parkinson's Disease Society Brain Bank - UKPDSBB, Gelb, Bower).¹⁻³

All studies were approved by local ethical committees following the procedures of each country, and material transfer agreements were set up between participating sites and the University of Tübingen (Germany).

According to the study's consortium agreement, participating sites contributed DNA and demographic/environmental data. DNAs (25µl of DNA at a concentration of 50 to 100 ng/µl) were shipped for quality control to University of Tübingen (Germany) and genotyped in a central laboratory in Munich (Institute of Human Genetics, Helmholtz Zentrum, Germany). The samples from two sites (Gasser, Morris/Wood) were genotyped at the Laboratory of Neurogenetics (National Institute on Aging, National Institutes of Health, Bethesda, USA). Demographic data were harmonized and collected using a standardized form and cleaned at Inserm U1018 (Villejuif, France).

Genotyping

The Neurochip chip was used to genotype all the samples.⁴ Briefly, this chip is a custom-designed array containing a tagging variant backbone with good genome-wide resolution of about 306,670, complemented with a manually curated custom content comprised of 179,467 variants implicated in diverse neurological diseases, including PD.

Genotyping was performed with an automated protocol according to the manufacturer's instructions (Illumina, San Diego, CA, USA). All arrays were scanned with an Illumina iScan and raw data were analysed with the Illumina Beeline and GenomeStudio software packages using the manifest file `Neuro_Consortium_20013217_A1.bpm`. Clustering was performed in GenomeStudio with the GenTrain cluster 2.0 algorithm. Genotypes were post-processed with zCall (DOI: 10.1093/bioinformatics/bts479) to improve detection of rare alleles.

Quality control

Genotyped data exported from Genome Studio to PLINK format were used for quality control and downstream analysis. The pooled dataset from the 35 sites consists of 27,538 subjects. Phenotypic data were missing for 245 subjects and three sites were removed as they only included cases, leaving 26,535 subjects (14,859 cases, 11,431 controls) for quality control using "COMRARE" an automated pipeline under development at the University of Tübingen. The pipeline uses PLINK (<https://www.cog-genomics.org/plink>) and R scripts (R Foundation for Statistical Computing, Vienna, Austria) and the following steps were implemented separately for each site:

- 1- *Per individual quality control:*

- Identification of individuals with elevated missing genotyping rates or outlying heterozygosity rate: individuals with a genotype failure rate $\geq 4\%$ or heterozygosity rate ± 4 standard deviations from the mean were excluded.
- Identification of Individuals with discordant sex information: the homozygosity rate was calculated for X-linked SNPs for each individual and compared to the expected rate. Participants for whom phenotypic and genotypic sex were discordant were removed.
- Identification of duplicated or related Individuals: pairs of individuals with an identity by descent (IBD) greater than 0.185 were removed.
- Eigensoft software was used to compute principal components in order to correct for population stratification by merging our dataset with HapMap.^{5, 6} A scatter plot of the first two principal components was used to identify outliers in each study.

2- Per marker quality control:

- Identification of markers with high missing data rate: a call-rate threshold of 96% was used and SNPs with a lower rate were removed.
- SNPs with a significant ($P < 10^{-5}$) difference in rates of missing values between cases and controls were removed.
- We excluded variants with a minor allele frequency (MAF) $< 5 \times 10^{-8}$ and those in Hardy-Weinberg disequilibrium ($P < 5 \times 10^{-8}$).

Imputation

After QC, we used the HRC/1000G imputation preparation and checking tool (<https://www.well.ox.ac.uk/~wrayner/tools/HRC-1000G-check-bim-v4.3.0.zip>) to check for Ref/Alt allele assignments, incorrect strands, deviation from allele frequency, and palindromic SNPs. Imputation of autosomal variants was performed separately for each dataset based on based on 271,398 to 373,664 SNPs in each study, through the Michigan Imputation server using the HRC reference panel and the GRCh37/hg19 assembly with a R^2 filter of 0.3. The mean of the number of SNPs available in each study after imputation was 13,710,549 (SD=2,986,478).

Association analysis and meta-analysis

We excluded from our analyses samples overlapping with the international Parkinson Disease Genomics Consortium (iPDGC): all the samples from three sites (Pastor/Diez-Fairen, Spain; Toft, Norway; Morris/Wood, UK), 1000 samples from the Gasser/Sharma (Germany) site (642 cases, 358 controls), and 266 samples of PD cases from the Tolosa site (Spain). Analyses are also restricted to sites that provided samples for both cases and controls and to participants of Caucasian ancestry; only sites with at least 50 cases or 50 controls were included. The main characteristics of 8919 cases and 7600 controls from 23 sites included in the analyses are shown in eTable 1.

We excluded SNPs with a MAF $< 1\%$, in Hardy-Weinberg disequilibrium ($P < 5 \times 10^{-8}$), and those with low imputation quality ($r^2 < 0.8$). The final number of SNPs available for analysis in each study was comprised between 5,934,239 and 7,168,307. For our MR analyses, we selected a total of 543 SNPs, of which 5 were not available and 15 were excluded (eTable 2); of the remaining 523 SNPs, 74% were available in all studies and 96% (N=501) were available in at least 75% (N=17) of them. Only 501 SNPs available in 75% of the studies or more were

retained for further analyses. Of these SNPs, 79 were genotyped and 422 were imputed; when genotyped SNPs were available, we selected them in priority.

For each site, logistic regression adjusted for sex and the first four principal components was performed for each SNP under an additive genetic model (number of alleles for genotyped SNPs, dosage for imputed SNPs) using PLINK software (version 1.9).⁷

Summary statistics from the GWAS of the 23 studies were meta-analysed using the GWAMA software.⁸ Effects size and standard errors of SNPs with low heterogeneity across studies ($I^2 \leq 25\%$) were combined using a fixed-effect model, while we used a random-effects model for SNPs with high heterogeneity ($I^2 > 25\%$).

Analyses were first performed overall. We then repeated our analyses: (i) in two groups defined by median age at study (≤ 67 years, > 67 years; 7324 cases and 6210 controls from 19 studies); (ii) in two groups defined by median disease duration in PD cases (≤ 7 years, $n=4,358$; > 7 years, $n=3917$) from 22 studies (cases from each group were compared to all controls).

eReferences

1. Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson disease. *Arch Neurol*. 1999;56(1):33-9.
2. Gibb WR, Lees AJ. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 1988;51(6):745-52.
3. Bower JH, Maraganore DM, McDonnell SK, Rocca WA. Incidence and distribution of parkinsonism in Olmsted County, Minnesota, 1976-1990. *Neurology*. 1999;52(6):1214-20.
4. Blauwendraat C, Faghri F, Pihlstrom L, et al. NeuroChip, an updated version of the NeuroX genotyping platform to rapidly screen for variants associated with neurological diseases. *Neurobiol Aging*. 2017;57:247.e9-.e13.
5. Price AL, Patterson NJ, Plenge RM, Weinblatt ME, Shadick NA, Reich D. Principal components analysis corrects for stratification in genome-wide association studies. *Nat Genet*. 2006;38(8):904-9.
6. Patterson N, Price AL, Reich D. Population Structure and Eigenanalysis. *PLOS Genetics*. 2006;2(12):e190.
7. Purcell S, Neale B, Todd-Brown K, et al. PLINK: a tool set for whole-genome association and population-based linkage analyses. *Am J Hum Genet*. 2007;81(3):559-75.
8. Magi R, Morris AP. GWAMA: software for genome-wide association meta-analysis. *BMC Bioinformatics*. 2010;11:288.

eTable 1: Power calculations for forward Mendelian randomisation analyses.

Population	N cases	N controls	R ²	Odds ratio				
				0.5	0.6	0.7	0.8	0.9
Courage-PD								
All	8919	7600	5.03%	1.00	1.00	1.00	0.90	0.33
Women	3554	4153	4.60%	1.00	1.00	0.91	0.55	0.17
Men	5365	3447	4.50%	1.00	1.00	0.95	0.61	0.18
Age ≤ 67y	3502	3306	5.03%	1.00	1.00	0.92	0.55	0.16
Age > 67y	3822	2904	4.99%	1.00	1.00	0.92	0.54	0.16
PD Duration ≤7y	4358	7416	5.03%	1.00	1.00	0.98	0.72	0.23
PD Duration >7y	3917	7416	5.03%	1.00	1.00	0.97	0.69	0.22
iPDGC ^a								
Women	7384	12389	4.90%	1.00	1.00	1.00	0.90	0.35
Men	12054	11999	4.80%	1.00	1.00	1.00	0.97	0.43
iPDGC + Courage-PD								
Women	10938	16542	4.88%	1.00	1.00	1.00	0.98	0.46
Men	17419	15446	4.77%	1.00	1.00	1.00	0.99	0.56

^a Summary statistics from sex-stratified analyses in iPDGC with exclusion of UK Biobank participants (Blauwendraat et al. Investigation of Autosomal Genetic Sex Differences in Parkinson's Disease 2021).

eTable 2: Characteristics of cases and controls from the Courage-PD consortium by study site (after quality control).

Continent	Principal investigators	Country	Status	n	Sex (%)		Age at study			Age at PD onset			Age at PD diagnosis			Disease duration ^b		Family history or mutations
					Male	Female	Mean	SD	MD	Mean	SD	MD	Mean	SD	MD	Mean	SD	n
Africa	Bardien/Carr ^a	South Africa	Cases	170	61.2	38.8	68.7	10.6		60.0	11.9		60.0	11.9		8.7	6.4	53
			Controls	85	56.5	43.5	51.1	12.7		-	-	85	-	-		-	-	5
North America	Farrer ^a	United States	Cases	389	65.6	34.4	67.7	10.3	1	56.5	11.1	1	59.0	11.0	130	11.2	6.2	127
			Controls	409	31.8	68.2	69.4	12.4		-	-	409	-	-		-	-	15
	Rogaeva/Lang ^a	Canada	Cases	215	66.0	34.0	63.6	12.4	6	54.0	12.2	6			215	9.6	5.9	56
			Controls	153	37.9	62.1	73.8	8.6		-	-	153	-	-		-	-	4
Australia	Mellick ^a	Australia	Cases	399	64.0	36.0	68.3	9.3		59.1	11.3		60.7	10.7	13	9.2	7	81
			Controls	399	45.3	54.7	66.9	9.6		-	-	508	-	-		-	-	109
Europe	Aasly ^a	Norway	Cases	510	60.0	40.0	77.7	11.6		60.5	11.0				510	17.2	5.7	47
			Controls	509	54.8	45.2	73.0	14.1	79	-	-	509	-	-		-	-	22
	Annesi ^a	Italy	Cases	93	64.5	35.5	66.5	9.0		59.2	10.1		66.5	9.0		7.3	5.6	4
			Controls	94	45.7	54.3	58.2	20.3		-	-	94	-	-		-	-	1
	Brice/Corvol/Lesage ^a	France	Cases	851	58.4	41.6	60.7	10.9	32	51.9	11.1	32			851	8.8	6.2	106
			Controls	280	56.4	43.6	62.4	10.7		-	-	280	-	-		-	-	5
	Carmine Belin/Ran ^a	Sweden	Cases	286	61.5	38.5	67.4	10.3		59.4	11.1				286	8.1	6.1	72
			Controls	629	55.2	44.8	66.5	10.4	597	-	-	629	-	-	-	-	-	18
	Chartier-Harlin/Muttez ^a	France	Cases	370	54.3	45.7	64.3	9.0		52.7	10.5		53.8	10.2		11.6	5.9	85
			Controls	228	39.9	60.1	59.9	12.6		-	-	228	-	-		-	-	11
	Deutschländer ^a	Germany	Cases	285	61.8	38.2	69.4	9.9		60.4	11.5		59.0	11.1	213	9.1	6.5	21
			Controls	46	30.4	69.6	66.0	10.3		-	-	46	-	-		-	-	6
	Elbaz ^a	France	Cases	455	59.8	40.2	70.1	7.4		64.9	7.7		65.8	7.5	1	5.2	4.1	68
			Controls	1066	59.2	40.8	69.8	7.6		-	-	1066	-	-		-	-	68
	Ferreira	Portugal	Cases	415	57.1	42.9	69.0	10.1		57.9	11.9		59.5	11.9		11.2	7.6	102
			Controls	67	25.4	74.6	47.1	17.8		-	-	67	-	-		-	-	14
	Gasser/Sharma ^c	Germany	Cases	681	63.6	36.4	64.9	10.9		59.8	11.3		61.6	10.8	251	5.1	5.1	249
			Controls	549	43.4	56.6	61.9	7.8		-	-	549	-	-		-	-	161
	Duga/Cilia ^a	Italy	Cases	1391	59.2	40.8	65.8	10.8		59.1	11.2		60.7	11		6.7	5.6	51
			Controls	1370	33.7	66.3	61.9	10.9		-	-	1370	-	-		-	-	42
	Hadjigeorgiou ^a	Greece	Cases	283	48.4	51.6	67.9	10.3		63.1	10.1		64.0	10.2		4.8	4.4	27
			Controls	314	47.1	52.9	69.8	8.7		-	-	314	-	-		-	-	4
	Koks/Taba ^a	Estonia	Cases	216	39.8	60.2	73.0	8.2		66.8	9.8				216	6.2	5.3	6
			Controls	170	41.8	58.2	72.3	10.2		-	-	170	-	-		-	-	7
	Kruger ^a	Luxembourg	Cases	333	67.3	32.7	67.4	11.2		59.7	13.0		61.9	12.1	17	7.2	6.6	48
			Controls	360	55.8	44.2	58.1	11.9		-	-	360	-	-		-	-	77

Continent	Principal investigators	Country	Status	n	Sex (%)		Age at study			Age at PD onset			Age at PD diagnosis			Disease duration ^b		Family history or mutations
					Male	Female	Mean	SD	MD	Mean	SD	MD	Mean	SD	MD	Mean	SD	n
	Puschmann ^a	Sweden	Cases	110	62.7	37.3	68.8	10.6		60.5	10.6		47.0	-	109	8.2	5.4	60
			Controls	105	29.5	70.5	66.7	8.9		-	-	105	-	-		-	-	
	Stefanis/Simitsi ^a	Greece	Cases	242	61.6	38.4	67.1	13.5		60.7	13.6		61.3	12.7	68	6.4	6.7	68
			Controls	181	35.9	64.1	67.0	9.6		-	-	181	-	-		-	-	3
	Tolosa ^d	Spain	Cases	155	60	40.0	67.6	10.2		60.6	10.9				155	7	5.8	14
			Controls	68	16.2	83.8	62.3	12.1	8	-	-	68	-	-		-	-	2
	Valente	Italy	Cases	326	62.3	37.7	67.0	12.1	7	55.3	10.9	7	59.0	7.9	239	11.7	8	103
			Controls	54	38.9	61.1	78.4	9.6		-	-	54	-	-		-	-	
	Wirdefeldt ^a	Sweden	Cases	65	53.8	46.2	75.7	8.1		66.6	9.9				65	8.6	5.5	4
			Controls	171	45.6	54.4	73.6	9.8		-	-	171	-	-		-	-	6
Zimprich	Austria	Cases	598	63.4	36.6	66.8	11.3		58.8	11.3				598	8	0	98	
		Controls	184	40.8	59.2			184	-	-	184	-	-		-	-	2	
Total			Cases	8919														
			Controls	7600														

MD, missing data; SD, standard deviation.

^a Sites from the Geo-PD consortium.

^b Duration disease = age at study - age at PD onset. Missing values are the same as those for age at study.

^c For the Gasser/Sharma site, we excluded 1,000 samples overlapping with IPDGC (642 cases, 358 controls).

^d For the Tolosa site, we excluded 266 samples of PD cases overlapping with IPDGC.

eTable 3: SNPs used for Mendelian randomisation analyses: individual associations with BMI and PD (Courage-PD), and R².

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EA	Beta	SE	P	n studies	n sample	EA	Beta	SE	P	I ² (%)	
BMI (per 1SD=4.8kg/m ²)														
rs79113395	1:1590521	G/A	0.73	0.020	0.002	2.03E-20	22	16283	0.73	0.055	0.029	5.85E-02	0	1.56E-04
rs10909880	1:2727804	C/T	0.55	0.014	0.002	2.21E-16	23	16519	0.54	0.019	0.032	5.37E-01	25.4	9.03E-05
rs11121210	1:8708529	C/T	0.66	0.011	0.002	2.37E-10	23	16519	0.56	-0.051	0.025	4.23E-02	0	5.56E-05
rs10779751	1:11284336	A/G	0.28	0.013	0.002	2.66E-13	23	16519	0.29	0.022	0.028	4.29E-01	17.2	6.90E-05
rs61740466	1:19934900	G/A	0.77	0.014	0.002	2.24E-10	23	16519	0.75	-0.001	0.028	9.79E-01	0	7.24E-05
rs4655141 ^a	1:23312025	C/T	0.16	0.017	0.002	6.20E-15	22	16332	0.17	0.053	0.047	2.62E-01	43.2	8.20E-05
rs2228552 ^a	1:32165495	T/G	0.57	0.012	0.002	1.80E-11	22	16332	0.64	-0.029	0.025	2.54E-01	0	7.55E-05
rs4653017	1:33776728	T/C	0.67	0.012	0.002	1.11E-10	23	16519	0.65	-0.015	0.026	5.62E-01	12	6.18E-05
rs7512146	1:34283008	G/T	0.47	0.010	0.002	1.29E-08	23	16519	0.50	0.025	0.025	3.20E-01	11.9	4.69E-05
rs11577094	1:38026600	T/C	0.08	0.019	0.003	3.28E-10	23	16519	0.06	0.059	0.050	2.39E-01	0	5.04E-05
rs112646560	1:39560250	T/C	0.21	0.018	0.002	1.29E-14	23	16519	0.23	-0.012	0.029	6.80E-01	0	1.08E-04
rs2984618	1:47690438	T/G	0.44	0.016	0.002	3.80E-24	23	16519	0.37	0.057	0.025	2.25E-02	0	1.34E-04
rs657452 ^a	1:49589847	A/G	0.40	0.019	0.002	3.17E-30	22	16332	0.38	0.031	0.029	2.72E-01	17	1.70E-04
rs587271	1:54743111	T/C	0.69	0.012	0.002	6.21E-11	9	5180	Excluded for MR					
rs79906980	1:57887985	T/C	0.16	0.016	0.003	1.69E-09	23	16519	0.16	-0.004	0.034	9.18E-01	0	6.56E-05
rs12140153 ^a	1:62579891	G/T	0.91	0.035	0.003	1.44E-25	22	16332	0.92	0.022	0.046	6.24E-01	0	2.06E-04
rs2503185	1:66461401	A/G	0.51	0.013	0.002	1.33E-14	23	16519	0.52	-0.007	0.024	7.84E-01	24	8.45E-05
rs3101336	1:72751185	C/T	0.62	0.025	0.002	4.80E-54	23	16519	0.63	-0.051	0.026	4.70E-02	0	3.05E-04
rs6656785	1:75005776	G/A	0.39	0.018	0.002	3.06E-27	23	16519	0.37	-0.006	0.025	8.28E-01	11.3	1.50E-04
rs34517439	1:78450517	A/C	0.12	0.039	0.003	3.40E-39	21	15909	0.09	0.021	0.046	6.52E-01	0	3.15E-04
rs6696828	1:80812020	C/G	0.30	0.012	0.002	6.42E-11	23	16519	0.28	0.012	0.027	6.70E-01	0	6.02E-05
rs321237	1:96478125	A/G	0.75	0.013	0.002	1.49E-10	23	16519	0.73	-0.067	0.028	1.50E-02	0	5.96E-05
rs11165643	1:96924097	T/C	0.58	0.018	0.002	4.49E-30	23	16519	0.56	-0.051	0.025	3.84E-02	0	1.67E-04
rs12072739	1:98315893	G/A	0.22	0.017	0.002	1.50E-13	23	16519	0.21	-0.029	0.031	3.44E-01	16.7	9.92E-05
rs17024393 ^a	1:110154688	C/T	0.03	0.064	0.005	7.11E-39	22	16330	0.03	0.025	0.075	7.37E-01	0	2.50E-04
rs197374	1:112289983	T/C	0.40	0.014	0.002	3.16E-16	23	16519	0.38	0.019	0.025	4.50E-01	0	9.56E-05
rs17544384	1:115295160	C/T	0.20	0.013	0.002	2.28E-08	23	16519	0.21	-0.044	0.030	1.39E-01	17.9	5.59E-05
rs7534091	1:118864616	G/A	0.28	0.012	0.002	6.65E-11	23	16519	0.24	-0.008	0.028	7.73E-01	0	5.83E-05
rs74887628	1:147032779	A/G	0.03	0.030	0.005	1.76E-08	8	5656	Excluded for MR					
rs4970991	1:151004003	T/C	0.22	0.012	0.002	1.81E-08	23	16519	0.22	0.030	0.030	3.21E-01	0	4.54E-05
rs61813324	1:156049877	T/C	0.13	0.029	0.003	3.20E-24	2	1934	Excluded for MR					
rs1750307	1:156488420	A/T	0.37	0.013	0.002	2.78E-13	23	16519	0.35	0.005	0.025	8.38E-01	0	7.72E-05
rs10733051	1:167280354	A/G	0.51	0.009	0.002	6.96E-09	23	16519	0.57	-0.024	0.026	3.50E-01	7.7	4.32E-05
rs61828641	1:174321997	A/G	0.11	0.022	0.003	2.49E-13	23	16519	0.12	-0.013	0.037	7.38E-01	0	9.67E-05
rs543874 ^a	1:177889480	G/A	0.22	0.048	0.002	3.06E-125	22	16332	0.18	-0.108	0.042	1.04E-02	31.8	7.91E-04
rs10920678	1:190239907	A/G	0.42	0.015	0.002	7.15E-20	23	16519	0.42	0.013	0.025	5.89E-01	14.1	1.09E-04
rs2400414	1:194965200	C/T	0.65	0.013	0.002	5.52E-13	23	16519	0.63	-0.001	0.025	9.55E-01	0	7.19E-05
rs2820295 ^a	1:201800868	A/G	0.33	0.024	0.002	5.56E-39	22	16332	0.30	-0.037	0.032	2.45E-01	23.5	2.43E-04
rs10920336	1:202115945	G/A	0.47	0.010	0.002	4.20E-09	23	16519	0.48	-0.032	0.025	1.90E-01	0	5.08E-05
rs1006317	1:209552636	T/G	0.13	0.016	0.003	3.75E-10	23	16519	0.13	-0.028	0.036	4.38E-01	8.5	5.67E-05
rs6661316	1:210095527	T/C	0.59	0.012	0.002	1.72E-13	23	16519	0.57	-0.044	0.024	6.97E-02	12	6.97E-05
rs10864728	1:230304914	A/G	0.40	0.011	0.002	1.20E-08	23	16519	0.41	0.005	0.025	8.57E-01	0	5.80E-05
rs946824	1:243684019	T/C	0.14	0.020	0.002	4.82E-15	18	12515	0.15	0.019	0.042	6.52E-01	0	9.09E-05
rs6710091	2:239597	C/G	0.67	0.010	0.002	5.78E-09	23	16519	0.67	-0.022	0.026	4.02E-01	7.2	4.72E-05

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)						I ² (%)	R ²
			EA	Beta	SE	P	n studies	n sample	EA	Beta	SE	P		
rs77165542	2:430975	C/T	0.97	0.094	0.005	1.51E-70	3	1439					Excluded for MR	
rs13021737	2:632348	G/A	0.84	0.058	0.002	2.89E-161	23	16519	0.80	-0.013	0.031	6.88E-01	0	8.83E-04
rs10929925	2:6155557	C/A	0.59	0.014	0.002	3.05E-18	23	16519	0.55	0.038	0.024	1.15E-01	0	9.76E-05
rs11902450	2:12845368	T/C	0.11	0.017	0.003	1.06E-09	23	16519	0.11	-0.065	0.053	2.17E-01	30.3	5.25E-05
rs10182181	2:25150296	G/A	0.49	0.033	0.002	2.45E-91	23	16519	0.46	0.024	0.024	3.24E-01	0	5.35E-04
rs935166	2:26949366	G/A	0.51	0.015	0.002	8.69E-16	23	16519	0.49	0.004	0.025	8.69E-01	0	1.16E-04
rs10168563	2:35552173	A/G	0.70	0.013	0.002	9.33E-12	23	16519	0.70	-0.008	0.027	7.67E-01	0	6.63E-05
rs3770890	2:36657992	G/T	0.03	0.030	0.005	2.10E-08	11	7008					Excluded for MR	
rs10185199	2:40282202	G/A	0.71	0.014	0.002	3.18E-13	22	16139	0.70	-0.007	0.037	8.47E-01	32.1	8.35E-05
rs10169594	2:41637688	C/T	0.35	0.012	0.002	1.34E-11	23	16519	0.35	0.011	0.026	6.73E-01	0	6.57E-05
rs7561278	2:48954905	T/C	0.77	0.017	0.002	4.89E-16	23	16519	0.78	-0.006	0.038	8.66E-01	27.6	1.02E-04
rs930295	2:50233352	A/C	0.15	0.021	0.002	2.03E-19	23	16519	0.16	-0.022	0.033	5.16E-01	3.1	1.13E-04
rs805412	2:54120820	G/A	0.57	0.010	0.002	1.14E-08	23	16519	0.60	-0.012	0.025	6.34E-01	0	4.72E-05
rs4671328 ^a	2:58935282	T/G	0.45	0.021	0.002	3.42E-36	22	16331	0.43	-0.016	0.025	5.22E-01	4.5	2.27E-04
rs6545714	2:59307725	G/A	0.39	0.019	0.002	4.01E-32	23	16519	0.38	0.023	0.025	3.52E-01	8.8	1.79E-04
rs2861685	2:67837553	T/C	0.59	0.016	0.002	7.82E-18	23	16519	0.60	0.027	0.036	4.53E-01	43.8	1.32E-04
rs17020497	2:81826131	A/G	0.13	0.014	0.002	2.04E-08	23	16519	0.15	-0.029	0.034	3.98E-01	17.9	4.55E-05
rs12714199	2:86812549	C/T	0.39	0.014	0.002	3.22E-16	23	16519	0.39	-0.002	0.025	9.49E-01	7.2	9.42E-05
rs4303732	2:100830040	T/C	0.61	0.017	0.002	1.26E-22	23	16519	0.62	0.020	0.025	4.37E-01	10.4	1.35E-04
rs264941	2:104297420	C/A	0.53	0.012	0.002	1.84E-13	23	16519	0.56	0.019	0.040	6.35E-01	54.2	7.66E-05
rs10197031	2:105454590	C/T	0.27	0.016	0.002	5.05E-18	23	16519	0.26	0.026	0.027	3.36E-01	24.3	1.03E-04
rs13033310	2:133523605	A/G	0.25	0.015	0.002	3.40E-11	23	16519	0.26	0.008	0.034	8.17E-01	25.8	8.03E-05
rs4988235 ^a	2:136608646	A/G	0.72	0.012	0.002	7.09E-13	22	16332	0.49	0.071	0.027	1.01E-02	0.7	6.19E-05
rs17814208	2:144037998	G/A	0.24	0.013	0.002	7.24E-11	23	16519	0.24	0.009	0.029	7.65E-01	1.2	6.11E-05
rs1451077	2:147901207	G/A	0.42	0.017	0.002	1.43E-18	23	16519	0.41	-0.006	0.025	8.23E-01	0	1.39E-04
rs2119753	2:151224579	A/G	0.62	0.010	0.002	1.00E-08	23	16519	0.64	-0.048	0.026	6.27E-02	5.9	4.70E-05
rs11695013	2:157057487	C/T	0.37	0.010	0.002	2.43E-09	23	16519	0.36	-0.021	0.026	4.23E-01	0	5.03E-05
rs3764835	2:159519368	G/A	0.85	0.013	0.002	3.84E-08	23	16519	0.85	-0.011	0.035	7.44E-01	16.4	4.32E-05
rs12692596	2:161265910	T/C	0.36	0.012	0.002	1.03E-12	23	16519	0.36	-0.043	0.025	8.53E-02	0	6.65E-05
rs62176243	2:166190881	A/T	0.76	0.015	0.002	2.41E-11	23	16519	0.77	0.030	0.029	2.99E-01	6.8	8.06E-05
rs56133507	2:172818467	G/T	0.19	0.013	0.002	4.31E-08	23	16519	0.19	-0.079	0.031	1.10E-02	0	5.36E-05
rs34234296	2:175166636	G/A	0.61	0.015	0.002	2.01E-13	16	11466					Excluded for MR	
rs7588437	2:181575281	G/A	0.63	0.016	0.002	2.32E-22	23	16519	0.65	-0.011	0.026	6.71E-01	16.8	1.26E-04
rs6716898	2:198944271	A/G	0.49	0.013	0.002	2.33E-11	23	16519	0.51	0.031	0.025	2.09E-01	12.3	8.06E-05
rs7593917	2:203931012	G/A	0.55	0.012	0.002	9.67E-13	23	16519	0.57	-0.018	0.025	4.60E-01	0	6.56E-05
rs4482463	2:205375909	C/A	0.08	0.031	0.003	4.85E-23	NA in Courage-PD							
rs11692326	2:208263279	T/C	0.23	0.015	0.002	1.69E-14	23	16519	0.20	0.029	0.030	3.43E-01	0	7.66E-05
rs73985439	2:212299249	C/A	0.31	0.013	0.002	1.84E-10	23	16519	0.30	-0.006	0.026	8.29E-01	1.3	7.32E-05
rs7599312 ^a	2:213413231	G/A	0.73	0.018	0.002	1.52E-23	22	16331	0.74	0.025	0.031	4.19E-01	12.6	1.32E-04
rs12987009 ^a	2:219658170	T/A	0.41	0.011	0.002	1.83E-10	22	16332	0.43				Excluded for MR	
rs6725931	2:220205146	T/C	0.85	0.019	0.002	2.30E-15	6	3040					Excluded for MR	
rs4973618	2:229002620	G/A	0.34	0.015	0.002	1.25E-16	23	16519	0.37	-0.048	0.025	6.08E-02	13.9	9.80E-05
rs6720868	2:230663576	T/C	0.31	0.015	0.002	1.82E-17	23	16519	0.34	-0.054	0.026	3.72E-02	0	1.01E-04
rs7568228	2:236848488	G/C	0.46	0.010	0.002	1.00E-09	23	16519	0.50				Excluded for MR	
rs59302296	3:9507314	A/T	0.10	0.022	0.003	9.12E-12	23	16519	0.10	-0.057	0.054	2.86E-01	31.5	8.41E-05
rs6783054	3:11672805	A/C	0.50	0.010	0.002	6.22E-09	23	16519	0.49	-0.020	0.024	4.24E-01	21.7	4.90E-05
rs10510419	3:12426936	G/T	0.85	0.017	0.002	2.23E-13	23	16519	0.85	-0.005	0.034	8.73E-01	16.9	7.07E-05

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							I² (%)	R²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P			
rs2600226 ^a	3:12928762	C/T	0.33	0.012	0.002	1.42E-10	22	16332	0.33	0.029	0.027	2.93E-01	8.7	5.94E-05	
rs1048637	3:13358171	G/T	0.45	0.009	0.002	2.94E-08	23	16519	0.44	-0.027	0.025	2.77E-01	0	4.38E-05	
rs4858193	3:20441050	T/C	0.72	0.013	0.002	2.44E-12	23	16519	0.75	0.023	0.028	4.28E-01	10.2	7.13E-05	
rs6804842 ^a	3:25106437	G/A	0.57	0.014	0.002	7.57E-18	22	16332	0.57	0.007	0.024	7.64E-01	0	9.75E-05	
rs11921432	3:35117776	C/T	0.11	0.019	0.003	5.38E-12	23	16519	0.11	0.007	0.040	8.70E-01	7.8	6.96E-05	
rs1799923	3:42306294	G/A	0.89	0.022	0.003	1.12E-17	21	16109	0.88	-0.021	0.040	5.93E-01	0	9.96E-05	
rs28350	3:42418446	A/G	0.17	0.017	0.002	1.07E-14	11	6642	Excluded for MR						
rs4017425	3:44028764	C/T	0.53	0.012	0.002	2.91E-12	23	16519	0.54	0.017	0.024	4.82E-01	0	6.93E-05	
rs11919665	3:48085349	A/T	0.32	0.012	0.002	7.30E-09	23	16519	0.35	0.024	0.026	3.52E-01	0	6.01E-05	
rs11713193	3:49924424	A/G	0.52	0.025	0.002	3.02E-48	23	16519	0.48	0.003	0.024	8.97E-01	0	3.02E-04	
rs2365389	3:61236462	C/T	0.60	0.017	0.002	6.49E-25	23	16519	0.61	-0.006	0.025	7.95E-01	5.8	1.35E-04	
rs6445258	3:62112198	T/C	0.21	0.013	0.002	2.48E-08	7	4426	Excluded for MR						
rs925018	3:62713143	G/C	0.33	0.013	0.002	4.33E-14	23	16519	0.33	-0.009	0.026	7.15E-01	0	7.51E-05	
rs11915371	3:70539559	C/A	0.20	0.015	0.002	2.29E-13	23	16519	0.21	-0.036	0.030	2.33E-01	0	7.53E-05	
rs12636480 ^a	3:82719412	T/G	0.35	0.013	0.002	6.96E-13	22	16332	0.37	-0.046	0.025	6.69E-02	0	7.46E-05	
rs9827823	3:84221774	T/C	0.86	0.018	0.002	3.39E-15	23	16519	0.85	-0.022	0.034	5.22E-01	0	8.20E-05	
rs9818122	3:85861064	C/T	0.21	0.023	0.002	3.97E-30	23	16519	0.21	-0.004	0.030	9.05E-01	0	1.70E-04	
rs34184235	3:86192846	C/T	0.56	0.012	0.002	2.14E-09	23	16519	0.58	-0.044	0.024	7.41E-02	12.1	6.50E-05	
rs11128021	3:88139016	G/A	0.84	0.018	0.002	1.63E-14	23	16519	0.86	0.047	0.035	1.76E-01	0.6	8.87E-05	
rs1492014	3:94071481	C/T	0.43	0.017	0.002	1.44E-23	23	16519	0.40	-0.061	0.025	1.53E-02	0	1.44E-04	
rs1436344	3:104606144	C/G	0.57	0.015	0.002	1.07E-17	23	16519	0.58	Excluded for MR					
rs7640424	3:107820063	C/T	0.69	0.014	0.002	1.23E-14	23	16519	0.72	-0.053	0.027	5.11E-02	0	7.80E-05	
rs17681451	3:114399296	G/A	0.92	0.022	0.003	7.37E-13	23	16519	0.91	0.072	0.045	1.14E-01	0	7.13E-05	
rs6808814 ^a	3:116852469	T/C	0.73	0.012	0.002	1.31E-09	22	16332	0.73	-0.018	0.027	5.21E-01	0	5.44E-05	
rs7631156	3:131751628	A/G	0.31	0.021	0.002	3.33E-32	23	16519	0.31	-0.003	0.035	9.39E-01	33.9	1.97E-04	
rs687339 ^a	3:135932359	T/C	0.77	0.019	0.002	4.32E-22	22	16331	0.76	0.030	0.033	3.64E-01	17.6	1.25E-04	
rs16851483	3:141275436	T/G	0.07	0.035	0.003	4.87E-25	23	16519	0.06	-0.074	0.052	1.57E-01	0	1.65E-04	
rs355777	3:154034950	C/G	0.40	0.015	0.002	2.13E-18	23	16519	0.41	0.039	0.025	1.17E-01	0	1.09E-04	
rs9826775	3:156295341	A/G	0.85	0.016	0.002	6.61E-11	23	16519	0.86	-0.019	0.035	5.91E-01	0	6.08E-05	
rs2047648	3:157033438	T/A	0.25	0.013	0.002	7.95E-12	23	16519	0.26	0.030	0.028	2.74E-01	0	6.69E-05	
rs3732927	3:170586057	T/C	0.29	0.010	0.002	1.13E-08	23	16519	0.32	-0.009	0.026	7.33E-01	0	4.04E-05	
rs12635553	3:171113714	A/T	0.49	0.010	0.002	4.10E-09	23	16519	0.46	Excluded for MR					
rs39654	3:173095123	G/A	0.55	0.016	0.002	1.75E-21	23	16519	0.53	0.034	0.036	3.44E-01	40.8	1.32E-04	
rs6443750	3:181329682	C/T	0.80	0.015	0.002	7.25E-13	NA in Courage-PD								
rs865809	3:183997735	A/G	0.22	0.012	0.002	6.50E-10	23	16519	0.22	0.004	0.030	8.88E-01	0	5.36E-05	
rs9816226 ^a	3:185834499	T/A	0.82	0.032	0.002	1.45E-50	22	16331	0.82	0.013	0.035	7.17E-01	12	2.87E-04	
rs7616009 ^a	3:194881756	G/A	0.84	0.016	0.002	4.33E-11	22	16332	0.86	-0.055	0.038	1.47E-01	10.4	6.61E-05	
rs6803161	3:196205694	T/C	0.39	0.011	0.002	2.71E-08	23	16519	0.42	-0.022	0.026	3.99E-01	10.3	5.47E-05	
rs2051559	4:3298800	C/T	0.14	0.017	0.002	3.78E-11	23	16519	0.12	0.019	0.038	6.15E-01	0	6.76E-05	
rs12642970	4:16601492	G/C	0.56	0.011	0.002	1.71E-08	23	16519	0.60	Excluded for MR					
rs994596	4:18459828	T/C	0.32	0.013	0.002	1.06E-12	23	16519	0.33	0.013	0.026	6.04E-01	0	7.41E-05	
rs34811474	4:25408838	G/A	0.78	0.029	0.002	8.50E-38	NA in Courage-PD								
rs73213484	4:28489339	A/T	0.86	0.021	0.003	2.04E-14	23	16519	0.83	-0.056	0.032	8.40E-02	0	1.06E-04	
rs337637 ^a	4:38604470	G/A	0.64	0.014	0.002	6.24E-16	22	16332	0.68	0.012	0.026	6.35E-01	0	8.64E-05	
rs10938397	4:45182527	G/A	0.43	0.032	0.002	2.42E-86	23	16519	0.42	-0.008	0.025	7.48E-01	12.9	5.08E-04	
rs2271046	4:52752812	T/A	0.31	0.012	0.002	3.03E-10	23	16519	0.25	-0.014	0.028	6.16E-01	0	5.61E-05	
rs1492767	4:55221467	T/C	0.47	0.010	0.002	3.55E-09	23	16519	0.49	0.007	0.025	7.68E-01	0	4.49E-05	

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							I² (%)	R²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P			
rs2192158	4:55505360	A/G	0.45	0.014	0.002	7.42E-16	23	16519	0.49	0.008	0.025	7.43E-01	1.5	9.29E-05	
rs1346841 ^a	4:65651730	G/A	0.59	0.013	0.002	3.18E-13	22	16332	0.59	-0.003	0.028	9.12E-01	15.8	7.69E-05	
rs10002111	4:67815504	A/G	0.22	0.013	0.002	1.26E-09	23	16519	0.24	0.021	0.029	4.67E-01	0	5.41E-05	
rs10033843	4:77028783	A/G	0.22	0.014	0.002	1.07E-11	23	16519	0.23	-0.038	0.029	1.85E-01	6	6.62E-05	
rs72649373	4:80609966	C/T	0.14	0.017	0.003	3.20E-09	23	16519	0.15	0.022	0.045	6.20E-01	27.9	6.64E-05	
rs4148155	4:89054667	A/G	0.89	0.019	0.003	1.34E-13	23	16519	0.90	0.054	0.041	1.87E-01	0	7.41E-05	
rs4286488	4:94440026	A/G	0.76	0.012	0.002	1.70E-09	23	16519	0.76	0.004	0.029	8.81E-01	0	5.33E-05	
rs7678054	4:95093855	G/A	0.52	0.010	0.002	4.57E-09	23	16519	0.54	0.035	0.024	1.47E-01	0	4.89E-05	
rs3796432	4:96030402	G/T	0.63	0.011	0.002	2.21E-10	23	16519	0.62	-0.007	0.025	7.88E-01	18.4	5.93E-05	
rs13107325 ^a	4:103188709	T/C	0.08	0.047	0.003	3.81E-47	22	16332	0.07	-0.092	0.048	5.31E-02	0	3.30E-04	
rs326893	4:112691776	T/C	0.58	0.012	0.002	1.89E-12	23	16519	0.60	0.003	0.025	9.19E-01	0	7.13E-05	
rs7696649	4:120322177	A/G	0.28	0.012	0.002	4.73E-10	23	16519	0.28	-0.004	0.037	9.16E-01	36.6	5.40E-05	
rs4864201 ^a	4:130731284	T/C	0.35	0.014	0.002	4.30E-16	22	16332	0.35	0.007	0.025	7.97E-01	0	8.51E-05	
rs1296328	4:137083193	A/C	0.45	0.017	0.002	3.49E-22	23	16519	0.45	0.021	0.025	3.97E-01	0	1.36E-04	
rs17367750	4:140782542	C/T	0.69	0.012	0.002	1.97E-11	23	16519	0.67	-0.019	0.026	4.75E-01	22.1	6.39E-05	
rs9992189	4:144060728	G/C	0.39	0.010	0.002	2.04E-08	23	16519	0.42	Excluded for MR					
rs3914628	4:147438019	T/C	0.86	0.016	0.002	6.91E-13	23	16519	0.85	-0.046	0.034	1.80E-01	0	6.58E-05	
rs750090	4:152931436	T/C	0.63	0.011	0.002	2.50E-10	23	16519	0.66	-0.061	0.026	1.92E-02	0	5.98E-05	
rs13110266	4:162129844	G/A	0.60	0.012	0.002	3.96E-14	23	16519	0.61	0.008	0.025	7.43E-01	6.2	7.40E-05	
rs7685628	4:165310133	A/T	0.40	0.010	0.002	6.15E-09	23	16519	0.40	-0.022	0.025	3.74E-01	0	4.90E-05	
rs1522569	4:171632637	T/G	0.82	0.014	0.002	1.60E-10	23	16519	0.81	-0.024	0.031	4.35E-01	0	5.91E-05	
rs1437842	4:173597016	G/A	0.51	0.011	0.002	8.49E-10	23	16519	0.53	-0.018	0.025	4.63E-01	0	5.62E-05	
rs6850421	4:180187034	A/G	0.46	0.011	0.002	3.66E-09	23	16519	0.47	0.052	0.024	3.30E-02	0	6.34E-05	
rs35408866	4:187743245	A/G	0.13	0.016	0.003	1.50E-08	23	16519	0.14	0.010	0.037	7.85E-01	18.6	5.86E-05	
rs698147 ^a	5:3513485	A/G	0.45	0.012	0.002	9.67E-12	22	16332	0.48	0.017	0.024	4.83E-01	0	6.65E-05	
rs6890310	5:27193573	G/A	0.71	0.012	0.002	3.29E-10	23	16519	0.71	0.063	0.027	1.87E-02	0	5.86E-05	
rs7730004	5:43191033	T/C	0.66	0.014	0.002	1.46E-14	23	16519	0.68	-0.031	0.027	2.37E-01	0	8.65E-05	
rs116374395	5:50723410	A/G	0.03	0.032	0.005	7.05E-10	23	16519	0.04	-0.029	0.060	6.27E-01	19.6	6.92E-05	
rs150215901	5:50935903	T/A	0.96	0.028	0.005	1.54E-08	14	9978	Excluded for MR						
rs4865796	5:53272664	G/A	0.30	0.010	0.002	4.21E-08	23	16519	0.32	0.001	0.026	9.80E-01	0	3.84E-05	
rs13186194	5:60795485	T/C	0.62	0.010	0.002	2.20E-09	23	16519	0.64	-0.014	0.025	5.93E-01	0	4.73E-05	
rs4700608	5:63026280	C/T	0.48	0.016	0.002	4.32E-20	23	16519	0.48	-0.003	0.024	9.12E-01	24.7	1.20E-04	
rs10050620	5:63927239	C/T	0.67	0.013	0.002	1.20E-10	23	16519	0.68	-0.045	0.033	1.76E-01	28.5	7.48E-05	
rs1159692	5:63977815	A/C	0.48	0.014	0.002	5.54E-15	23	16519	0.52	0.004	0.025	8.85E-01	23.7	9.09E-05	
rs2112347	5:75015242	T/G	0.63	0.028	0.002	1.17E-61	23	16519	0.64	0.018	0.025	4.62E-01	0	3.55E-04	
rs10942267	5:80841914	A/G	0.69	0.015	0.002	6.53E-16	23	16519	0.72	-0.026	0.027	3.41E-01	2.9	9.33E-05	
rs2962334	5:86879056	T/G	0.03	0.040	0.006	1.78E-11	23	16519	0.02	0.083	0.081	3.06E-01	0	8.30E-05	
rs1501673	5:87963600	A/G	0.14	0.029	0.002	2.73E-31	23	16519	0.14	-0.031	0.051	5.50E-01	45	1.96E-04	
rs12652212 ^a	5:88808594	G/A	0.44	0.013	0.002	1.63E-15	22	16332	0.43	0.023	0.024	3.46E-01	0	8.45E-05	
rs7713317	5:95716722	G/A	0.28	0.017	0.002	1.96E-20	23	16519	0.28	0.002	0.027	9.44E-01	2.7	1.11E-04	
rs6882366	5:95864693	C/T	0.60	0.013	0.002	4.39E-14	23	16519	0.62	-0.002	0.025	9.39E-01	0	8.21E-05	
rs11739877 ^a	5:105876806	T/C	0.62	0.012	0.002	4.01E-11	22	16331	0.61	0.009	0.026	7.25E-01	5.3	6.32E-05	
rs6888194	5:106910657	C/T	0.16	0.013	0.002	3.58E-08	23	16519	0.14	-0.014	0.035	6.85E-01	0	4.24E-05	
rs40067	5:107439012	G/A	0.83	0.025	0.002	9.73E-29	23	16519	0.83	0.007	0.032	8.24E-01	4.7	1.79E-04	
rs459552	5:112176756	T/A	0.23	0.013	0.002	8.36E-12	17	11948	0.25	0.002	0.036	9.64E-01	11.2	6.17E-05	
rs6893539	5:122705737	C/A	0.30	0.012	0.002	6.17E-11	23	16519	0.29	-0.023	0.027	3.96E-01	0	6.27E-05	
rs6864049	5:124330522	G/A	0.51	0.012	0.002	1.48E-13	23	16519	0.52	-0.010	0.025	6.73E-01	15.7	7.32E-05	

SNP	Chr.Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)						I ² (%)	R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P		
rs6886072	5:136598460	C/T	0.53	0.010	0.002	4.13E-09	23	16519	0.52	-0.023	0.024	3.38E-01	0	4.98E-05
rs13174863	5:139080745	G/A	0.15	0.020	0.002	1.94E-17	23	16519	0.17	-0.017	0.034	6.06E-01	10.9	9.67E-05
rs17405603	5:144608340	T/A	0.29	0.013	0.002	4.43E-11	23	16519	0.28	0.026	0.028	3.51E-01	0	6.48E-05
rs2910026	5:152529936	C/T	0.28	0.013	0.002	5.69E-10	23	16519	0.28	-0.015	0.028	5.98E-01	0	6.99E-05
rs7715256	5:153537893	G/T	0.44	0.016	0.002	3.98E-22	23	16519	0.43	0.008	0.024	7.30E-01	5.9	1.23E-04
rs7734385 ^a	5:158460212	G/A	0.56	0.010	0.002	6.08E-10	22	16332	0.60	-0.030	0.031	3.39E-01	27.1	5.04E-05
rs4921301	5:159984492	C/T	0.79	0.013	0.002	4.03E-08	23	16519	0.79	0.042	0.031	1.67E-01	2.9	5.57E-05
rs2861089	5:164557954	A/T	0.38	0.011	0.002	1.55E-09	23	16519	0.41	0.031	0.025	2.08E-01	0	5.20E-05
rs7727781	5:165185571	T/C	0.52	0.009	0.002	4.27E-08	23	16519	0.52	0.038	0.024	1.21E-01	1.7	4.32E-05
rs2053682	5:170599327	A/C	0.68	0.017	0.002	2.59E-20	23	16519	0.66	-0.059	0.034	8.79E-02	32.4	1.26E-04
rs6556301 ^a	5:176527577	G/T	0.63	0.011	0.002	8.14E-11	22	16332	0.67	-0.026	0.027	3.38E-01	5.9	5.96E-05
rs2228213	6:12124855	G/A	0.66	0.014	0.002	5.50E-17	23	16519	0.64	0.010	0.025	6.81E-01	0	9.27E-05
rs11757278	6:13180454	T/C	0.70	0.013	0.002	6.92E-13	23	16519	0.70	-0.003	0.027	9.19E-01	0	7.48E-05
rs3806114	6:20482335	G/A	0.31	0.012	0.002	1.46E-11	23	16519	0.31	0.004	0.027	8.91E-01	0	6.14E-05
rs2066295	6:26168903	A/G	0.76	0.014	0.002	2.29E-12	23	16519	0.76	0.016	0.028	5.67E-01	21.3	7.40E-05
rs3115667	6:31643399	C/T	0.72	0.018	0.002	5.92E-21	23	16519	0.76	-0.072	0.028	1.15E-02	12.3	1.30E-04
rs2281819	6:33771673	T/A	0.77	0.015	0.002	2.09E-14	23	16519	0.77	0.022	0.029	4.46E-01	7.2	8.38E-05
rs2744974	6:34579431	T/C	0.32	0.026	0.002	1.28E-51	23	16519	0.34	-0.010	0.026	6.95E-01	23.1	2.98E-04
rs2436728 ^a	6:40365601	A/G	0.41	0.019	0.002	1.97E-29	22	16332	0.39	-0.027	0.024	2.75E-01	0.2	1.72E-04
rs1358980 ^a	6:43764551	C/T	0.53	0.013	0.002	5.15E-15	22	16332	0.52	0.015	0.027	5.78E-01	13.5	8.30E-05
rs2206277	6:50798526	T/C	0.16	0.041	0.002	1.82E-83	23	16519	0.19	-0.038	0.031	2.22E-01	0	4.38E-04
rs1327259	6:51177811	A/G	0.61	0.016	0.002	1.47E-19	23	16519	0.60	-0.044	0.025	7.91E-02	0	1.17E-04
rs6915002	6:54028069	T/C	0.41	0.010	0.002	8.71E-09	23	16519	0.41	-0.014	0.026	5.79E-01	0	4.75E-05
rs9370410 ^a	6:55171842	A/G	0.73	0.011	0.002	2.58E-08	22	16331	0.72	0.001	0.029	9.61E-01	8.6	4.35E-05
rs2622274	6:64240516	G/T	0.54	0.011	0.002	3.23E-10	23	16519	0.58	0.012	0.025	6.30E-01	6.1	5.68E-05
rs1293037	6:70248345	T/C	0.75	0.013	0.002	5.73E-09	23	16519	0.75	0.012	0.028	6.71E-01	0	6.17E-05
rs6921533	6:73742334	T/C	0.29	0.010	0.002	1.37E-08	23	16519	0.29	-0.028	0.027	3.02E-01	0.8	4.48E-05
rs9294260	6:83433228	A/G	0.47	0.014	0.002	8.16E-18	23	16519	0.46	-0.001	0.024	9.57E-01	0	9.76E-05
rs6909685	6:97753952	C/T	0.67	0.015	0.002	2.78E-16	23	16519	0.68	-0.047	0.026	7.54E-02	0	9.81E-05
rs9320823	6:98429337	C/T	0.59	0.016	0.002	2.07E-21	23	16519	0.59	-0.006	0.025	8.08E-01	18.1	1.32E-04
rs57989773	6:100629078	C/T	0.24	0.014	0.002	5.63E-10	23	16519	0.24	0.066	0.029	2.48E-02	0	7.41E-05
rs156201	6:104847441	C/G	0.75	0.012	0.002	1.65E-10	23	16519	0.75	-0.015	0.028	5.97E-01	0	5.83E-05
rs768023	6:108876002	A/G	0.60	0.016	0.002	1.13E-22	23	16519	0.57	0.012	0.025	6.43E-01	12.9	1.24E-04
rs2357760 ^a	6:120213880	A/G	0.67	0.014	0.002	2.11E-16	22	16332	0.66	0.008	0.027	7.71E-01	6.8	8.99E-05
rs2875762	6:124925032	C/G	0.25	0.013	0.002	1.07E-10	23	16519	0.26	-0.042	0.028	1.42E-01	0	6.27E-05
rs1268065	6:126042783	G/A	0.50	0.010	0.002	7.12E-10	23	16519	0.51	0.045	0.025	7.31E-02	4.2	5.00E-05
rs9375702	6:130384187	C/T	0.32	0.011	0.002	5.52E-09	23	16519	0.31	0.031	0.026	2.41E-01	7.8	4.90E-05
rs2246012	6:131898208	C/T	0.15	0.016	0.002	1.15E-13	23	16519	0.15	-0.011	0.035	7.43E-01	0	6.57E-05
rs6922607	6:142703483	G/A	0.19	0.013	0.002	1.85E-09	23	16519	0.20	-0.027	0.043	5.30E-01	39.7	5.24E-05
rs765875 ^a	6:143185683	C/T	0.53	0.013	0.002	1.08E-14	22	16332	0.52	0.002	0.024	9.38E-01	0	8.68E-05
rs7760482	6:147354276	G/A	0.38	0.010	0.002	6.25E-09	23	16519	0.37	-0.051	0.025	4.52E-02	0	4.92E-05
rs12527426	6:153392002	A/G	0.30	0.015	0.002	5.54E-16	23	16519	0.29	-0.028	0.027	2.88E-01	11.8	9.45E-05
rs9478496	6:154333183	C/T	0.15	0.016	0.002	8.17E-12	23	16519	0.16	-0.019	0.033	5.56E-01	0	6.45E-05
rs13191362 ^a	6:163033350	A/G	0.86	0.024	0.002	4.08E-21	22	16332	0.88	-0.018	0.037	6.23E-01	0	1.35E-04
rs9458814	6:163771305	C/T	0.23	0.011	0.002	2.33E-08	23	16519	0.22	0.031	0.040	4.43E-01	37.6	4.43E-05
rs6950388	7:1270699	A/G	0.78	0.014	0.002	1.59E-09	22	16283	0.75	-0.021	0.030	4.86E-01	0	6.29E-05
rs4721089	7:1872921	T/C	0.78	0.017	0.002	5.60E-13	23	16519	0.74	-0.007	0.028	7.97E-01	0	9.48E-05

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)						I ² (%)	R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P		
rs6463489	7:5542513	T/C	0.10	0.017	0.003	2.50E-10	13	8121					Excluded for MR	
rs4307239	7:24354300	G/A	0.46	0.012	0.002	1.47E-11	23	16519	0.47	0.004	0.024	8.70E-01	0	6.58E-05
rs213518	7:26941065	C/T	0.15	0.015	0.002	2.49E-10	23	16519	0.14	-0.065	0.036	6.72E-02	15.5	5.98E-05
rs215669	7:32378979	G/A	0.40	0.015	0.002	8.94E-18	23	16519	0.41	-0.025	0.033	4.46E-01	32.8	1.06E-04
rs2108719	7:39481056	A/G	0.73	0.011	0.002	2.28E-08	23	16519	0.74	0.007	0.028	8.02E-01	16.7	4.54E-05
rs217433	7:44553496	C/T	0.20	0.012	0.002	3.00E-08	23	16519	0.18	0.030	0.031	3.35E-01	0	4.18E-05
rs2289379	7:44804225	C/T	0.61	0.014	0.002	7.02E-15	23	16519	0.59	-0.012	0.025	6.27E-01	21	8.94E-05
rs10499694 ^a	7:50614173	A/G	0.49	0.013	0.002	1.29E-15	22	16332	0.48	0.051	0.033	1.20E-01	36.5	8.45E-05
rs11772246	7:71603692	T/C	0.82	0.015	0.002	3.69E-11	23	16519	0.81	0.026	0.040	5.22E-01	30.8	6.11E-05
rs17207196	7:75101065	C/T	0.58	0.022	0.002	1.58E-36	23	16519	0.61	0.006	0.027	8.32E-01	0	2.36E-04
rs17149254	7:76634463	T/C	0.21	0.024	0.002	2.99E-25	17	11889	0.21	0.021	0.038	5.73E-01	0	1.85E-04
rs6973656	7:77422583	G/A	0.42	0.010	0.002	6.31E-09	23	16519	0.39	0.046	0.032	1.51E-01	31	4.96E-05
rs1965529	7:77825707	A/G	0.77	0.016	0.002	7.66E-14	23	16519	0.79	-0.025	0.030	3.99E-01	0	9.10E-05
rs274628	7:86265855	C/A	0.66	0.010	0.002	1.36E-08	23	16519	0.64	0.019	0.034	5.84E-01	35.1	4.65E-05
rs2283006	7:93085722	A/G	0.49	0.013	0.002	8.06E-15	23	16519	0.49	-0.001	0.042	9.87E-01	57.6	8.71E-05
rs13240600	7:99064466	A/G	0.83	0.018	0.002	7.90E-16	23	16519	0.85	-0.025	0.034	4.55E-01	16.1	8.96E-05
rs1721447 ^a	7:109214139	G/T	0.49	0.010	0.002	3.79E-09	22	16332	0.48	0.022	0.029	4.49E-01	20.9	5.00E-05
rs2396625	7:113028634	T/A	0.58	0.018	0.002	2.81E-24	23	16519	0.57				Excluded for MR	
rs13245051	7:113362799	A/G	0.46	0.015	0.002	1.12E-18	21	15952	0.46	0.022	0.026	3.94E-01	8.5	1.12E-04
rs10261050	7:114337652	T/C	0.48	0.011	0.002	4.53E-11	23	16519	0.44	0.006	0.025	8.18E-01	8.4	6.37E-05
rs2283093	7:126721231	T/C	0.19	0.012	0.002	1.10E-08	23	16519	0.21	0.015	0.030	6.20E-01	0	4.59E-05
rs7802342	7:137435925	G/T	0.30	0.012	0.002	6.23E-11	23	16519	0.30	-0.025	0.027	3.60E-01	0	6.40E-05
rs11525873	7:138817193	T/C	0.90	0.023	0.003	2.98E-13	23	16519	0.91	-0.080	0.043	6.45E-02	0	9.73E-05
rs11773362 ^a	7:147668180	C/T	0.66	0.011	0.002	6.39E-09	22	16332	0.69	-0.034	0.026	1.88E-01	0	4.95E-05
rs2907948	7:150638484	G/A	0.76	0.015	0.002	1.95E-14	23	16519	0.76	-0.030	0.028	2.85E-01	10.2	7.76E-05
rs56211164	7:158016764	G/A	0.76	0.013	0.002	8.90E-09	23	16519	0.78	0.047	0.042	2.64E-01	41.4	5.97E-05
rs1700082	8:4121727	C/G	0.66	0.009	0.002	3.38E-08	23	16519	0.66	0.008	0.027	7.76E-01	0	3.97E-05
rs4240673	8:10787612	T/C	0.45	0.018	0.002	1.58E-26	23	16519	0.48	0.028	0.024	2.50E-01	20.4	1.52E-04
rs13263601	8:14095900	C/A	0.34	0.015	0.002	4.87E-16	23	16519	0.33	0.019	0.035	5.85E-01	37.9	9.46E-05
rs10110189	8:15393380	C/T	0.89	0.016	0.003	2.20E-08	10	6802					Excluded for MR	
rs10101364	8:20634888	T/C	0.68	0.012	0.002	5.61E-11	23	16519	0.68	0.030	0.027	2.55E-01	0	6.27E-05
rs73225274	8:21088909	G/A	0.14	0.016	0.003	2.33E-08	23	16519	0.13	-0.010	0.036	7.90E-01	0	5.69E-05
rs13249650	8:25664336	A/T	0.44	0.011	0.002	1.02E-08	23	16519	0.44				Excluded for MR	
rs1421334	8:30865733	A/C	0.45	0.014	0.002	3.11E-15	23	16519	0.46	-0.010	0.025	6.95E-01	0	9.04E-05
rs2466103	8:32412304	G/T	0.31	0.012	0.002	8.00E-12	23	16519	0.31	-0.029	0.026	2.70E-01	0	6.23E-05
rs6468266	8:34380276	T/A	0.58	0.011	0.002	7.71E-11	23	16519	0.62	0.017	0.025	5.14E-01	7.6	6.21E-05
rs12681792	8:62054463	A/C	0.20	0.015	0.002	2.88E-12	23	16519	0.17	-0.001	0.032	9.73E-01	0	7.26E-05
rs12334877 ^a	8:67194171	G/A	0.81	0.014	0.002	2.17E-11	22	16332	0.79	0.040	0.030	1.85E-01	0	6.42E-05
rs1808629	8:73435964	G/A	0.33	0.020	0.002	2.19E-23	23	16519	0.33	-0.005	0.026	8.38E-01	23.9	1.79E-04
rs17405819	8:76806584	T/C	0.68	0.021	0.002	6.04E-33	23	16519	0.70	0.003	0.033	9.20E-01	25.4	1.92E-04
rs2196618	8:85089437	G/A	0.74	0.014	0.002	1.49E-12	23	16519	0.73	0.006	0.028	8.17E-01	0	7.28E-05
rs12386885	8:87766769	T/C	0.16	0.015	0.003	9.90E-09	23	16519	0.15	-0.020	0.042	6.36E-01	25.5	6.02E-05
rs2120710	8:93210803	A/G	0.65	0.010	0.002	1.98E-08	23	16519	0.67	0.015	0.026	5.76E-01	0	4.62E-05
rs12680842	8:95582606	A/G	0.68	0.014	0.002	3.41E-16	23	16519	0.67	-0.008	0.026	7.57E-01	9.7	8.72E-05
rs1383592	8:106430676	A/G	0.21	0.012	0.002	4.92E-09	23	16519	0.22	0.004	0.042	9.28E-01	40.2	4.97E-05
rs3808477 ^a	8:116670347	C/T	0.73	0.018	0.002	8.73E-22	22	16331	0.75	-0.026	0.031	4.08E-01	14.5	1.32E-04
rs72673947	8:118884379	G/A	0.11	0.022	0.003	4.11E-13	23	16519	0.11	-0.062	0.039	1.11E-01	9.2	9.72E-05

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							I² (%)	R²
			EA	Beta	SE	P	n studies	n sample	EA	Beta	SE	P			
rs6470144 ^a	8:124152245	T/G	0.65	0.010	0.002	3.06E-08	22	16332	0.66	-0.006	0.026	8.03E-01	0	4.37E-05	
rs7842934	8:132838921	C/T	0.08	0.018	0.003	1.55E-08	23	16519	0.06	0.002	0.049	9.75E-01	0	4.61E-05	
rs305256	8:137568252	C/T	0.77	0.012	0.002	2.79E-08	17	11018	0.75	-0.004	0.046	9.35E-01	26.6	4.63E-05	
rs16906838	8:138213836	C/T	0.95	0.025	0.004	4.31E-10	23	16519	0.94	0.041	0.053	4.38E-01	0	5.64E-05	
rs11782074	8:142617096	T/G	0.37	0.012	0.002	4.24E-12	23	16519	0.36	-0.009	0.026	7.44E-01	0	7.15E-05	
rs10099330	8:143383694	G/A	0.46	0.012	0.002	3.22E-12	23	16519	0.44	-0.016	0.024	5.23E-01	24.4	7.04E-05	
rs10975933	9:6954557	C/G	0.66	0.011	0.002	2.07E-10	23	16519	0.67	-0.025	0.026	3.28E-01	0	5.80E-05	
rs1948080	9:11852043	T/G	0.63	0.014	0.002	1.13E-14	23	16519	0.63	0.002	0.025	9.29E-01	14.9	8.62E-05	
rs10961649	9:14670949	T/C	0.32	0.010	0.002	1.51E-08	23	16519	0.34	0.006	0.034	8.53E-01	32.5	4.74E-05	
rs4740619	9:15634326	T/C	0.54	0.019	0.002	3.15E-31	23	16519	0.56	-0.027	0.025	2.75E-01	0	1.77E-04	
rs10962550	9:16720329	C/G	0.18	0.019	0.002	5.68E-17	23	16519	0.19	0.002	0.031	9.49E-01	12.1	1.00E-04	
rs10811868	9:23199959	G/A	0.68	0.010	0.002	3.18E-08	23	16519	0.67	-0.012	0.026	6.33E-01	0	4.35E-05	
rs10968114 ^a	9:27800007	A/C	0.53	0.011	0.002	3.30E-11	22	16332	0.54	0.035	0.024	1.54E-01	0	6.36E-05	
rs1412235	9:28410996	C/G	0.32	0.024	0.002	2.28E-42	23	16519	0.28	0.046	0.027	9.41E-02	7.2	2.42E-04	
rs10121187	9:29737191	C/G	0.51	0.010	0.002	2.02E-09	23	16519	0.52	Excluded for MR					
rs2275003	9:34124860	A/G	0.50	0.011	0.002	9.44E-12	23	16519	0.51	-0.010	0.025	6.88E-01	15.7	6.16E-05	
rs13296413	9:37258105	C/T	0.62	0.015	0.002	2.49E-17	23	16519	0.63	-0.063	0.032	5.19E-02	30.7	1.03E-04	
rs2134858	9:73837155	C/T	0.49	0.012	0.002	5.87E-12	23	16519	0.48	-0.020	0.030	5.19E-01	25.7	6.84E-05	
rs7861160	9:80799579	T/C	0.59	0.010	0.002	3.68E-08	23	16519	0.61	0.013	0.025	6.11E-01	6.6	4.35E-05	
rs1999433	9:81371441	C/T	0.56	0.011	0.002	2.90E-10	23	16519	0.57	0.004	0.025	8.68E-01	0	5.64E-05	
rs2777768	9:84186734	A/G	0.72	0.012	0.002	6.38E-10	23	16519	0.72	-0.015	0.028	5.91E-01	0	5.67E-05	
rs7357754	9:92207308	G/A	0.50	0.012	0.002	1.81E-12	23	16519	0.49	-0.010	0.025	6.79E-01	14.6	7.20E-05	
rs10992867 ^a	9:96461013	A/G	0.27	0.016	0.002	3.20E-17	22	16332	0.27	-0.018	0.029	5.31E-01	7.8	1.03E-04	
rs7025938	9:103088321	G/C	0.32	0.016	0.002	1.47E-19	23	16519	0.34	0.009	0.026	7.14E-01	0	1.14E-04	
rs7024334	9:109072075	T/G	0.23	0.014	0.002	4.71E-12	23	16519	0.28	-0.052	0.040	1.94E-01	37	6.36E-05	
rs1928295 ^a	9:120378483	T/C	0.57	0.013	0.002	2.23E-16	22	16332	0.55	0.044	0.024	7.40E-02	0	8.80E-05	
rs1877875	9:120664469	C/T	0.57	0.011	0.002	2.51E-10	23	16519	0.58	0.003	0.025	9.07E-01	24.8	5.84E-05	
rs13298487	9:126112104	T/C	0.61	0.012	0.002	1.43E-08	5	2790	Excluded for MR						
rs10733682	9:129460914	A/G	0.46	0.015	0.002	1.76E-19	23	16519	0.50	0.010	0.032	7.63E-01	28.6	1.09E-04	
rs2267958	9:131015279	G/A	0.49	0.013	0.002	2.01E-13	3	1660	Excluded for MR						
rs4740383	9:133783566	A/G	0.42	0.013	0.002	7.03E-14	23	16519	0.37	0.053	0.026	3.85E-02	0	8.35E-05	
rs10858334	9:137989785	G/C	0.15	0.015	0.002	4.91E-09	23	16519	0.14	-0.048	0.050	3.43E-01	36.3	5.63E-05	
rs7907470 ^b	10:10268989	G/A	0.09	0.018	0.003	7.36E-09	22	16332	0.08	0.015	0.060	8.07E-01	37.1	4.93E-05	
rs7893571	10:16750129	T/G	0.67	0.013	0.002	5.83E-12	23	16519	0.66	-0.036	0.026	1.75E-01	0	6.87E-05	
rs76638898	10:21099584	G/A	0.98	0.038	0.006	8.15E-09	2	1255	Excluded for MR						
rs7084454	10:21821274	A/G	0.31	0.020	0.002	4.51E-27	22	15388	0.34	0.007	0.027	7.86E-01	0	1.67E-04	
rs10829164	10:27318370	T/C	0.15	0.015	0.002	2.37E-10	22	15388	0.15	-0.043	0.035	2.20E-01	0	5.71E-05	
rs4097319	10:33860515	T/G	0.56	0.011	0.002	4.32E-10	22	15388	0.56	-0.006	0.026	8.04E-01	8.2	5.63E-05	
rs12765914	10:34013507	T/C	0.08	0.023	0.003	1.96E-13	22	15388	0.09	-0.050	0.045	2.63E-01	16.2	7.53E-05	
rs1624134	10:34834482	C/G	0.39	0.010	0.002	6.51E-09	22	15388	0.40	0.014	0.026	5.88E-01	0	4.77E-05	
rs12259464 ^a	10:53680099	A/G	0.48	0.011	0.002	1.48E-10	22	16332	0.46	0.038	0.027	1.64E-01	12.1	5.93E-05	
rs7070670	10:61842645	C/T	0.68	0.013	0.002	7.14E-10	23	16519	0.69	0.016	0.027	5.63E-01	0	6.94E-05	
rs10761785	10:65318766	G/T	0.49	0.013	0.002	3.47E-16	23	16519	0.50	-0.060	0.033	6.65E-02	33.4	8.84E-05	
rs12098284	10:76047464	T/C	0.12	0.018	0.003	9.87E-13	23	16519	0.13	-0.008	0.037	8.30E-01	0	7.21E-05	
rs11001259	10:76807650	T/A	0.82	0.014	0.002	1.22E-08	NA in Courage-PD								
rs7899106	10:87410904	G/A	0.05	0.033	0.004	1.72E-18	22	15388	0.05	-0.046	0.060	4.44E-01	23.5	1.02E-04	
rs10788494	10:88110925	C/G	0.48	0.013	0.002	5.51E-15	22	15388	0.46	Excluded for MR					

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							I² (%)	R²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P			
rs147568678	10:93061851	T/C	0.77	0.013	0.002	3.42E-09	21	15201	0.77	-0.015	0.032	6.35E-01	0	6.39E-05	
rs2439823	10:99778226	G/A	0.55	0.016	0.002	6.51E-22	22	15388	0.52	-0.014	0.026	5.87E-01	7.2	1.35E-04	
rs17094222 ^a	10:102395440	C/T	0.21	0.017	0.002	4.04E-18	22	16332	0.20	0.049	0.031	1.12E-01	3	9.89E-05	
rs11594179	10:104392580	C/T	0.77	0.011	0.002	2.16E-08	23	16519	0.79	0.020	0.039	6.01E-01	29.1	4.24E-05	
rs79780963	10:104952499	T/C	0.08	0.024	0.004	2.63E-12	23	16519	0.09	-0.036	0.043	3.94E-01	17.8	8.80E-05	
rs7903146	10:114758349	C/T	0.72	0.018	0.002	1.67E-23	23	16519	0.70	0.022	0.035	5.33E-01	28.3	1.27E-04	
rs2257791	10:118643670	G/A	0.24	0.014	0.002	1.63E-12	23	16519	0.28	-0.001	0.029	9.81E-01	0	7.13E-05	
rs845084	10:125220036	A/G	0.27	0.014	0.002	3.22E-12	23	16519	0.28	-0.009	0.027	7.42E-01	0	7.23E-05	
rs17636031	10:126594078	C/T	0.28	0.015	0.002	3.87E-17	6	3891				Excluded for MR			
rs4880341	10:133992689	C/T	0.43	0.013	0.002	3.06E-14	22	16283	0.47	-0.002	0.025	9.49E-01	10.2	8.27E-05	
rs11246136	11:371265	C/A	0.90	0.017	0.003	2.03E-08	11	8087				Excluded for MR			
rs12421848 ^a	11:891338	G/A	0.60	0.014	0.002	3.99E-13	18	14351	0.61	0.009	0.026	7.22E-01	0	9.51E-05	
rs4256980	11:8673939	G/C	0.67	0.019	0.002	8.63E-29	23	16519	0.61	-0.003	0.025	9.20E-01	0	1.55E-04	
rs900144	11:13294268	T/C	0.58	0.015	0.002	1.53E-18	23	16519	0.54	0.041	0.025	1.06E-01	0	1.07E-04	
rs2074314 ^a	11:17411821	T/C	0.64	0.011	0.002	1.37E-09	22	16332	0.64	-0.023	0.027	3.89E-01	6	5.11E-05	
rs6265 ^a	11:27679916	C/T	0.82	0.041	0.002	7.40E-89	22	16332	0.79	0.030	0.030	3.21E-01	0	5.11E-04	
rs570463	11:28739318	C/A	0.67	0.012	0.002	4.33E-11	23	16519	0.69	-0.018	0.034	5.95E-01	33.2	6.44E-05	
rs11030618	11:29243293	T/C	0.58	0.011	0.002	1.67E-10	23	16519	0.54	0.006	0.025	8.19E-01	0	5.90E-05	
rs2065418 ^a	11:30422068	T/G	0.65	0.014	0.002	6.07E-15	22	16332	0.64	-0.007	0.025	7.70E-01	0	8.84E-05	
rs2862996 ^a	11:43653833	G/T	0.30	0.022	0.002	3.60E-35	22	16332	0.31	0.034	0.028	2.25E-01	7.2	1.96E-04	
rs10742752	11:45438374	C/T	0.62	0.012	0.002	1.20E-13	23	16519	0.62	0.009	0.025	7.30E-01	0	7.10E-05	
rs118081010	11:46174948	T/C	0.02	0.052	0.007	5.28E-12	17	13417	0.02	-0.055	0.103	5.95E-01	1.8	8.71E-05	
rs7124681 ^a	11:47529947	A/C	0.42	0.026	0.002	3.96E-55	22	16332	0.40	0.025	0.027	3.50E-01	10.2	3.21E-04	
rs6591407	11:56914157	C/A	0.80	0.012	0.002	3.58E-09	23	16519	0.81	-0.039	0.031	1.99E-01	0	4.89E-05	
rs562664	11:63823619	C/T	0.81	0.014	0.002	4.15E-10	23	16519	0.82	-0.013	0.032	6.84E-01	19.9	5.80E-05	
rs7102454 ^a	11:65594820	C/T	0.36	0.017	0.002	3.84E-21	22	16332	0.33	0.008	0.031	8.11E-01	24.6	1.29E-04	
rs592483	11:69445173	C/T	0.41	0.014	0.002	1.53E-16	23	16519	0.41	0.033	0.025	1.99E-01	11.5	9.06E-05	
rs12282785	11:76476030	C/A	0.78	0.016	0.002	1.43E-11	23	16519	0.76	-0.039	0.029	1.74E-01	0	8.47E-05	
rs349088 ^a	11:84814393	C/A	0.52	0.013	0.002	3.50E-14	22	16332	0.50	-0.053	0.024	2.68E-02	0.3	8.43E-05	
rs10741329	11:89997796	A/G	0.69	0.012	0.002	3.91E-10	23	16519	0.67	-0.005	0.026	8.40E-01	0	5.61E-05	
rs3019466	11:92476178	C/T	0.83	0.013	0.002	4.91E-08	23	16519	0.84	0.056	0.034	9.60E-02	0	4.57E-05	
rs2605603	11:93221105	G/A	0.52	0.010	0.002	2.04E-10	23	16519	0.51	-0.024	0.024	3.27E-01	5.1	5.30E-05	
rs2513999	11:103019633	G/A	0.84	0.015	0.003	3.07E-09	21	15909	0.82	-0.047	0.035	1.78E-01	4.2	6.35E-05	
rs12286929 ^a	11:115022404	G/A	0.50	0.018	0.002	1.93E-27	22	16332	0.54	-0.036	0.024	1.35E-01	0	1.57E-04	
rs76942203	11:116973247	A/G	0.06	0.026	0.004	9.08E-11	23	16519	0.06	-0.136	0.051	7.58E-03	0	7.64E-05	
rs3825061	11:118944675	T/C	0.39	0.014	0.002	6.15E-16	23	16519	0.38	0.009	0.025	7.14E-01	8.6	9.29E-05	
rs11218510	11:121922587	G/A	0.61	0.014	0.002	6.79E-13	23	16519	0.62	0.018	0.025	4.66E-01	0	9.37E-05	
rs35483388	11:122545146	T/C	0.38	0.013	0.002	2.61E-10	23	16519	0.37	-0.001	0.025	9.55E-01	0	7.36E-05	
rs7944782	11:130795698	G/T	0.50	0.014	0.002	3.61E-17	23	16519	0.50	-0.009	0.025	7.02E-01	18.7	1.04E-04	
rs2007518	11:132639606	G/A	0.44	0.013	0.002	1.96E-14	23	16519	0.42	-0.015	0.025	5.50E-01	1.4	8.32E-05	
rs1941213 ^a	11:133125329	A/C	0.71	0.011	0.002	1.59E-08	22	16331	0.72	0.008	0.035	8.24E-01	30.3	4.79E-05	
rs329651	11:133767622	T/G	0.81	0.016	0.002	2.13E-14	23	16519	0.78	-0.080	0.030	8.58E-03	0	8.01E-05	
rs12364470	11:134601012	G/T	0.15	0.019	0.002	2.18E-17	12	7523				Excluded for MR			
rs11611246	12:939480	T/G	0.20	0.022	0.002	2.04E-28	23	16519	0.19	-0.024	0.031	4.43E-01	0	1.59E-04	
rs765125 ^a	12:2156207	C/T	0.41	0.010	0.002	1.27E-08	22	16332	0.43	-0.015	0.025	5.31E-01	0	4.66E-05	
rs10772983 ^a	12:17141582	C/T	0.46	0.001	0.002	6.21E-10	19	11322	0.49	0.055	0.030	6.85E-02	0	4.97E-05	
rs11044430	12:19287416	A/T	0.84	0.016	0.002	3.77E-12	23	16519	0.83	0.035	0.034	2.93E-01	21.2	6.83E-05	

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)						I ² (%)	R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P		
rs11046972	12:23705969	T/C	0.07	0.018	0.003	3.72E-08	23	16519	0.09	-0.023	0.043	5.97E-01	0	4.11E-05
rs10842240	12:24060075	C/G	0.13	0.020	0.002	1.21E-14	23	16519	0.14	-0.019	0.036	6.02E-01	0	8.35E-05
rs11170468	12:39430048	A/C	0.78	0.013	0.002	1.12E-11	23	16519	0.77	-0.021	0.029	4.73E-01	0	5.75E-05
rs1350430	12:41819215	C/T	0.47	0.013	0.002	2.08E-13	23	16519	0.43	0.026	0.024	2.87E-01	0	7.78E-05
rs1126930	12:49399132	C/G	0.03	0.034	0.005	1.00E-10	4	2385	Excluded for MR					
rs7138803 ^a	12:50247468	A/G	0.39	0.030	0.002	3.10E-71	22	16332	0.37	0.065	0.025	9.28E-03	0	4.19E-04
rs2271189	12:56494991	G/A	0.60	0.014	0.002	9.26E-16	23	16519	0.63	0.008	0.026	7.42E-01	0	9.51E-05
rs7975187	12:60964108	G/A	0.23	0.014	0.002	3.86E-11	23	16519	0.20	0.079	0.030	8.59E-03	0	6.62E-05
rs650198	12:69674595	C/T	0.27	0.014	0.002	6.43E-13	23	16519	0.33	0.005	0.026	8.46E-01	0	7.41E-05
rs11115176	12:82465797	T/C	0.78	0.013	0.002	6.79E-12	23	16519	0.76	-0.034	0.028	2.30E-01	0	5.81E-05
rs10506971	12:89757937	G/A	0.45	0.014	0.002	4.69E-17	23	16519	0.47	0.032	0.032	3.16E-01	27.7	9.97E-05
rs11105839	12:91237920	T/A	0.63	0.011	0.002	1.25E-11	23	16519	0.63	-0.007	0.025	7.68E-01	13.9	5.97E-05
rs2712665	12:99594947	C/T	0.30	0.011	0.002	5.40E-09	23	16519	0.33	0.016	0.027	5.39E-01	10.4	4.93E-05
rs6539064	12:103706754	C/G	0.75	0.019	0.002	1.14E-23	23	16519	0.73	0.008	0.027	7.78E-01	0	1.42E-04
rs1860561	12:110783241	A/G	0.21	0.016	0.002	1.71E-16	23	16519	0.19	-0.014	0.031	6.56E-01	0	8.35E-05
rs11066188	12:112610714	G/A	0.62	0.011	0.002	3.05E-12	20	15621	0.58	0.038	0.027	1.66E-01	0	6.10E-05
rs2707183	12:116957607	G/T	0.47	0.009	0.002	4.89E-08	23	16519	0.47	<0.001	0.025	9.86E-01	0	4.31E-05
rs11615578	12:121714935	T/C	0.26	0.012	0.002	3.04E-09	18	12286	0.23	-0.008	0.035	8.25E-01	8.7	5.23E-05
rs12369179	12:122963550	C/T	0.92	0.034	0.003	2.32E-28	22	16332	0.92	0.028	0.048	5.69E-01	0	1.80E-04
rs11060853	12:123424071	G/A	0.41	0.011	0.002	3.10E-08	23	16519	0.40	0.088	0.031	4.85E-03	27.6	5.53E-05
rs11614340	12:133426483	C/T	0.29	0.012	0.002	1.87E-10	23	16519	0.28	0.009	0.027	7.40E-01	0	5.68E-05
rs9512648	13:27933910	A/G	0.47	0.010	0.002	4.11E-08	23	16519	0.50	-0.039	0.032	2.23E-01	30.5	4.50E-05
rs7323	13:28009031	G/C	0.73	0.017	0.002	2.18E-18	23	16519	0.75	-0.036	0.028	1.89E-01	1.8	1.08E-04
rs4771218 ^a	13:28655311	G/A	0.38	0.014	0.002	3.18E-15	22	16332	0.41	-0.031	0.025	2.09E-01	0	9.33E-05
rs9595908	13:33184288	T/C	0.64	0.015	0.002	3.73E-20	23	16519	0.62	-0.004	0.025	8.73E-01	0	1.09E-04
rs9603697 ^a	13:40783323	T/C	0.32	0.013	0.002	1.69E-13	22	16332	0.33	-0.008	0.026	7.56E-01	0	7.79E-05
rs12429545 ^a	13:54102206	A/G	0.12	0.031	0.002	1.42E-37	22	16332	0.12	-0.050	0.042	2.30E-01	15.2	2.10E-04
rs962796 ^a	13:54385284	T/C	0.19	0.014	0.002	1.88E-11	22	16332	0.20	-0.006	0.033	8.45E-01	9.2	6.12E-05
rs9569777	13:58484786	G/T	0.81	0.020	0.002	3.43E-21	23	16519	0.84	-0.026	0.033	4.25E-01	0	1.23E-04
rs9527895	13:59367767	C/T	0.18	0.016	0.002	3.69E-12	23	16519	0.17	0.008	0.033	8.11E-01	0	7.40E-05
rs8181823	13:65477940	C/A	0.77	0.013	0.002	4.36E-10	23	16519	0.76	-0.020	0.039	6.03E-01	37.2	5.61E-05
rs9599161	13:67434016	T/C	0.57	0.010	0.002	2.32E-09	23	16519	0.57	0.035	0.025	1.65E-01	0	4.71E-05
rs1441264 ^a	13:79580919	A/G	0.58	0.017	0.002	7.60E-25	22	16332	0.62	-0.036	0.026	1.74E-01	7.4	1.47E-04
rs9531786	13:85983968	G/C	0.63	0.011	0.002	4.11E-10	23	16519	0.63	0.026	0.033	4.34E-01	31.9	5.75E-05
rs77432547	13:86494817	G/A	0.28	0.017	0.002	1.44E-15	23	16519	0.26	-0.007	0.035	8.31E-01	28.6	1.16E-04
rs1927790	13:96922191	C/T	0.39	0.014	0.002	1.57E-17	23	16519	0.43	-0.024	0.025	3.24E-01	23.6	9.36E-05
rs9168	13:99101583	C/A	0.72	0.014	0.002	1.08E-13	23	16519	0.72	-0.012	0.027	6.44E-01	14.8	7.71E-05
rs9888533	13:107854612	T/C	0.53	0.013	0.002	1.38E-10	9	5180	Excluded for MR					
rs9522183	13:111977280	G/T	0.45	0.014	0.002	2.10E-12	23	16519	0.44	0.041	0.025	1.04E-01	8.1	9.02E-05
rs12868881	13:112218924	A/T	0.41	0.014	0.002	1.40E-15	23	16519	0.41	0.004	0.025	8.61E-01	0	9.19E-05
rs10132280	14:25928179	C/A	0.69	0.021	0.002	2.28E-33	23	16519	0.70	-0.023	0.027	4.00E-01	22.3	1.96E-04
rs4981693 ^a	14:29680331	A/G	0.77	0.020	0.002	7.89E-24	22	16332	0.77	0.029	0.029	3.22E-01	0	1.43E-04
rs225882	14:30480123	T/C	0.75	0.011	0.002	8.56E-10	23	16519	0.70	0.002	0.034	9.46E-01	27.6	4.77E-05
rs1958898	14:40886886	G/C	0.79	0.015	0.002	4.23E-12	23	16519	0.80	0.008	0.031	7.94E-01	0	7.07E-05
rs61983990	14:41475003	A/G	0.08	0.020	0.004	1.91E-08	23	16519	0.07	-0.055	0.062	3.69E-01	30.6	5.78E-05
rs4900714	14:47302219	T/G	0.48	0.015	0.002	1.00E-18	23	16519	0.53	-0.017	0.030	5.65E-01	25.2	1.12E-04
rs217669	14:62360075	C/T	0.28	0.017	0.002	6.27E-16	23	16519	0.25	-0.001	0.036	9.72E-01	27.6	1.19E-04

SNP	Chr.Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)						I ² (%)	R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P		
rs4430672	14:63094407	T/C	0.20	0.012	0.002	5.00E-09	23	16519	0.22	0.009	0.039	8.15E-01	29.8	4.84E-05
rs3902951	14:69789755	G/T	0.23	0.013	0.002	2.88E-12	20	15470	0.23	-0.002	0.031	9.42E-01	0	6.38E-05
rs17182027	14:73348130	G/A	0.44	0.011	0.002	1.46E-10	23	16519	0.48	-0.002	0.025	9.25E-01	0	5.95E-05
rs7144011	14:79940383	T/G	0.23	0.026	0.002	2.37E-40	23	16519	0.19	0.003	0.042	9.52E-01	35.6	2.48E-04
rs4517716	14:83013876	G/C	0.21	0.012	0.002	4.27E-09	23	16519	0.22	0.010	0.030	7.25E-01	0	4.50E-05
rs12888545	14:88308044	G/A	0.25	0.013	0.002	1.76E-11	23	16519	0.23	-0.014	0.029	6.19E-01	0	6.70E-05
rs1951455	14:91512339	C/T	0.72	0.015	0.002	6.05E-15	23	16519	0.69	0.006	0.027	8.20E-01	0	8.86E-05
rs942066	14:94031914	G/A	0.63	0.020	0.002	2.36E-24	23	16519	0.62	0.009	0.026	7.39E-01	0	1.91E-04
rs7161194	14:101529005	A/G	0.34	0.019	0.002	2.23E-24	NA in Courage-PD							
rs10145749	14:102782109	T/C	0.15	0.016	0.003	8.33E-10	23	16519	0.14	-0.033	0.036	3.59E-01	13.1	6.79E-05
rs4906263	14:103249127	G/C	0.34	0.018	0.002	8.11E-23	23	16519	0.35	-0.019	0.026	4.64E-01	0	1.40E-04
rs2273175	14:104160141	C/T	0.32	0.012	0.002	3.69E-11	23	16519	0.29	-0.003	0.039	9.45E-01	44.2	6.38E-05
rs12594043	15:27034988	C/G	0.52	0.010	0.002	1.31E-09	23	16519	0.50	Excluded for MR				
rs7172627	15:31877690	G/A	0.48	0.011	0.002	1.81E-11	23	16519	0.47	0.013	0.024	5.79E-01	0	6.48E-05
rs11636611	15:36391965	T/C	0.50	0.010	0.002	8.85E-10	23	16519	0.48	-0.010	0.025	6.78E-01	0	5.41E-05
rs9944219	15:46500612	G/A	0.40	0.012	0.002	8.14E-13	23	16519	0.40	-0.040	0.034	2.37E-01	35.9	6.77E-05
rs12912198	15:47103953	C/T	0.73	0.010	0.002	3.44E-08	23	16519	0.74	0.015	0.028	5.94E-01	7.7	3.97E-05
rs6493498	15:51754451	T/C	0.45	0.014	0.002	4.84E-17	23	16519	0.47	-0.009	0.025	7.09E-01	0	9.28E-05
rs10518694	15:53072673	A/C	0.14	0.014	0.002	3.43E-09	23	16519	0.13	-0.047	0.037	2.05E-01	0	4.98E-05
rs12439632	15:59103963	C/G	0.17	0.015	0.002	3.68E-10	23	16519	0.13	-0.082	0.037	2.95E-02	13.9	5.88E-05
rs339991	15:60913637	G/A	0.58	0.013	0.002	3.51E-13	23	16519	0.55	-0.016	0.032	6.19E-01	30.1	7.61E-05
rs1559673	15:62156514	A/C	0.97	0.036	0.005	2.21E-13	20	15434	0.98	0.102	0.083	2.19E-01	0	7.79E-05
rs2241423 ^a	15:68086838	G/A	0.77	0.030	0.002	3.60E-54	22	16332	0.77	0.022	0.029	4.56E-01	1	3.13E-04
rs7171864	15:73227249	A/G	0.69	0.013	0.002	2.60E-14	23	16519	0.67	-0.039	0.027	1.45E-01	0	7.41E-05
rs2470893 ^a	15:75019449	T/C	0.30	0.011	0.002	9.43E-10	22	16332	0.27	0.026	0.036	4.66E-01	31.8	4.85E-05
rs56151256	15:78024806	A/C	0.76	0.017	0.002	6.19E-14	23	16519	0.76	-0.039	0.028	1.73E-01	0	1.02E-04
rs12914623	15:80993570	G/C	0.73	0.016	0.002	2.00E-16	23	16519	0.75	-0.023	0.035	5.21E-01	28.9	1.00E-04
rs72757415	15:92572762	G/T	0.79	0.016	0.002	1.34E-11	23	16519	0.82	0.016	0.032	6.14E-01	0	8.46E-05
rs11633626	15:95271378	C/A	0.37	0.016	0.002	7.27E-19	23	16519	0.38	0.012	0.026	6.48E-01	0	1.15E-04
rs6496248	15:98262923	A/T	0.64	0.010	0.002	2.93E-09	23	16519	0.63	<0.001	0.025	9.92E-01	0	5.01E-05
rs12591120	15:99236869	T/C	0.74	0.012	0.002	3.84E-08	23	16519	0.75	-0.004	0.039	9.17E-01	36.8	5.55E-05
rs2715423	15:99511873	G/A	0.72	0.012	0.002	1.90E-09	21	15909	0.74	0.016	0.031	5.92E-01	0	5.34E-05
rs214249 ^a	16:348687	T/G	0.61	0.014	0.002	2.72E-15	21	16096	0.62	-0.045	0.025	7.31E-02	0	9.09E-05
rs12448257	16:3599655	A/G	0.22	0.016	0.002	9.04E-16	23	16519	0.21	-0.072	0.031	1.83E-02	0	8.85E-05
rs879620 ^a	16:4015729	T/C	0.60	0.023	0.002	8.45E-39	22	16330	0.61	-0.018	0.025	4.57E-01	0	2.46E-04
rs2058527 ^a	16:6704749	G/T	0.73	0.012	0.002	1.80E-09	22	16332	0.75	0.016	0.029	5.87E-01	3.5	5.23E-05
rs9926784 ^a	16:19941968	T/C	0.80	0.024	0.002	1.08E-30	22	16332	0.82	0.024	0.037	5.19E-01	18.3	1.79E-04
rs194809	16:23804956	A/G	0.19	0.013	0.002	4.86E-09	23	16519	0.19	0.009	0.031	7.77E-01	0	4.83E-05
rs2342892	16:24540806	T/G	0.49	0.013	0.002	1.33E-13	23	16519	0.49	0.026	0.024	2.84E-01	0	7.93E-05
rs7498665	16:28883241	G/A	0.38	0.028	0.002	1.14E-66	23	16519	0.35	-0.035	0.026	1.73E-01	0	3.84E-04
rs3814883	16:29994922	T/C	0.48	0.023	0.002	1.47E-40	23	16519	0.43	0.005	0.031	8.85E-01	26.5	2.57E-04
rs6500208	16:49011249	A/G	0.20	0.015	0.002	3.21E-13	23	16519	0.18	-0.016	0.032	6.22E-01	0	6.87E-05
rs1477199	16:53712135	G/A	0.16	0.022	0.002	5.15E-21	21	15542	0.15	0.038	0.038	3.12E-01	0	1.30E-04
rs7206790	16:53797908	G/C	0.48	0.061	0.002	1.00E-200	23	16519	0.47	Excluded for MR				
rs8057911	16:54143352	T/C	0.23	0.013	0.002	3.66E-08	23	16519	0.24	0.008	0.030	7.95E-01	0	5.60E-05
rs889398	16:69556715	C/T	0.58	0.020	0.002	3.23E-32	18	12171	0.59	0.007	0.047	8.78E-01	50.5	1.85E-04
rs35949039	16:70572605	G/T	0.89	0.021	0.003	6.30E-12	23	16519	0.89	-0.011	0.040	7.80E-01	0	8.73E-05

SNP	Chr.Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)						I ² (%)	R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P		
rs12926250	16:72213316	T/G	0.11	0.018	0.003	1.78E-10	23	16519	0.10	-0.054	0.040	1.82E-01	0	6.09E-05
rs756717	16:72996162	G/A	0.61	0.013	0.002	2.38E-15	19	14932	0.61	-0.025	0.028	3.65E-01	0	8.57E-05
rs4390583	16:81694835	C/A	0.43	0.010	0.002	1.63E-08	23	16519	0.41	-0.016	0.032	6.16E-01	25.1	4.90E-05
rs12922346	16:82438337	C/G	0.26	0.013	0.002	1.48E-11	23	16519	0.26	-0.059	0.028	3.85E-02	0	6.88E-05
rs7206608	16:82872628	G/C	0.32	0.013	0.002	1.20E-12	23	16519	0.29	-0.014	0.026	6.01E-01	19.3	7.41E-05
rs3923783	17:1843189	C/A	0.82	0.022	0.002	4.12E-23	23	16519	0.83	0.004	0.033	9.12E-01	17.5	1.44E-04
rs11078883	17:2138828	G/C	0.35	0.013	0.002	1.30E-12	23	16519	0.35	0.016	0.038	6.65E-01	43.9	7.18E-05
rs7774	17:4801163	A/C	0.32	0.013	0.002	4.22E-10	23	16519	0.33	0.002	0.027	9.51E-01	5.7	7.13E-05
rs1075901	17:15943910	C/T	0.55	0.012	0.002	4.43E-13	23	16519	0.56	-0.056	0.025	2.70E-02	2.1	6.90E-05
rs4986044 ^a	17:21261560	C/T	0.54	0.018	0.002	1.27E-27	22	16332	0.52	-0.011	0.025	6.52E-01	6	1.55E-04
rs8065172 ^a	17:31456969	G/A	0.76	0.012	0.002	5.29E-10	22	16331	0.75	0.052	0.034	1.27E-01	21.7	5.58E-05
rs12150665	17:34914787	T/C	0.59	0.017	0.002	1.74E-24	23	16519	0.59	0.034	0.025	1.73E-01	0	1.36E-04
rs6607337	17:35057373	C/T	0.70	0.012	0.002	2.55E-11	23	16519	0.67	-0.034	0.026	1.96E-01	3.8	6.43E-05
rs56161855	17:46288649	T/A	0.13	0.023	0.003	1.41E-16	23	16519	0.15	<0.001	0.034	9.99E-01	24	1.25E-04
rs9299 ^a	17:46669430	T/C	0.64	0.012	0.002	1.87E-11	22	16332	0.64	0.009	0.025	7.14E-01	0	6.49E-05
rs11655587	17:47140794	C/T	0.64	0.021	0.002	6.87E-26	23	16519	0.67	-0.027	0.034	4.23E-01	28.9	2.03E-04
rs11649864 ^a	17:56093061	A/G	0.09	0.019	0.003	2.52E-10	22	16332	0.09	0.044	0.042	3.04E-01	0	5.79E-05
rs12602912	17:65870073	T/C	0.21	0.017	0.002	2.90E-16	23	16519	0.20	<0.001	0.031	9.92E-01	0	9.21E-05
rs312750	17:68343539	A/G	0.50	0.010	0.002	2.57E-09	23	16519	0.50	<0.001	0.036	9.89E-01	47.1	4.70E-05
rs12939549	17:78611724	A/G	0.56	0.018	0.002	3.68E-28	23	16519	0.57	-0.002	0.024	9.23E-01	12.9	1.60E-04
rs35867081	17:79047278	A/G	0.49	0.015	0.002	6.65E-15	23	16519	0.51	0.019	0.025	4.47E-01	0	1.12E-04
rs8097672	18:1839601	T/A	0.15	0.021	0.002	3.26E-18	23	16519	0.15	-0.024	0.034	4.82E-01	5.3	1.09E-04
rs478707	18:7543207	C/T	0.80	0.015	0.002	1.98E-10	23	16519	0.79	0.003	0.030	9.10E-01	9	7.29E-05
rs891387	18:21103909	T/C	0.50	0.021	0.002	9.26E-35	23	16519	0.54	-0.008	0.025	7.29E-01	19	2.16E-04
rs1945160	18:22164216	G/A	0.62	0.010	0.002	5.65E-09	23	16519	0.62	0.021	0.025	3.97E-01	19.7	5.11E-05
rs1941696	18:31252129	A/G	0.52	0.011	0.002	4.74E-11	23	16519	0.49	<0.001	0.024	9.87E-01	0	6.26E-05
rs474605	18:39612720	G/A	0.53	0.013	0.002	2.72E-13	20	15529	0.51	-0.005	0.027	8.42E-01	5.5	7.78E-05
rs1356506	18:40708038	T/C	0.63	0.014	0.002	8.39E-15	23	16519	0.65	-0.133	0.036	2.40E-04	41.9	8.76E-05
rs2612576	18:42967950	T/A	0.71	0.011	0.002	8.49E-09	23	16519	0.71	-0.003	0.027	9.10E-01	0	4.85E-05
rs9951619	18:56882326	G/T	0.78	0.015	0.002	2.33E-15	23	16519	0.74	0.023	0.045	6.12E-01	49.7	8.03E-05
rs6567160	18:57829135	C/T	0.25	0.055	0.002	7.82E-184	23	16519	0.23	0.004	0.029	8.80E-01	16.9	1.14E-03
rs17066856	18:58049656	T/C	0.89	0.035	0.003	7.10E-38	23	16519	0.91	0.014	0.043	7.43E-01	10.9	2.37E-04
rs66595146	18:58204315	A/C	0.63	0.014	0.002	9.09E-12	23	16519	0.61	0.052	0.025	3.63E-02	0	8.50E-05
rs17783165	18:63461638	C/T	0.33	0.013	0.002	2.74E-13	23	16519	0.35	-0.009	0.027	7.46E-01	12.4	7.23E-05
rs11150911	18:73498528	A/C	0.28	0.012	0.002	3.72E-11	23	16519	0.32	-0.002	0.027	9.33E-01	17.2	5.67E-05
rs12981256	19:1865901	A/G	0.53	0.015	0.002	1.43E-18	23	16519	0.52	0.011	0.025	6.69E-01	0	1.14E-04
rs45486197	19:2244849	A/G	0.06	0.028	0.004	1.80E-12	3	1489	Excluded for MR					
rs895330	19:4060707	C/G	0.81	0.020	0.002	1.59E-19	23	16519	0.80	-0.047	0.031	1.29E-01	0	1.20E-04
rs273512	19:18224729	T/C	0.41	0.016	0.002	4.48E-19	23	16519	0.43	-0.025	0.025	3.00E-01	0	1.18E-04
rs17724992 ^a	19:18454825	A/G	0.72	0.017	0.002	5.23E-21	22	16332	0.74	0.036	0.027	1.87E-01	0	1.19E-04
rs7258722	19:18808915	T/A	0.59	0.020	0.002	1.81E-30	23	16519	0.62	0.057	0.033	8.61E-02	33.7	1.94E-04
rs12611148	19:19865077	C/A	0.86	0.014	0.002	1.42E-08	23	16519	0.84	-0.043	0.033	1.94E-01	3.2	4.60E-05
rs12462975	19:30272202	A/G	0.32	0.019	0.002	1.47E-25	23	16519	0.30	0.007	0.027	8.05E-01	0	1.63E-04
rs7245985	19:30710410	T/G	0.80	0.012	0.002	1.88E-08	23	16519	0.79	-0.014	0.030	6.50E-01	16.1	4.61E-05
rs11882409	19:34019685	A/C	0.03	0.012	0.002	3.31E-10	23	16519	0.29	-0.003	0.028	9.04E-01	19	6.18E-05
rs185350	19:34306816	T/C	0.49	0.014	0.002	9.10E-17	23	16519	0.51	-0.044	0.025	7.72E-02	21.3	9.38E-05
rs429358	19:45411941	T/C	0.85	0.026	0.003	2.60E-22	23	16519	0.88	-0.009	0.037	8.09E-01	0	1.72E-04

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							I² (%)	R²	
			EA/BA	Beta	SE	P	n studies	n sample	EA/BA	Beta	SE	P				
rs11672660	19:46180184	C/T	0.81	0.034	0.002	6.83E-60	23	16519	0.80	-0.030	0.031	3.32E-01	0	3.48E-04		
rs9304665	19:47602577	A/T	0.74	0.023	0.002	2.20E-31	3	2170	Excluded for MR							
rs3764625	19:49649051	T/G	0.40	0.010	0.002	2.42E-08	23	16519	0.42	0.026	0.025	3.04E-01	8.7	4.42E-05		
rs1884389	20:1410582	C/T	0.56	0.011	0.002	3.72E-10	23	16519	0.59	0.033	0.025	1.88E-01	0	5.74E-05		
rs4813619	20:2815715	G/T	0.47	0.011	0.002	1.70E-09	23	16519	0.48	0.058	0.025	1.92E-02	15	5.60E-05		
rs1884897 ^a	20:6612832	G/A	0.63	0.018	0.002	2.70E-28	22	16332	0.64	-0.005	0.026	8.58E-01	2.7	1.59E-04		
rs2423668	20:12430673	T/C	0.42	0.011	0.002	7.84E-09	23	16519	0.45	0.013	0.026	6.16E-01	20.5	5.47E-05		
rs852056	20:17102860	T/C	0.25	0.012	0.002	2.15E-10	23	16519	0.25	-0.013	0.029	6.39E-01	0	5.73E-05		
rs1409818 ^a	20:21381121	T/C	0.11	0.020	0.003	2.59E-12	22	16332	0.11	0.003	0.039	9.42E-01	0	7.29E-05		
rs8122855	20:25192049	A/G	0.34	0.014	0.002	4.11E-14	23	16519	0.31	0.036	0.033	2.71E-01	28	8.40E-05		
rs4812405	20:35276585	C/A	0.92	0.020	0.003	1.28E-09	3	2032	Excluded for MR							
rs742748	20:39293397	C/T	0.41	0.011	0.002	1.13E-11	23	16519	0.39	0.019	0.025	4.43E-01	0	6.19E-05		
rs79186842	20:47689036	A/G	0.86	0.020	0.003	2.60E-13	23	16519	0.88	0.043	0.049	3.80E-01	30.1	9.84E-05		
rs17806224	20:51065854	G/A	0.82	0.026	0.002	7.91E-32	23	16519	0.82	0.050	0.032	1.18E-01	22.6	2.00E-04		
rs1304549	20:54378256	G/A	0.77	0.012	0.002	1.35E-08	23	16519	0.79	-0.063	0.030	3.44E-02	0	4.87E-05		
rs6010784 ^a	20:61540319	T/C	0.51	0.011	0.002	6.91E-11	22	16332	0.48	-0.041	0.026	1.14E-01	7.2	5.62E-05		
rs6512302	20:62691550	C/G	0.74	0.013	0.002	1.52E-11	18	14896	0.73	0.029	0.042	4.81E-01	37.5	6.92E-05		
rs2064044	21:22119890	C/A	0.19	0.012	0.002	1.02E-08	14	8814	Excluded for MR							
rs2832283	21:30690558	A/G	0.23	0.012	0.002	4.72E-09	23	16519	0.22	-0.079	0.031	1.03E-02	0	4.62E-05		
rs13047416	21:40309436	C/G	0.63	0.015	0.002	6.93E-18	23	16519	0.63	0.024	0.033	4.62E-01	30.9	1.08E-04		
rs8134638	21:40644170	C/T	0.37	0.013	0.002	1.57E-11	23	16519	0.38	0.057	0.025	2.44E-02	0	8.27E-05		
rs8126575	21:46435610	T/G	0.87	0.015	0.002	5.88E-10	18	12171	0.86	-0.056	0.044	2.00E-01	20.1	5.32E-05		
rs427943	21:46570896	C/A	0.57	0.018	0.002	3.60E-25	23	16519	0.54	-0.040	0.031	1.91E-01	25.8	1.53E-04		
rs11538 ^a	22:18220831	G/A	0.17	0.014	0.002	1.09E-09	22	16332	0.16	0.012	0.035	7.44E-01	9.6	5.41E-05		
rs2238799	22:20109325	A/G	0.62	0.010	0.002	8.65E-09	23	16519	0.62	0.015	0.031	6.38E-01	25.3	4.91E-05		
rs12628891	22:38317137	C/T	0.68	0.012	0.002	5.85E-10	23	16519	0.72	0.019	0.028	5.02E-01	0	5.74E-05		
rs12628051 ^a	22:40654276	T/C	0.64	0.016	0.002	2.90E-19	22	16332	0.68	-0.034	0.032	2.89E-01	25.7	1.19E-04		
rs28489620	22:41804716	G/A	0.72	0.015	0.002	1.42E-12	23	16519	0.72	-0.040	0.028	1.50E-01	0	9.23E-05		
rs9615337	22:48898559	G/C	0.42	0.011	0.002	2.05E-08	23	16519	0.41	Excluded for MR						

^a SNPs genotyped.

^b Proxy SNP used in Courage-PD: rs7079940 (genotyped)

NA, not available; EA/BA, effect allele/base allele; SE, standard error. R², proportion of the variance of the exposure explained by the SNP: $2 \times \text{Beta}_{\text{exposure}}^2 \times \text{EAF}_{\text{exposure}} \times (1 - \text{EAF}_{\text{exposure}})$
 Bold coefficient with their corresponding SE and p-values are significant at p≤0.05; those underlined with a solid line are negative and those underlined with a dashed line are positive.

eTable 4: SNPs used for Mendelian randomisation analyses: individual associations with PD (Courage-PD) and BMI stratified by sex.

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EA	Beta	SE	P	n studies	n sample	EA	Beta	SE	P	I ² (%)	
FEMALES BMI (per 1SD=4.8kg/m ²)														
rs79113395	1:1590521	G/A	0.73	0.021	0.003	1.45E-12	22	7584	0.73	0.060	0.042	1.48E-01	15%	1.73E-04
rs10909880	1:2727804	C/T	0.55	0.012	0.002	1.97E-08	23	7707	0.54	0.017	0.037	6.50E-01	65%	7.62E-05
rs78886584	1:16859325	G/A	0.50	0.015	0.003	1.30E-08	9	2156	Excluded for MR					
rs4295917	1:32173360	A/G	0.65	0.014	0.002	1.62E-08	23	7707	0.63	-0.032	0.037	3.86E-01	39%	8.27E-05
rs112646560	1:39560250	T/C	0.21	0.020	0.003	1.14E-09	23	7707	0.23	-0.035	0.041	4.04E-01	40%	1.28E-04
rs2984618	1:47690438	T/G	0.44	0.017	0.002	2.21E-14	23	7707	0.37	0.064	0.037	7.92E-02	8%	1.38E-04
rs657452	1:49589847	A/G	0.40	0.020	0.002	1.14E-19	23	7707	0.38	0.039	0.038	3.07E-01	31%	1.99E-04
rs12140153	1:62579891	G/T	0.91	0.033	0.005	2.87E-12	23	7707	0.93	-0.039	0.066	5.52E-01	55%	1.75E-04
rs2568958	1:72765116	A/G	0.62	0.023	0.002	1.32E-24	23	7707	0.63	-0.043	0.038	2.57E-01	26%	2.43E-04
rs6669189	1:75011358	T/C	0.41	0.021	0.002	4.69E-21	23	7707	0.38	-0.012	0.036	7.52E-01	75%	2.13E-04
rs34517439	1:78450517	A/C	0.12	0.039	0.004	2.00E-21	21	7414	0.08	0.065	0.068	3.41E-01	34%	3.15E-04
rs12089815	1:91189933	G/A	0.45	0.015	0.003	6.02E-09	23	7707	0.48	-0.044	0.042	3.03E-01	30%	1.16E-04
rs11165643	1:96924097	T/C	0.58	0.018	0.002	1.71E-16	23	7707	0.56	-0.046	0.036	1.90E-01	19%	1.60E-04
rs4421623	1:98316285	T/G	0.21	0.018	0.003	1.13E-11	10	2987	Excluded for MR					
rs7550711	1:110082886	T/C	0.03	0.064	0.007	3.37E-21	22	7566	0.03	0.072	0.110	5.14E-01	51%	2.26E-04
rs197374	1:112289983	T/C	0.41	0.017	0.002	2.82E-13	23	7707	0.39	0.007	0.036	8.46E-01	85%	1.41E-04
rs61813324	1:156049877	T/C	0.13	0.030	0.004	3.60E-14	2	826	Excluded for MR					
rs1750307	1:156488420	A/T	0.37	0.014	0.002	8.22E-09	23	7707	0.35	-0.027	0.037	4.54E-01	45%	8.70E-05
rs12564992	1:174478100	G/A	0.11	0.021	0.004	2.37E-09	23	7707	0.12	0.001	0.054	9.85E-01	99%	8.56E-05
rs543874	1:177889480	G/A	0.22	0.058	0.003	8.70E-100	23	7707	0.17	-0.131	0.048	6.39E-03	1%	1.15E-03
rs10920678	1:190239907	A/G	0.42	0.016	0.002	7.46E-14	23	7707	0.42	0.015	0.036	6.69E-01	67%	1.30E-04
rs4474229	1:195037001	G/A	0.63	0.017	0.003	1.64E-10	23	7707	0.62	0.007	0.036	8.43E-01	84%	1.39E-04
rs2820295	1:201800868	A/G	0.33	0.021	0.002	8.03E-19	23	7707	0.31	-0.073	0.043	9.39E-02	9%	2.01E-04
rs17014375	1:209543560	G/T	0.13	0.019	0.003	1.46E-08	23	7707	0.13	-0.031	0.052	5.54E-01	55%	8.14E-05
rs12042959	1:243533273	A/G	0.86	0.019	0.003	2.33E-09	23	7707	0.85	-0.032	0.050	5.31E-01	53%	8.81E-05
rs62106258	2:417167	T/C	0.95	0.099	0.006	8.72E-58	1	123	Excluded for MR					
rs6548237	2:621461	C/A	0.84	0.058	0.003	4.43E-89	23	7707	0.79	0.034	0.045	4.55E-01	46%	8.91E-04
rs7571496	2:6169351	A/G	0.74	0.015	0.003	1.45E-08	23	7707	0.74	-0.015	0.040	7.08E-01	71%	8.02E-05
rs7601870	2:15384392	G/A	0.55	0.013	0.002	1.23E-08	23	7707	0.57	0.038	0.036	2.90E-01	29%	8.63E-05
rs10182181	2:25150296	G/A	0.50	0.036	0.002	5.00E-63	23	7707	0.45	0.046	0.035	1.92E-01	19%	6.55E-04
rs10048652	2:35449306	T/C	0.45	0.014	0.002	3.47E-09	23	7707	0.45	-0.031	0.035	3.78E-01	38%	9.02E-05
rs786420	2:44719893	T/C	0.77	0.016	0.003	8.84E-09	23	7707	0.75	0.017	0.042	6.78E-01	68%	8.47E-05
rs35722922	2:47002226	A/G	0.63	0.019	0.003	3.65E-12	23	7707	0.65	-0.024	0.039	5.40E-01	54%	1.66E-04
rs1421598	2:50264710	C/A	0.16	0.019	0.003	6.78E-10	23	7707	0.17	-0.018	0.048	7.13E-01	71%	9.85E-05
rs7601895	2:55281901	C/G	0.69	0.016	0.003	9.61E-11	23	7707	0.72	-0.001	0.039	9.85E-01	98%	1.11E-04
rs1861412	2:58893065	G/A	0.58	0.022	0.002	9.13E-21	23	7707	0.55	0.049	0.035	1.59E-01	16%	2.26E-04
rs6728037	2:59297346	A/G	0.39	0.021	0.002	6.49E-19	23	7707	0.39	-0.009	0.050	8.63E-01	86%	2.03E-04
rs2861685	2:67837553	T/C	0.59	0.018	0.003	1.05E-11	23	7707	0.60	0.037	0.051	4.73E-01	47%	1.57E-04

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs12714199	2:86812549	C/T	0.39	0.015	0.002	5.12E-10	23	7707	0.39	0.017	0.037	6.37E-01	64%	1.01E-04
rs11677607	2:100751150	C/T	0.75	0.024	0.003	2.87E-19	23	7707	0.75	0.001	0.040	9.82E-01	98%	2.14E-04
rs1457457	2:104340148	A/T	0.53	0.014	0.002	3.79E-10	23	7707	0.56	Excluded for MR				
rs6739199	2:105452326	T/C	0.27	0.016	0.003	3.20E-10	23	7707	0.26	0.055	0.040	1.66E-01	17%	9.95E-05
rs1984559	2:135678888	A/G	0.81	0.016	0.003	3.27E-08	21	7467	0.72	-0.028	0.041	5.01E-01	50%	8.23E-05
rs13002158	2:144021712	G/A	0.19	0.021	0.003	1.15E-12	23	7707	0.19	-0.012	0.045	7.94E-01	79%	1.32E-04
rs76900466	2:145057760	T/G	0.88	0.023	0.004	4.53E-08	3	941	Excluded for MR					
rs12692596	2:161265910	T/C	0.36	0.015	0.002	9.74E-11	23	7707	0.35	-0.025	0.037	5.01E-01	50%	9.83E-05
rs12692738	2:165558252	C/T	0.24	0.016	0.003	2.82E-10	23	7707	0.26	-0.051	0.041	2.09E-01	21%	9.46E-05
rs7588437	2:181575281	G/A	0.63	0.018	0.002	8.38E-15	23	7707	0.65	-0.031	0.037	4.00E-01	40%	1.44E-04
rs7594237	2:198187164	T/A	0.72	0.014	0.003	1.81E-08	23	7707	0.72	0.011	0.040	7.77E-01	78%	8.19E-05
rs4482463	2:205375909	C/A	0.08	0.037	0.004	5.21E-18	NA in Courage-PD							
rs11692326	2:208263279	T/C	0.23	0.016	0.003	2.04E-09	23	7707	0.20	0.023	0.064	7.21E-01	72%	8.61E-05
rs4673553	2:211608379	G/T	0.44	0.015	0.002	2.59E-11	23	7707	0.43	0.027	0.036	4.48E-01	45%	1.16E-04
rs12612009	2:228982603	G/T	0.34	0.014	0.002	3.78E-09	23	7707	0.37	-0.094	0.037	1.04E-02	1%	8.89E-05
rs6720868	2:230663576	T/C	0.31	0.017	0.002	4.65E-12	23	7707	0.34	-0.066	0.037	7.68E-02	8%	1.21E-04
rs1801282	3:12393125	G/C	0.10	0.018	0.003	4.72E-08	23	7707	0.12	-0.059	0.055	2.81E-01	28%	6.10E-05
rs2470520	3:15762920	C/T	0.42	0.013	0.002	4.16E-08	23	7707	0.41	-0.043	0.036	2.32E-01	23%	7.75E-05
rs4858223	3:20581149	C/T	0.67	0.016	0.003	8.26E-11	23	7707	0.69	0.056	0.039	1.47E-01	15%	1.14E-04
rs13062093	3:35667057	G/T	0.37	0.014	0.002	8.00E-09	23	7707	0.35	-0.028	0.037	4.49E-01	45%	8.73E-05
rs1799923	3:42306294	G/A	0.89	0.024	0.004	5.10E-12	21	7504	0.88	-0.061	0.058	2.94E-01	29%	1.16E-04
rs13076052	3:44456573	G/C	0.28	0.017	0.003	1.30E-08	23	7707	0.26	0.084	0.061	1.71E-01	17%	1.10E-04
rs6446187	3:49907111	A/C	0.51	0.028	0.003	1.22E-26	23	7707	0.48	0.013	0.036	7.17E-01	72%	3.86E-04
rs1916801	3:61187046	A/T	0.62	0.017	0.002	1.75E-14	23	7707	0.61	0.023	0.036	5.13E-01	51%	1.36E-04
rs1452075	3:62481063	T/C	0.73	0.016	0.003	1.47E-10	23	7707	0.73	-0.059	0.045	1.92E-01	19%	9.92E-05
rs925018	3:62713143	G/C	0.33	0.014	0.002	9.81E-10	23	7707	0.33	-0.027	0.038	4.72E-01	47%	8.98E-05
rs7647242	3:82642734	T/C	0.39	0.015	0.002	3.92E-10	23	7707	0.40	-0.030	0.035	3.92E-01	39%	1.00E-04
rs13068138	3:85809425	T/C	0.19	0.023	0.003	3.60E-17	23	7707	0.20	0.057	0.043	1.87E-01	19%	1.65E-04
rs1949197	3:86273850	A/G	0.40	0.014	0.002	3.04E-09	23	7707	0.41	-0.073	0.036	4.18E-02	4%	9.28E-05
rs1492014	3:94071481	C/T	0.43	0.015	0.002	2.84E-10	23	7707	0.40	-0.068	0.036	6.22E-02	6%	1.03E-04
rs1436348	3:104612668	G/A	0.57	0.013	0.002	6.31E-09	23	7707	0.58	-0.004	0.049	9.34E-01	93%	8.81E-05
rs1289736	3:107950892	T/C	0.54	0.014	0.002	1.43E-09	23	7707	0.56	0.040	0.036	2.74E-01	27%	9.59E-05
rs17619973	3:114417675	A/G	0.94	0.024	0.004	1.29E-08	23	7707	0.92	0.043	0.070	5.36E-01	54%	7.01E-05
rs7428670	3:131579810	C/G	0.27	0.020	0.003	3.09E-15	23	7707	0.26	0.021	0.040	5.99E-01	60%	1.61E-04
rs7621025	3:136272246	C/T	0.74	0.020	0.003	1.62E-15	23	7707	0.73	-0.029	0.040	4.60E-01	46%	1.54E-04
rs16851483	3:141275436	T/G	0.07	0.036	0.005	2.28E-15	23	7707	0.06	0.070	0.077	3.61E-01	36%	1.78E-04
rs355754	3:154024165	C/T	0.40	0.014	0.002	4.26E-10	23	7707	0.41	0.027	0.036	4.44E-01	44%	9.64E-05
rs247975	3:173107443	C/T	0.53	0.018	0.002	3.62E-15	23	7707	0.54	-0.003	0.042	9.47E-01	95%	1.65E-04
rs10513801	3:185822353	T/G	0.88	0.035	0.003	1.26E-27	23	7707	0.86	0.071	0.053	1.79E-01	18%	2.66E-04
rs4677812	3:194863794	C/A	0.71	0.014	0.003	9.38E-09	23	7707	0.72	-0.037	0.039	3.41E-01	34%	8.59E-05
rs994596	4:18459828	T/C	0.33	0.015	0.003	1.02E-09	23	7707	0.33	0.032	0.048	5.07E-01	51%	9.88E-05

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs34811474	4:25408838	G/A	0.78	0.032	0.003	5.19E-24	NA in Courage-PD							
rs73213484	4:28489339	A/T	0.86	0.025	0.004	2.28E-11	23	7707	0.83	-0.074	0.047	1.09E-01	11%	1.54E-04
rs337637	4:38604470	G/A	0.64	0.013	0.002	3.04E-08	23	7707	0.68	-0.027	0.037	4.72E-01	47%	7.18E-05
rs10938397	4:45182527	G/A	0.43	0.032	0.002	1.66E-45	23	7707	0.42	0.010	0.044	8.30E-01	83%	4.86E-04
rs2271046	4:52752812	T/A	0.31	0.014	0.003	2.38E-08	23	7707	0.25	0.009	0.040	8.26E-01	83%	7.97E-05
rs11727273	4:55509748	C/T	0.45	0.017	0.003	1.28E-10	23	7707	0.48	0.008	0.036	8.17E-01	82%	1.41E-04
rs11945861	4:65700865	G/A	0.75	0.015	0.003	3.13E-08	23	7707	0.78	-0.021	0.042	6.26E-01	63%	8.36E-05
rs10002111	4:67815504	A/G	0.22	0.017	0.003	9.26E-10	23	7707	0.24	-0.002	0.042	9.61E-01	96%	9.94E-05
rs4148155	4:89054667	A/G	0.89	0.020	0.004	6.20E-09	23	7707	0.90	0.040	0.060	5.13E-01	51%	8.29E-05
rs12645001	4:96018337	G/A	0.64	0.014	0.002	4.11E-09	23	7707	0.66	-0.010	0.037	7.83E-01	78%	9.11E-05
rs13107325	4:103188709	T/C	0.08	0.045	0.004	9.33E-25	23	7707	0.07	-0.155	0.070	2.71E-02	3%	3.10E-04
rs4834272	4:113313986	C/T	0.31	0.014	0.002	8.24E-10	23	7707	0.35	-0.055	0.037	1.36E-01	14%	8.80E-05
rs1403846	4:119101723	T/C	0.83	0.016	0.003	1.62E-08	23	7707	0.82	0.043	0.046	3.53E-01	35%	7.30E-05
rs4864201	4:130731284	T/C	0.35	0.013	0.002	6.34E-09	23	7707	0.35	0.009	0.046	8.43E-01	84%	7.77E-05
rs57800857	4:140863365	A/C	0.63	0.019	0.003	1.07E-11	23	7707	0.66	0.008	0.038	8.26E-01	83%	1.61E-04
rs35107973	4:143125948	T/C	0.12	0.023	0.004	7.66E-09	23	7707	0.10	0.015	0.058	8.02E-01	80%	1.13E-04
rs750090	4:152931436	T/C	0.62	0.016	0.002	7.40E-11	23	7707	0.66	-0.038	0.038	3.15E-01	31%	1.14E-04
rs13110266	4:162129844	G/A	0.60	0.014	0.002	1.55E-10	23	7707	0.62	0.004	0.047	9.26E-01	93%	9.70E-05
rs1491333	4:172186288	G/T	0.74	0.015	0.003	9.85E-09	23	7707	0.74	-0.050	0.041	2.24E-01	22%	8.39E-05
rs6890310	5:27193573	G/A	0.71	0.015	0.003	1.38E-09	23	7707	0.71	0.057	0.039	1.44E-01	14%	9.85E-05
rs782971	5:43124688	G/A	0.25	0.017	0.003	4.89E-12	23	7707	0.25	-0.066	0.041	1.10E-01	11%	1.10E-04
rs1812587	5:62991802	T/G	0.46	0.015	0.003	6.95E-09	23	7707	0.47	-0.029	0.036	4.24E-01	42%	1.15E-04
rs10471636	5:63979856	G/A	0.48	0.017	0.002	4.66E-13	23	7707	0.52	0.023	0.036	5.27E-01	53%	1.44E-04
rs2112347	5:75015242	T/G	0.63	0.031	0.002	2.13E-42	23	7707	0.64	0.026	0.036	4.72E-01	47%	4.45E-04
rs6870983	5:87697533	C/T	0.79	0.021	0.003	9.61E-16	23	7707	0.75	0.052	0.053	3.29E-01	33%	1.47E-04
rs141729694	5:87999371	T/C	0.07	0.039	0.005	2.53E-14	22	7584	0.09	-0.109	0.063	8.50E-02	8%	2.02E-04
rs159032	5:94206202	T/C	0.23	0.015	0.003	4.52E-08	23	7707	0.24	-0.073	0.042	8.31E-02	8%	7.89E-05
rs2161097	5:103945178	T/C	0.44	0.013	0.002	2.31E-08	23	7707	0.43	-0.009	0.036	8.02E-01	80%	8.21E-05
rs158186	5:107440856	G/A	0.83	0.029	0.003	3.23E-20	23	7707	0.83	0.000	0.047	9.94E-01	99%	2.28E-04
rs4895231	5:119388659	C/G	0.47	0.014	0.002	9.26E-10	23	7707	0.49	Excluded for MR				
rs13174863	5:139080745	G/A	0.15	0.027	0.003	4.53E-18	23	7707	0.17	-0.072	0.049	1.41E-01	14%	1.81E-04
rs4569924	5:153540025	T/C	0.44	0.016	0.002	7.44E-13	23	7707	0.43	0.020	0.035	5.72E-01	57%	1.23E-04
rs6556810	5:164585949	C/T	0.47	0.012	0.002	4.98E-08	23	7707	0.50	0.006	0.036	8.59E-01	86%	7.65E-05
rs2053682	5:170599327	A/C	0.68	0.018	0.003	1.89E-13	23	7707	0.66	-0.044	0.038	2.51E-01	25%	1.46E-04
rs2228213	6:12124855	G/A	0.66	0.015	0.002	9.21E-11	22	7478	0.64	0.031	0.037	4.00E-01	40%	9.79E-05
rs9367369	6:13189941	A/G	0.71	0.017	0.003	2.32E-09	22	7478	0.72	-0.022	0.040	5.81E-01	58%	1.23E-04
rs3806114	6:20482335	G/A	0.31	0.014	0.002	4.49E-09	22	7478	0.30	0.005	0.040	9.01E-01	90%	8.44E-05
rs2178899	6:31606756	A/T	0.89	0.025	0.003	7.16E-14	22	7478	0.88	-0.007	0.056	9.05E-01	91%	1.25E-04
rs11751591	6:33794215	G/A	0.85	0.019	0.003	1.16E-08	23	7707	0.86	0.058	0.051	2.53E-01	25%	8.85E-05
rs2814992	6:34617144	G/A	0.33	0.029	0.002	1.25E-35	23	7707	0.34	-0.015	0.037	6.82E-01	68%	3.66E-04
rs1579557	6:40371918	T/C	0.29	0.021	0.003	3.09E-17	23	7707	0.28	-0.022	0.040	5.86E-01	59%	1.84E-04

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs943005	6:50865820	T/C	0.15	0.040	0.003	1.99E-43	23	7707	0.17	0.030	0.055	5.88E-01	59%	3.98E-04
rs2465043	6:51180765	G/A	0.65	0.014	0.002	3.22E-09	23	7707	0.63	-0.037	0.037	3.16E-01	32%	9.19E-05
rs62412826	6:61881167	T/C	0.06	0.033	0.006	7.98E-09	NA in Courage-PD							
rs209416	6:83534729	A/T	0.32	0.017	0.002	8.71E-12	23	7707	0.29	-0.019	0.038	6.14E-01	61%	1.21E-04
rs13209872	6:97753223	G/C	0.65	0.014	0.002	6.07E-09	23	7707	0.66	-0.037	0.037	3.25E-01	33%	9.11E-05
rs12202969	6:98576223	G/A	0.52	0.015	0.002	1.93E-10	23	7707	0.51	0.045	0.035	2.01E-01	20%	1.05E-04
rs1417665	6:104816944	T/C	0.80	0.020	0.003	5.68E-12	23	7707	0.82	0.031	0.046	4.98E-01	50%	1.26E-04
rs768023	6:108876002	A/G	0.60	0.019	0.002	1.38E-16	23	7707	0.58	-0.012	0.036	7.32E-01	73%	1.64E-04
rs2357760	6:120213880	A/G	0.67	0.016	0.002	1.09E-11	23	7707	0.66	0.000	0.037	9.90E-01	99%	1.11E-04
rs11754747	6:141494602	T/C	0.27	0.015	0.003	1.27E-08	22	7623	0.26	-0.083	0.043	5.37E-02	5%	8.43E-05
rs198665	6:143154886	A/C	0.39	0.013	0.002	4.42E-09	23	7707	0.37	0.041	0.036	2.53E-01	25%	8.57E-05
rs2185027	6:153381622	C/A	0.30	0.015	0.002	1.11E-10	23	7707	0.29	-0.014	0.039	7.19E-01	72%	1.00E-04
rs12207125	6:154301575	A/G	0.78	0.018	0.003	7.67E-09	23	7707	0.78	0.030	0.043	4.80E-01	48%	1.15E-04
rs13213408	6:162998049	A/T	0.85	0.020	0.003	4.33E-09	23	7707	0.87	-0.089	0.051	7.86E-02	8%	1.01E-04
rs6973700	7:1856669	A/G	0.79	0.019	0.003	1.77E-09	23	7707	0.76	0.027	0.055	6.19E-01	62%	1.24E-04
rs836525	7:6465909	T/C	0.17	0.018	0.003	9.75E-09	23	7707	0.16	0.018	0.048	6.98E-01	70%	8.86E-05
rs4307239	7:24354300	G/A	0.46	0.014	0.002	1.31E-09	23	7707	0.47	-0.023	0.035	5.11E-01	51%	9.89E-05
rs11971098	7:26699061	G/A	0.09	0.024	0.004	6.49E-09	23	7707	0.09	-0.103	0.063	1.01E-01	10%	9.26E-05
rs10499694	7:50614173	A/G	0.49	0.014	0.002	3.99E-10	23	7707	0.47	0.033	0.035	3.53E-01	35%	9.25E-05
rs10237317	7:70045941	G/A	0.41	0.014	0.002	6.82E-10	23	7707	0.41	-0.006	0.046	8.89E-01	89%	9.23E-05
rs73124396	7:71579606	T/C	0.80	0.019	0.003	1.05E-08	23	7707	0.79	0.045	0.044	2.98E-01	30%	1.13E-04
rs2267812	7:74138121	C/A	0.19	0.017	0.003	1.74E-09	23	7707	0.21	-0.052	0.045	2.49E-01	25%	9.21E-05
rs1167800	7:75176196	A/G	0.55	0.020	0.002	3.66E-19	23	7707	0.56	0.030	0.036	4.10E-01	41%	1.98E-04
rs7805441	7:78121458	T/C	0.55	0.015	0.002	2.01E-10	23	7707	0.52	0.021	0.035	5.55E-01	55%	1.06E-04
rs2528531	7:93236510	C/A	0.35	0.015	0.002	1.35E-09	23	7707	0.35	0.012	0.051	8.13E-01	81%	9.56E-05
rs10271582	7:99121950	A/G	0.83	0.019	0.003	8.41E-09	23	7707	0.85	-0.041	0.049	4.05E-01	41%	1.06E-04
rs2299383	7:103418846	T/C	0.40	0.018	0.002	2.73E-16	23	7707	0.42	-0.025	0.036	4.76E-01	48%	1.58E-04
rs7788008	7:112972483	G/A	0.57	0.017	0.002	1.09E-13	23	7707	0.56	0.066	0.036	6.62E-02	7%	1.43E-04
rs2045293	7:114350102	T/C	0.42	0.019	0.002	4.06E-16	23	7707	0.38	-0.007	0.037	8.54E-01	85%	1.74E-04
rs2289705	7:121983843	G/A	0.20	0.015	0.003	1.47E-08	23	7707	0.23	0.005	0.042	9.12E-01	91%	7.30E-05
rs2968864	7:150622162	T/C	0.76	0.016	0.003	9.35E-10	23	7707	0.76	-0.039	0.041	3.39E-01	34%	9.79E-05
rs4240673	8:10787612	T/C	0.46	0.018	0.002	1.03E-15	23	7707	0.48	0.020	0.045	6.60E-01	66%	1.54E-04
rs2959592	8:17002725	T/C	0.81	0.017	0.003	6.26E-10	23	7707	0.79	-0.071	0.042	8.95E-02	9%	8.92E-05
rs1362910	8:30856464	A/G	0.41	0.013	0.002	3.03E-09	23	7707	0.42	0.060	0.046	1.96E-01	20%	8.70E-05
rs4320543	8:34422967	G/A	0.58	0.013	0.002	2.95E-08	23	7707	0.62	0.029	0.037	4.34E-01	43%	8.10E-05
rs12681792	8:62054463	A/C	0.20	0.018	0.003	2.61E-10	23	7707	0.18	-0.028	0.047	5.51E-01	55%	1.09E-04
rs7827848	8:64790774	A/T	0.51	0.015	0.002	1.88E-11	23	7707	0.54	Excluded for MR				
rs1808629	8:73435964	G/A	0.33	0.023	0.003	5.76E-16	23	7707	0.33	-0.004	0.038	9.18E-01	92%	2.24E-04
rs17405819	8:76806584	T/C	0.68	0.022	0.002	7.81E-20	23	7707	0.71	-0.057	0.039	1.40E-01	14%	2.06E-04
rs12680842	8:95582606	A/G	0.68	0.013	0.002	3.36E-08	23	7707	0.66	0.011	0.037	7.62E-01	76%	7.30E-05
rs2721965	8:116662038	A/C	0.67	0.019	0.002	2.10E-14	23	7707	0.71	-0.047	0.039	2.29E-01	23%	1.53E-04

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs10099330	8:143383694	G/A	0.46	0.013	0.002	9.94E-09	23	7707	0.43	0.013	0.035	7.02E-01	70%	8.53E-05
rs10124645	9:11321119	A/G	0.59	0.014	0.002	4.98E-09	23	7707	0.60	-0.004	0.037	9.11E-01	91%	8.93E-05
rs10756714	9:15885041	A/G	0.55	0.021	0.002	1.46E-19	23	7707	0.57	-0.042	0.036	2.47E-01	25%	2.14E-04
rs10962550	9:16720329	C/G	0.17	0.019	0.003	1.70E-10	23	7707	0.19	-0.053	0.045	2.38E-01	24%	1.06E-04
rs16912921	9:28413461	A/C	0.31	0.025	0.002	1.56E-26	23	7707	0.27	0.065	0.040	1.02E-01	10%	2.67E-04
rs973345	9:29713169	T/C	0.61	0.014	0.002	1.09E-09	23	7707	0.59	-0.032	0.036	3.74E-01	37%	9.59E-05
rs563132	9:37245476	A/T	0.61	0.018	0.002	1.96E-14	23	7707	0.62	-0.059	0.047	2.12E-01	21%	1.55E-04
rs10116186	9:80532374	G/A	0.54	0.015	0.003	4.10E-08	23	7707	0.53	-0.008	0.036	8.27E-01	83%	1.04E-04
rs10797115	9:92191256	T/C	0.53	0.016	0.002	4.07E-12	23	7707	0.54	-0.071	0.046	1.23E-01	12%	1.27E-04
rs10992867	9:96461013	A/G	0.27	0.019	0.003	8.89E-13	23	7707	0.27	-0.039	0.039	3.21E-01	32%	1.35E-04
rs10118701	9:103061366	G/A	0.33	0.018	0.002	2.20E-13	23	7707	0.34	0.038	0.037	2.97E-01	30%	1.37E-04
rs7024334	9:109072075	T/G	0.23	0.016	0.003	1.63E-09	23	7707	0.27	-0.051	0.043	2.29E-01	23%	8.84E-05
rs1928295	9:120378483	T/C	0.57	0.016	0.002	2.85E-13	23	7707	0.54	0.060	0.035	8.43E-02	8%	1.25E-04
rs3829849	9:129390800	T/C	0.35	0.014	0.002	1.93E-09	23	7707	0.37	0.005	0.037	8.91E-01	89%	8.42E-05
rs10733682	9:129460914	A/G	0.46	0.016	0.002	1.85E-12	23	7707	0.50	-0.029	0.048	5.48E-01	55%	1.24E-04
rs2267958	9:131015279	G/A	0.49	0.016	0.002	1.88E-11	3	766	Excluded for MR					
rs1009473	9:138777312	C/T	0.47	0.013	0.002	3.36E-08	23	7707	0.40	-0.027	0.037	4.70E-01	47%	8.04E-05
rs7084454	10:21821274	A/G	0.31	0.023	0.003	7.43E-20	21	7063	0.33	0.041	0.039	2.94E-01	29%	2.15E-04
rs34930419	10:33987329	C/T	0.03	0.046	0.008	1.37E-09	20	6960	0.03	0.000	0.111	9.98E-01	100%	1.29E-04
rs10823893	10:53677313	A/G	0.41	0.018	0.003	5.22E-11	22	7539	0.39	-0.014	0.045	7.49E-01	75%	1.48E-04
rs10761785	10:65318766	G/T	0.49	0.017	0.002	4.17E-15	23	7707	0.50	-0.048	0.048	3.18E-01	32%	1.48E-04
rs10824347	10:77645229	A/T	0.77	0.018	0.003	5.47E-11	23	7707	0.74	-0.014	0.040	7.36E-01	74%	1.09E-04
rs7899106	10:87410904	G/A	0.05	0.038	0.005	7.65E-14	22	7231	0.05	-0.165	0.088	5.99E-02	6%	1.35E-04
rs563296	10:99772404	A/G	0.56	0.018	0.002	8.85E-14	22	7231	0.53	0.015	0.038	6.96E-01	70%	1.51E-04
rs3977755	10:104420210	C/T	0.71	0.014	0.003	8.50E-09	23	7707	0.74	-0.062	0.039	1.16E-01	12%	8.37E-05
rs6585198	10:114762237	G/A	0.56	0.015	0.002	1.22E-12	23	7707	0.55	-0.097	0.036	7.36E-03	1%	1.17E-04
rs1681743	10:118565501	C/T	0.60	0.013	0.002	3.70E-08	23	7707	0.62	-0.022	0.036	5.36E-01	54%	8.25E-05
rs1561589	10:126695673	A/G	0.36	0.016	0.002	4.24E-12	23	7707	0.37	0.001	0.043	9.73E-01	97%	1.15E-04
rs4880341	10:133992689	C/T	0.43	0.014	0.002	4.53E-10	22	7584	0.47	-0.030	0.036	4.01E-01	40%	1.00E-04
rs7395632	11:958789	C/T	0.64	0.013	0.002	3.87E-08	23	7707	0.62	0.040	0.037	2.81E-01	28%	7.76E-05
rs4929923	11:8639200	C/T	0.66	0.022	0.002	2.51E-22	23	7707	0.60	0.004	0.036	9.22E-01	92%	2.18E-04
rs11022762	11:13335926	C/T	0.63	0.015	0.002	5.56E-11	23	7707	0.62	0.000	0.036	9.95E-01	100%	1.10E-04
rs6265	11:27679916	C/T	0.82	0.037	0.003	7.95E-40	23	7707	0.79	0.076	0.044	8.29E-02	8%	4.05E-04
rs2862961	11:43656535	G/A	0.30	0.024	0.003	5.30E-22	23	7707	0.32	0.009	0.039	8.24E-01	82%	2.40E-04
rs10742752	11:45438374	C/T	0.62	0.013	0.002	3.98E-09	23	7707	0.62	-0.005	0.036	8.92E-01	89%	8.17E-05
rs7124681	11:47529947	A/C	0.42	0.025	0.002	9.27E-29	23	7707	0.41	-0.033	0.035	3.51E-01	35%	2.97E-04
rs893006	11:64365796	A/C	0.72	0.017	0.002	4.05E-13	23	7707	0.70	-0.044	0.039	2.52E-01	25%	1.20E-04
rs625652	11:65641931	T/A	0.36	0.020	0.003	9.05E-13	23	7707	0.34	0.071	0.037	5.74E-02	6%	1.75E-04
rs7107409	11:76492195	C/T	0.78	0.018	0.003	2.05E-08	23	7707	0.76	-0.061	0.041	1.34E-01	13%	1.09E-04
rs2605603	11:93221105	G/A	0.52	0.013	0.002	1.40E-09	23	7707	0.51	-0.071	0.035	4.35E-02	4%	8.70E-05
rs7105462	11:112912048	A/G	0.58	0.014	0.002	4.40E-10	23	7707	0.57	0.008	0.036	8.19E-01	82%	1.01E-04

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs1048932	11:115044850	C/A	0.56	0.018	0.002	2.52E-16	23	7707	0.60	-0.010	0.036	7.87E-01	79%	1.63E-04
rs1003081	11:118913993	T/C	0.43	0.014	0.002	6.27E-11	21	7186	0.42	0.028	0.039	4.68E-01	47%	1.02E-04
rs4459316	11:130756176	C/T	0.45	0.015	0.002	2.33E-11	23	7707	0.44	0.014	0.035	7.00E-01	70%	1.17E-04
rs4936175	11:132641959	C/T	0.44	0.016	0.002	6.69E-12	23	7707	0.42	0.004	0.036	9.09E-01	91%	1.23E-04
rs329651	11:133767622	T/G	0.81	0.018	0.003	1.96E-10	23	7707	0.78	-0.078	0.044	7.77E-02	8%	1.03E-04
rs12364470	11:134601012	G/T	0.15	0.020	0.003	2.54E-11	12	3456	Excluded for MR					
rs11611246	12:939480	T/G	0.20	0.021	0.003	1.27E-14	23	7707	0.19	-0.017	0.045	7.07E-01	71%	1.43E-04
rs7976757	12:19207948	C/T	0.82	0.019	0.003	2.94E-10	23	7707	0.79	0.150	0.046	1.16E-03	0%	1.07E-04
rs16926318	12:23678745	G/A	0.08	0.023	0.004	4.23E-08	23	7707	0.10	-0.068	0.061	2.63E-01	26%	7.52E-05
rs16926778	12:24002125	C/G	0.08	0.026	0.004	1.41E-09	23	7707	0.09	0.040	0.063	5.33E-01	53%	9.62E-05
rs7138803	12:50247468	A/G	0.39	0.029	0.002	9.70E-38	23	7707	0.36	0.052	0.036	1.47E-01	15%	4.02E-04
rs2271189	12:56494991	G/A	0.60	0.015	0.002	6.35E-10	23	7707	0.63	0.033	0.037	3.67E-01	37%	1.02E-04
rs11173522	12:60953472	A/C	0.23	0.017	0.003	9.01E-10	23	7707	0.20	0.068	0.043	1.15E-01	12%	1.02E-04
rs645026	12:69757931	G/A	0.26	0.016	0.003	4.79E-10	23	7707	0.29	0.034	0.038	3.71E-01	37%	9.76E-05
rs10746306	12:84477374	T/G	0.77	0.018	0.003	8.74E-09	23	7707	0.75	0.027	0.041	5.16E-01	52%	1.14E-04
rs2279574	12:89745477	C/A	0.45	0.017	0.002	1.96E-12	23	7707	0.48	0.052	0.048	2.81E-01	28%	1.35E-04
rs2712643	12:99638276	C/A	0.76	0.015	0.003	1.47E-09	23	7706	0.74	0.055	0.044	2.07E-01	21%	8.63E-05
rs17033633	12:103656343	C/T	0.83	0.021	0.003	7.26E-12	23	7707	0.82	0.019	0.046	6.75E-01	67%	1.23E-04
rs6606686	12:110903380	G/C	0.30	0.018	0.002	2.50E-14	23	7707	0.31	0.000	0.039	9.96E-01	100%	1.34E-04
rs17508240	12:117577358	A/G	0.21	0.019	0.003	2.83E-09	23	7707	0.19	-0.037	0.047	4.32E-01	43%	1.23E-04
rs6489156	12:123100397	T/C	0.73	0.022	0.003	9.97E-18	23	7707	0.72	0.067	0.051	1.88E-01	19%	1.93E-04
rs7133378	12:124409502	A/G	0.33	0.016	0.002	1.85E-11	23	7707	0.35	-0.022	0.037	5.46E-01	55%	1.11E-04
rs9579775	13:20616557	C/A	0.13	0.025	0.004	3.66E-10	1	434	Excluded for MR					
rs12872889	13:28674628	C/T	0.24	0.021	0.003	1.52E-11	22	7566	0.23	0.027	0.044	5.37E-01	54%	1.59E-04
rs9595630	13:33065443	T/G	0.66	0.015	0.002	2.04E-10	22	7566	0.63	0.020	0.036	5.90E-01	59%	9.50E-05
rs12429545	13:54102206	A/G	0.12	0.029	0.003	1.09E-18	23	7707	0.12	-0.050	0.074	5.01E-01	50%	1.79E-04
rs6561937	13:58257667	T/A	0.23	0.020	0.003	5.95E-13	22	7566	0.23	-0.060	0.044	1.74E-01	17%	1.39E-04
rs4055791	13:59266053	C/T	0.59	0.017	0.003	1.77E-10	22	7566	0.60	0.018	0.036	6.16E-01	62%	1.40E-04
rs9571687	13:67472713	C/A	0.66	0.015	0.002	3.24E-09	23	7707	0.67	-0.005	0.038	8.97E-01	90%	9.46E-05
rs1441264	13:79580919	A/G	0.58	0.017	0.002	5.19E-14	23	7707	0.61	-0.017	0.048	7.30E-01	73%	1.42E-04
rs9531786	13:85983968	G/C	0.63	0.014	0.002	8.39E-09	23	7707	0.62	0.042	0.037	2.49E-01	25%	8.89E-05
rs77432547	13:86494817	G/A	0.28	0.018	0.003	2.28E-09	23	7707	0.26	-0.024	0.050	6.30E-01	63%	1.23E-04
rs1927790	13:96922191	C/T	0.39	0.014	0.002	1.27E-09	23	7707	0.43	-0.002	0.036	9.67E-01	97%	8.68E-05
rs4586287	13:99245334	C/G	0.67	0.014	0.003	2.95E-08	20	7030	0.64	-0.067	0.062	2.82E-01	28%	8.36E-05
rs7335249	13:109962579	T/C	0.56	0.014	0.002	4.91E-09	23	7707	0.60	-0.023	0.036	5.16E-01	52%	8.99E-05
rs2479958	13:111984244	A/G	0.49	0.014	0.002	1.38E-08	23	7707	0.48	0.030	0.036	4.05E-01	40%	9.11E-05
rs2754079	14:25886140	G/A	0.43	0.016	0.002	2.31E-11	23	7707	0.44	0.017	0.036	6.37E-01	64%	1.19E-04
rs1569979	14:29681294	A/G	0.77	0.023	0.003	1.57E-17	23	7707	0.76	0.054	0.042	2.01E-01	20%	1.85E-04
rs17522122	14:33302882	T/G	0.47	0.017	0.002	6.46E-14	23	7707	0.48	-0.002	0.035	9.62E-01	96%	1.39E-04
rs35020117	14:73341655	T/G	0.55	0.017	0.003	1.23E-09	18	5471	0.55	-0.006	0.045	8.93E-01	89%	1.35E-04
rs7141420	14:79899454	T/C	0.55	0.021	0.002	7.84E-22	23	7707	0.53	0.022	0.039	5.86E-01	59%	2.18E-04

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs1285997	14:91513029	G/C	0.71	0.015	0.003	3.18E-09	23	7707	0.69	-0.018	0.039	6.35E-01	64%	9.24E-05
rs942066	14:94031914	G/A	0.63	0.020	0.003	1.04E-13	23	7707	0.62	0.042	0.037	2.60E-01	26%	1.91E-04
rs3803286	14:103246470	A/G	0.34	0.017	0.002	8.29E-13	23	7707	0.34	0.054	0.038	1.54E-01	15%	1.33E-04
rs709400	14:104149475	A/G	0.62	0.018	0.002	4.41E-16	23	7707	0.62	0.010	0.036	7.77E-01	78%	1.59E-04
rs12101625	15:26972431	C/G	0.61	0.014	0.002	5.54E-09	23	7707	0.65	-0.010	0.038	7.92E-01	79%	9.03E-05
rs8038522	15:46585105	G/T	0.59	0.014	0.002	1.27E-09	23	7705	0.58	-0.079	0.048	1.02E-01	10%	9.50E-05
rs6493498	15:51754451	T/C	0.45	0.016	0.002	1.53E-13	23	7707	0.47	-0.016	0.036	6.48E-01	65%	1.31E-04
rs8024806	15:53473990	T/C	0.94	0.027	0.005	9.76E-09	23	7707	0.94	0.039	0.075	5.99E-01	60%	8.79E-05
rs8033510	15:61445514	T/C	0.36	0.014	0.002	1.13E-08	23	7707	0.40	-0.008	0.048	8.65E-01	86%	8.69E-05
rs4776982	15:68114974	A/G	0.77	0.031	0.003	4.25E-33	23	7707	0.77	0.016	0.042	7.07E-01	71%	3.43E-04
rs12914489	15:74187937	A/G	0.08	0.023	0.004	1.64E-10	23	7707	0.08	0.009	0.080	9.14E-01	91%	7.66E-05
rs62007782	15:78029797	G/A	0.74	0.018	0.003	1.94E-09	23	7707	0.75	-0.089	0.040	2.68E-02	3%	1.23E-04
rs12593036	15:81058652	A/G	0.69	0.015	0.003	6.65E-10	23	7707	0.71	-0.044	0.038	2.39E-01	24%	1.01E-04
rs7498044	15:92573639	G/A	0.79	0.018	0.003	2.73E-08	23	7707	0.82	0.023	0.047	6.18E-01	62%	1.09E-04
rs11073383	15:95274349	G/A	0.52	0.016	0.002	3.26E-12	23	7707	0.51	0.047	0.037	1.96E-01	20%	1.26E-04
rs57221746	15:99230035	G/A	0.78	0.018	0.003	2.08E-08	23	7707	0.79	-0.034	0.044	4.35E-01	43%	1.08E-04
rs214249	16:348687	T/G	0.61	0.017	0.002	1.37E-12	22	7584	0.63	-0.091	0.039	2.12E-02	2%	1.33E-04
rs12448257	16:3599655	A/G	0.22	0.015	0.003	3.13E-08	23	7707	0.21	-0.028	0.044	5.31E-01	53%	7.69E-05
rs879620	16:4015729	T/C	0.60	0.025	0.002	5.45E-26	23	7706	0.60	-0.037	0.035	2.98E-01	30%	2.94E-04
rs9926784	16:19941968	T/C	0.80	0.025	0.003	6.01E-20	23	7707	0.83	0.043	0.059	4.67E-01	47%	2.04E-04
rs17767765	16:24539793	C/T	0.49	0.013	0.002	2.60E-08	23	7707	0.48	0.037	0.035	3.00E-01	30%	8.06E-05
rs7498665	16:28883241	G/A	0.38	0.026	0.002	1.94E-32	23	7707	0.35	-0.057	0.037	1.24E-01	12%	3.29E-04
rs2289292	16:30097630	C/T	0.67	0.019	0.003	1.13E-14	23	7707	0.66	0.068	0.039	7.96E-02	8%	1.60E-04
rs4889606	16:31011183	A/G	0.63	0.027	0.002	1.25E-32	23	7707	0.59	-0.092	0.036	1.12E-02	1%	3.35E-04
rs9937053	16:53799507	A/G	0.44	0.068	0.002	1.00E-200	23	7707	0.42	0.016	0.035	6.49E-01	65%	2.24E-03
rs4783718	16:69547741	T/C	0.42	0.020	0.002	1.77E-19	9	2428	Excluded for MR					
rs811054	16:72251132	T/C	0.53	0.016	0.002	3.18E-13	23	7707	0.55	0.002	0.036	9.50E-01	95%	1.31E-04
rs2012502	16:81728081	A/C	0.38	0.015	0.002	2.97E-11	23	7707	0.36	-0.016	0.040	6.94E-01	69%	1.11E-04
rs4790292	17:1824305	C/A	0.85	0.026	0.003	1.65E-15	23	7707	0.86	-0.058	0.053	2.77E-01	28%	1.74E-04
rs3826408	17:7101292	T/C	0.42	0.012	0.002	4.48E-08	23	7707	0.49	0.028	0.047	5.52E-01	55%	7.12E-05
rs1075901	17:15943910	C/T	0.55	0.014	0.002	4.36E-11	23	7707	0.56	-0.038	0.036	2.93E-01	29%	1.03E-04
rs4986044	17:21261560	C/T	0.55	0.017	0.002	2.20E-15	23	7707	0.52	0.001	0.037	9.77E-01	98%	1.48E-04
rs12150665	17:34914787	T/C	0.59	0.017	0.002	5.92E-14	23	7707	0.58	0.041	0.036	2.53E-01	25%	1.35E-04
rs56161855	17:46288649	T/A	0.13	0.026	0.004	1.48E-11	23	7707	0.14	0.035	0.050	4.85E-01	49%	1.57E-04
rs9906944	17:47091420	C/T	0.65	0.019	0.002	7.25E-15	23	7707	0.68	-0.011	0.039	7.74E-01	77%	1.65E-04
rs7211966	17:54374611	C/T	0.97	0.047	0.008	4.89E-09	20	6994	0.98	-0.010	0.149	9.45E-01	94%	1.23E-04
rs8075273	17:61728881	C/A	0.71	0.016	0.002	5.56E-11	23	7707	0.74	0.023	0.041	5.66E-01	57%	1.05E-04
rs2619976	17:71754545	T/C	0.40	0.015	0.002	6.17E-10	23	7707	0.42	-0.004	0.037	9.07E-01	91%	1.02E-04
rs12949279	17:78558411	T/C	0.56	0.018	0.002	6.09E-16	23	7707	0.58	-0.024	0.035	4.97E-01	50%	1.58E-04
rs4969387	17:79081724	G/C	0.26	0.015	0.003	6.90E-09	19	6802	0.27	-0.015	0.045	7.39E-01	74%	9.16E-05
rs9955276	18:1839339	T/C	0.14	0.022	0.003	8.02E-12	23	7707	0.14	0.052	0.049	2.90E-01	29%	1.22E-04

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs1808579	18:21104888	C/T	0.52	0.020	0.002	9.44E-20	23	7707	0.57	-0.037	0.036	2.96E-01	30%	1.96E-04
rs16975921	18:39914870	T/A	0.31	0.016	0.003	3.87E-11	23	7707	0.33	0.032	0.037	3.86E-01	39%	1.13E-04
rs1518159	18:40760146	C/T	0.75	0.019	0.003	6.66E-13	23	7707	0.76	-0.110	0.056	4.73E-02	5%	1.34E-04
rs7239114	18:45921214	A/G	0.54	0.016	0.002	3.90E-12	12	3396	Excluded for MR					
rs6567160	18:57829135	C/T	0.25	0.057	0.003	8.74E-108	23	7707	0.23	0.031	0.042	4.66E-01	47%	1.20E-03
rs17066856	18:58049656	T/C	0.89	0.040	0.004	1.39E-27	23	7707	0.91	-0.063	0.061	3.02E-01	30%	3.09E-04
rs12981256	19:1865901	A/G	0.53	0.018	0.002	3.93E-15	23	7707	0.52	-0.003	0.045	9.41E-01	94%	1.65E-04
rs895330	19:4060707	C/G	0.81	0.018	0.003	6.65E-10	23	7707	0.80	0.000	0.046	9.93E-01	99%	1.02E-04
rs273504	19:18215247	G/A	0.42	0.015	0.002	1.27E-10	23	7707	0.45	0.003	0.035	9.21E-01	92%	1.11E-04
rs17724992	19:18454825	A/G	0.72	0.017	0.003	6.65E-12	23	7707	0.74	-0.002	0.040	9.53E-01	95%	1.17E-04
rs11880870	19:18830704	A/G	0.52	0.020	0.002	3.31E-18	23	7707	0.53	0.009	0.047	8.45E-01	85%	1.94E-04
rs17751061	19:19413092	C/T	0.84	0.018	0.003	1.29E-08	23	7707	0.84	-0.112	0.047	1.68E-02	2%	8.78E-05
rs12462975	19:30272202	A/G	0.32	0.020	0.003	2.63E-16	23	7707	0.31	0.003	0.038	9.34E-01	93%	1.81E-04
rs11667280	19:30705747	C/G	0.80	0.016	0.003	3.14E-08	23	7707	0.79	-0.036	0.044	4.09E-01	41%	8.07E-05
rs7250833	19:33937277	T/C	0.31	0.015	0.002	7.22E-10	23	7707	0.30	-0.029	0.038	4.47E-01	45%	9.51E-05
rs185350	19:34306816	T/C	0.49	0.013	0.002	7.14E-09	23	7707	0.51	-0.042	0.045	3.52E-01	35%	8.19E-05
rs429358	19:45411941	T/C	0.85	0.028	0.004	3.17E-14	23	7707	0.88	-0.019	0.053	7.19E-01	72%	1.99E-04
rs11672660	19:46180184	C/T	0.81	0.032	0.003	5.93E-31	23	7707	0.80	-0.018	0.044	6.82E-01	68%	3.13E-04
rs9304665	19:47602577	A/T	0.74	0.020	0.003	1.84E-14	3	949	Excluded for MR					
rs1884389	20:1410582	C/T	0.56	0.014	0.002	1.20E-09	23	7707	0.59	0.010	0.037	7.85E-01	78%	9.66E-05
rs1884897	20:6612832	G/A	0.63	0.017	0.002	9.06E-14	23	7707	0.65	-0.025	0.036	4.80E-01	48%	1.34E-04
rs1409818	20:21381121	T/C	0.11	0.025	0.004	1.58E-11	23	7707	0.11	0.025	0.056	6.61E-01	66%	1.23E-04
rs117495226 ^a	20:25565515	G/C	0.95	0.037	0.006	6.20E-09	19	6946	0.97	-0.113	0.122	3.52E-01	35%	1.31E-04
rs6142096	20:32686658	A/G	0.52	0.013	0.002	4.17E-09	23	7707	0.54	0.034	0.036	3.43E-01	34%	8.96E-05
rs16989232	20:39291784	A/G	0.39	0.013	0.002	1.52E-08	23	7707	0.36	-0.006	0.038	8.80E-01	88%	7.76E-05
rs17806224	20:51065854	G/A	0.82	0.029	0.003	3.52E-22	23	7707	0.82	0.072	0.064	2.56E-01	26%	2.48E-04
rs6010784	20:61540319	T/C	0.51	0.013	0.002	1.08E-08	23	7707	0.48	-0.029	0.047	5.36E-01	54%	7.94E-05
rs2836754	21:40291740	C/T	0.63	0.015	0.002	3.73E-11	23	7707	0.63	0.023	0.036	5.24E-01	52%	1.03E-04
rs915814	21:46493003	G/A	0.75	0.018	0.003	5.88E-09	23	7707	0.77	-0.071	0.042	9.36E-02	9%	1.16E-04
rs427943	21:46570896	C/A	0.57	0.018	0.002	1.37E-14	23	7707	0.54	-0.017	0.049	7.22E-01	72%	1.53E-04
rs28489620	22:41804716	G/A	0.72	0.018	0.003	6.90E-10	23	7707	0.72	-0.043	0.040	2.87E-01	29%	1.33E-04
rs13053342	22:48871624	A/G	0.40	0.015	0.002	1.32E-10	23	7707	0.38	0.053	0.037	1.53E-01	15%	1.12E-04
MALES BMI (per 1SD=4.8kg/m ²)														
rs2803316	1:1865298	G/A	0.54	0.015	0.003	4.03E-09	23	8812	0.53	0.009	0.039	8.15E-01	14%	1.10E-04
rs3762444	1:2427712	C/T	0.54	0.019	0.003	1.47E-14	11	4888	Excluded for MR					
rs11121210	1:8708529	C/T	0.66	0.015	0.003	7.86E-09	23	8812	0.56	-0.047	0.036	1.88E-01	3%	1.00E-04
rs11581010	1:11212458	G/A	0.24	0.018	0.003	1.01E-09	23	8812	0.25	-0.023	0.061	6.99E-01	44%	1.15E-04
rs2235549	1:23391775	G/T	0.16	0.021	0.003	8.27E-11	23	8812	0.19	0.043	0.047	3.60E-01	9%	1.22E-04
rs2271928	1:32127953	G/A	0.62	0.014	0.002	9.92E-09	23	8812	0.61	-0.004	0.035	9.03E-01	0%	8.67E-05

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs12061406	1:40073479	C/T	0.92	0.027	0.005	1.70E-09	23	8812	0.92	0.024	0.064	7.13E-01	0%	1.07E-04
rs1768808	1:46503217	T/C	0.62	0.014	0.003	3.54E-08	16	6342	Excluded for MR					
rs977747	1:47684677	T/G	0.44	0.016	0.002	1.35E-11	23	8812	0.38	0.047	0.035	1.85E-01	2%	1.24E-04
rs7531656	1:49828663	A/G	0.33	0.020	0.003	2.32E-15	23	8812	0.31	0.025	0.044	5.76E-01	21%	1.73E-04
rs2481665	1:62594677	T/C	0.58	0.019	0.002	2.03E-15	23	8812	0.56	0.044	0.034	1.90E-01	0%	1.70E-04
rs11208779	1:66417145	C/G	0.52	0.019	0.003	1.53E-11	23	8812	0.51	Excluded for MR				
rs1993709	1:72838529	G/A	0.82	0.041	0.003	1.49E-42	21	7241	0.81	-0.071	0.068	2.91E-01	31%	4.99E-04
rs12566985	1:75002193	G/A	0.44	0.018	0.002	1.09E-14	23	8812	0.45	-0.009	0.035	8.08E-01	5%	1.62E-04
rs12049202	1:77967523	T/C	0.19	0.023	0.003	5.52E-13	23	8812	0.18	0.022	0.044	6.14E-01	0%	1.55E-04
rs12034762	1:96290845	T/C	0.39	0.017	0.003	4.80E-11	23	8812	0.38	-0.044	0.035	2.09E-01	0%	1.35E-04
rs11165643	1:96924097	T/C	0.58	0.020	0.002	1.69E-17	23	8812	0.56	-0.061	0.035	7.90E-02	0%	1.97E-04
rs17024393	1:110154688	C/T	0.03	0.071	0.007	1.70E-23	20	8349	0.03	-0.048	0.108	6.56E-01	0%	3.13E-04
rs61813324	1:156049877	T/C	0.13	0.028	0.004	1.29E-10	2	1108	Excluded for MR					
rs76194251	1:173931908	G/C	0.98	0.060	0.010	4.04E-10	19	8305	0.97	0.032	0.111	7.71E-01	25%	1.63E-04
rs543874	1:177889480	G/A	0.23	0.036	0.003	3.70E-35	23	8812	0.18	-0.050	0.047	2.87E-01	6%	4.52E-04
rs10920678	1:190239907	A/G	0.42	0.013	0.002	1.90E-08	23	8812	0.42	0.014	0.035	6.88E-01	0%	8.63E-05
rs2172935	1:201826340	T/C	0.32	0.027	0.003	3.56E-24	23	8812	0.29	0.002	0.037	9.66E-01	22%	3.11E-04
rs12217091	1:204813050	T/C	0.09	0.027	0.005	4.44E-08	23	8812	0.09	0.013	0.060	8.28E-01	0%	1.22E-04
rs823094	1:205689807	T/G	0.55	0.015	0.002	3.77E-10	23	8812	0.57	0.003	0.035	9.38E-01	0%	1.08E-04
rs4653942	1:228505204	G/A	0.79	0.016	0.003	4.41E-08	23	8812	0.79	0.087	0.042	3.58E-02	0%	8.46E-05
rs2125231	1:243762299	T/C	0.32	0.017	0.003	5.50E-11	23	8812	0.34	0.027	0.038	4.74E-01	14%	1.28E-04
rs77165542	2:430975	C/T	0.97	0.084	0.008	1.13E-25	3	750	Excluded for MR					
rs12714415	2:651430	T/C	0.85	0.060	0.003	1.09E-80	23	8812	0.83	-0.047	0.046	3.16E-01	10%	9.33E-04
rs2693826	2:6160943	G/A	0.57	0.016	0.003	4.96E-11	23	8812	0.54	0.021	0.034	5.45E-01	0%	1.32E-04
rs10182181	2:25150296	G/A	0.50	0.027	0.002	5.55E-32	23	8812	0.45	0.006	0.035	8.67E-01	15%	3.73E-04
rs1260326	2:27730940	C/T	0.61	0.018	0.002	2.05E-14	23	8812	0.55	0.075	0.035	3.52E-02	9%	1.60E-04
rs2888172	2:35439812	G/A	0.45	0.014	0.003	1.42E-08	23	8812	0.44	-0.016	0.034	6.41E-01	21%	9.85E-05
rs10185199	2:40282202	G/A	0.71	0.016	0.003	3.79E-08	22	8588	0.70	0.055	0.040	1.71E-01	17%	1.03E-04
rs7561278	2:48954905	T/C	0.76	0.018	0.003	1.06E-08	23	8812	0.78	0.030	0.063	6.33E-01	41%	1.11E-04
rs12986742	2:58975143	C/T	0.48	0.020	0.003	3.22E-15	23	8812	0.47	-0.023	0.034	4.99E-01	16%	1.94E-04
rs887912	2:59302877	T/C	0.30	0.023	0.003	2.75E-19	23	8812	0.29	0.026	0.038	4.92E-01	0%	2.20E-04
rs11685481	2:67736749	T/C	0.85	0.020	0.003	8.99E-09	23	8812	0.84	-0.051	0.047	2.81E-01	14%	9.90E-05
rs4410328	2:69600683	C/T	0.59	0.020	0.003	7.75E-12	23	8812	0.58	-0.073	0.035	3.86E-02	0%	1.92E-04
rs10209325	2:86806356	C/T	0.38	0.018	0.003	1.49E-09	23	8812	0.38	-0.025	0.036	4.91E-01	22%	1.49E-04
rs1437377	2:100744924	G/T	0.15	0.024	0.004	1.47E-11	23	8812	0.13	0.038	0.051	4.56E-01	0%	1.49E-04
rs10197031	2:105454590	C/T	0.27	0.017	0.003	7.69E-10	23	8812	0.26	0.006	0.039	8.79E-01	8%	1.11E-04
rs13405033	2:113994595	T/C	0.15	0.026	0.004	4.37E-11	23	8812	0.14	0.042	0.051	4.08E-01	0%	1.78E-04
rs11687120	2:119579558	A/G	0.45	0.014	0.003	4.74E-08	23	8812	0.43	-0.028	0.035	4.17E-01	5%	9.28E-05
rs961360	2:136393658	A/G	0.89	0.021	0.003	3.75E-10	23	8812	0.76	0.110	0.043	9.73E-03	0%	8.90E-05
rs453520	2:147907202	C/T	0.43	0.016	0.003	1.19E-10	23	8812	0.42	0.007	0.035	8.53E-01	0%	1.27E-04
rs34234296	2:175166636	G/A	0.61	0.018	0.003	2.86E-09	16	6342	Excluded for MR					

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs2216931	2:181599070	A/C	0.66	0.018	0.003	1.40E-11	23	8812	0.66	0.005	0.036	8.87E-01	0%	1.44E-04
rs10497807	2:198585087	G/C	0.50	0.015	0.002	4.95E-10	23	8812	0.50	Excluded for MR				
rs7569376	2:205385322	T/C	0.21	0.020	0.003	1.33E-10	23	8812	0.24	0.047	0.042	2.64E-01	0%	1.25E-04
rs17203016	2:208255518	G/A	0.20	0.017	0.003	9.91E-09	22	8558	0.17	0.074	0.046	1.12E-01	2%	9.18E-05
rs7599312	2:213413231	G/A	0.73	0.022	0.003	1.51E-16	23	8811	0.74	0.014	0.038	7.09E-01	0%	1.89E-04
rs1541777	2:219587291	G/A	0.45	0.016	0.002	1.82E-11	23	8812	0.46	0.022	0.035	5.41E-01	0%	1.20E-04
rs7600417	2:220169492	A/G	0.85	0.021	0.004	2.88E-09	23	8812	0.84	0.077	0.058	1.88E-01	24%	1.09E-04
rs11692572	2:227774503	G/C	0.40	0.014	0.003	3.72E-08	23	8812	0.36	-0.004	0.036	9.08E-01	1%	9.30E-05
rs2596902	3:12955982	G/A	0.35	0.015	0.003	1.30E-08	23	8812	0.35	-0.009	0.037	8.01E-01	0%	1.02E-04
rs6804842	3:25106437	G/A	0.57	0.018	0.002	1.29E-14	23	8812	0.58	-0.055	0.042	1.93E-01	24%	1.62E-04
rs762318	3:38516369	A/C	0.63	0.015	0.003	2.13E-09	23	8812	0.60	-0.016	0.051	7.55E-01	42%	1.09E-04
rs1524887	3:44016371	C/T	0.58	0.014	0.003	3.60E-08	23	8812	0.59	-0.044	0.034	2.06E-01	2%	9.41E-05
rs6803741	3:48123540	C/T	0.34	0.015	0.003	1.99E-08	23	8812	0.35	-0.055	0.037	1.39E-01	0%	1.00E-04
rs2188151	3:50201924	T/G	0.42	0.028	0.003	2.73E-29	23	8812	0.40	-0.031	0.046	4.99E-01	30%	3.92E-04
rs6787805	3:51204788	G/A	0.86	0.021	0.004	2.31E-09	23	8812	0.86	-0.005	0.052	9.25E-01	0%	1.01E-04
rs2365389	3:61236462	C/T	0.61	0.018	0.002	5.27E-14	23	8812	0.62	-0.042	0.035	2.35E-01	21%	1.50E-04
rs11915371	3:70539559	C/A	0.20	0.022	0.003	1.06E-12	23	8812	0.22	-0.075	0.042	7.81E-02	0%	1.50E-04
rs13078509	3:70881429	T/C	0.03	0.048	0.008	8.37E-09	8	3145	Excluded for MR					
rs3849570	3:81792112	A/C	0.35	0.015	0.003	2.56E-09	23	8812	0.32	0.058	0.037	1.14E-01	6%	1.02E-04
rs12495178	3:85886077	T/C	0.64	0.023	0.002	1.54E-20	23	8812	0.65	-0.064	0.045	1.58E-01	28%	2.35E-04
rs73140133	3:88067498	C/T	0.67	0.021	0.003	2.56E-12	23	8812	0.68	-0.003	0.037	9.44E-01	11%	2.00E-04
rs1492014	3:94071481	C/T	0.43	0.021	0.003	1.64E-17	23	8812	0.40	-0.050	0.036	1.57E-01	4%	2.23E-04
rs1436351	3:104617973	T/G	0.74	0.018	0.003	3.39E-11	23	8812	0.74	0.008	0.039	8.36E-01	0%	1.23E-04
rs6768228	3:108120008	G/A	0.37	0.015	0.003	6.77E-09	23	8812	0.38	0.039	0.035	2.71E-01	0%	1.03E-04
rs2918217	3:115546380	T/C	0.15	0.022	0.004	7.18E-10	23	8812	0.12	<u>0.107</u>	0.054	4.60E-02	0%	1.26E-04
rs1320903	3:131758077	A/G	0.31	0.026	0.003	1.65E-21	23	8812	0.30	0.003	0.037	9.27E-01	5%	2.78E-04
rs645040	3:135926622	T/G	0.77	0.019	0.003	3.16E-11	23	8812	0.74	0.042	0.040	3.01E-01	1%	1.24E-04
rs2035935	3:141306013	G/A	0.08	0.033	0.005	3.99E-13	23	8812	0.07	<u>-0.201</u>	0.072	5.31E-03	16%	1.55E-04
rs355777	3:154034950	C/G	0.40	0.017	0.003	1.81E-11	23	8812	0.41	0.051	0.035	1.39E-01	1%	1.38E-04
rs9870575	3:156296559	G/A	0.86	0.024	0.004	1.48E-11	23	8812	0.86	0.049	0.049	3.22E-01	0%	1.36E-04
rs7356034	3:170732599	A/G	0.29	0.022	0.003	6.24E-12	23	8812	0.30	-0.025	0.037	5.07E-01	14%	1.94E-04
rs2606227	3:183536836	T/C	0.37	0.014	0.003	4.61E-08	23	8812	0.34	-0.019	0.037	6.11E-01	1%	9.38E-05
rs9816226	3:185834499	T/A	0.83	0.034	0.003	5.05E-29	23	8811	0.82	0.022	0.049	6.58E-01	9%	3.34E-04
rs13135416	4:18346297	T/C	0.30	0.018	0.003	1.56E-08	23	8812	0.31	-0.024	0.037	5.26E-01	0%	1.32E-04
rs34811474	4:25408838	G/A	0.78	0.028	0.003	6.48E-16	NA in Courage-PD							
rs2242189	4:38691024	T/C	0.63	0.017	0.003	5.55E-11	23	8812	0.67	-0.011	0.046	8.08E-01	26%	1.34E-04
rs13130484	4:45175691	T/C	0.43	0.035	0.002	6.44E-50	23	8812	0.43	-0.036	0.034	2.93E-01	0%	6.08E-04
rs2237025	4:55541879	T/C	0.43	0.014	0.003	3.10E-08	23	8812	0.47	0.012	0.036	7.37E-01	10%	9.75E-05
rs13107325	4:103188709	T/C	0.09	0.050	0.005	3.22E-26	22	8708	0.08	-0.042	0.066	5.25E-01	0%	3.82E-04
rs2613726	4:112597321	G/A	0.63	0.016	0.003	4.34E-10	23	8812	0.64	0.043	0.037	2.44E-01	0%	1.22E-04
rs2391518	4:130817060	T/C	0.32	0.016	0.003	1.74E-10	23	8812	0.33	0.020	0.037	5.81E-01	0%	1.09E-04

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs1296328	4:137083193	A/C	0.44	0.020	0.003	2.07E-15	23	8812	0.45	0.023	0.035	5.16E-01	15%	1.97E-04
rs6537285	4:145310147	G/A	0.72	0.018	0.003	1.24E-10	23	8812	0.71	0.031	0.038	4.12E-01	0%	1.28E-04
rs6827083	4:153075491	G/A	0.42	0.015	0.002	1.34E-10	23	8812	0.42	-0.026	0.036	4.65E-01	0%	1.13E-04
rs828544	5:3520064	T/G	0.43	0.014	0.003	4.45E-08	23	8812	0.49	-0.023	0.035	5.20E-01	0%	9.22E-05
rs1503526	5:63020706	C/T	0.47	0.014	0.002	5.74E-09	23	8812	0.48	0.033	0.044	4.62E-01	30%	9.77E-05
rs253414	5:74956517	T/C	0.66	0.026	0.003	1.10E-24	23	8812	0.67	-0.023	0.036	5.28E-01	0%	3.02E-04
rs4532349	5:77473165	A/G	0.78	0.016	0.003	6.64E-09	23	8812	0.79	0.005	0.056	9.32E-01	33%	8.92E-05
rs7733438	5:87986284	G/T	0.14	0.035	0.004	2.07E-21	23	8812	0.14	-0.047	0.071	5.10E-01	42%	2.89E-04
rs6235	5:95728898	G/C	0.27	0.021	0.003	1.92E-13	23	8812	0.26	0.001	0.039	9.88E-01	0%	1.68E-04
rs11951673	5:95861012	C/T	0.61	0.019	0.002	7.83E-15	23	8812	0.63	-0.001	0.036	9.81E-01	6%	1.67E-04
rs289228	5:107405834	C/G	0.84	0.022	0.003	9.78E-12	23	8812	0.83	0.006	0.045	8.90E-01	24%	1.35E-04
rs7711753	5:122733317	G/A	0.58	0.013	0.002	2.64E-08	23	8812	0.58	-0.001	0.035	9.70E-01	0%	8.46E-05
rs7715256	5:153537893	G/T	0.44	0.016	0.002	4.52E-12	23	8812	0.44	-0.003	0.035	9.42E-01	14%	1.31E-04
rs7730898	5:170459675	A/G	0.73	0.017	0.003	9.94E-11	23	8812	0.73	-0.047	0.040	2.48E-01	7%	1.12E-04
rs6556301	5:176527577	G/T	0.63	0.014	0.003	1.57E-08	23	8812	0.67	-0.018	0.052	7.37E-01	42%	9.54E-05
rs2228213	6:12124855	G/A	0.66	0.015	0.003	6.77E-10	22	8622	0.64	-0.009	0.036	8.13E-01	0%	1.02E-04
rs9366639	6:26167613	C/G	0.80	0.019	0.003	3.82E-09	22	8622	0.81	0.084	0.045	6.02E-02	23%	1.19E-04
rs2269553	6:28876509	G/A	0.79	0.019	0.003	2.23E-11	23	8812	0.76	0.109	0.051	3.30E-02	28%	1.20E-04
rs9277992	6:33312455	A/G	0.19	0.028	0.004	8.69E-14	22	8622	0.18	0.070	0.060	2.46E-01	31%	2.31E-04
rs2744974	6:34579431	T/C	0.32	0.023	0.003	8.48E-20	22	8622	0.33	0.001	0.036	9.68E-01	0%	2.29E-04
rs34045288	6:40369081	T/C	0.33	0.025	0.003	3.95E-16	23	8812	0.30	0.021	0.037	5.72E-01	8%	2.74E-04
rs2206277	6:50798526	T/C	0.15	0.045	0.003	5.35E-50	23	8812	0.19	-0.115	0.058	5.00E-02	35%	5.28E-04
rs1327259	6:51177811	A/G	0.61	0.016	0.003	5.96E-10	23	8812	0.59	-0.049	0.035	1.69E-01	0%	1.20E-04
rs7773045	6:81443423	T/G	0.92	0.026	0.004	1.60E-09	22	8708	0.93	0.030	0.088	7.36E-01	27%	1.01E-04
rs12663742	6:97792735	G/A	0.63	0.018	0.003	1.69E-12	23	8812	0.64	-0.031	0.035	3.77E-01	0%	1.53E-04
rs4548017	6:98399521	G/A	0.61	0.024	0.003	1.13E-15	23	8812	0.59	-0.009	0.035	7.95E-01	24%	2.66E-04
rs17789218	6:100600097	C/T	0.25	0.015	0.003	3.33E-08	23	8812	0.24	0.041	0.042	3.25E-01	0%	8.59E-05
rs768023	6:108876002	A/G	0.60	0.013	0.002	3.05E-08	23	8812	0.57	0.042	0.036	2.40E-01	21%	8.48E-05
rs1159974	6:126090277	C/T	0.51	0.014	0.003	2.03E-08	23	8812	0.49	0.031	0.035	3.72E-01	6%	9.66E-05
rs6569648	6:130349119	C/T	0.24	0.015	0.003	3.66E-08	23	8812	0.22	0.058	0.040	1.47E-01	0%	8.31E-05
rs765875	6:143185683	C/T	0.53	0.014	0.003	3.43E-08	23	8812	0.52	0.017	0.035	6.17E-01	3%	9.48E-05
rs13191362	6:163033350	A/G	0.85	0.027	0.004	2.34E-13	23	8812	0.88	0.054	0.052	2.95E-01	0%	1.76E-04
rs9364687	6:163817911	G/T	0.60	0.014	0.002	3.97E-09	23	8812	0.59	0.033	0.037	3.80E-01	9%	9.39E-05
rs118182061 ^b	7:14655786	A/T	0.03	0.045	0.008	2.32E-09	21	8595	0.03	-0.141	0.114	2.19E-01	0%	1.18E-04
rs215635	7:32370220	C/T	0.38	0.018	0.003	1.16E-12	23	8812	0.38	0.009	0.036	8.12E-01	8%	1.58E-04
rs77095142	7:39096572	A/C	0.03	0.046	0.008	2.37E-08	12	4067	Excluded for MR					
rs10269783	7:49616203	A/G	0.42	0.017	0.002	7.59E-13	23	8812	0.39	-0.068	0.036	5.70E-02	0%	1.44E-04
rs1167827	7:75163169	G/A	0.56	0.022	0.002	2.88E-19	23	8812	0.58	-0.012	0.035	7.34E-01	0%	2.32E-04
rs2245368	7:76608143	C/T	0.19	0.033	0.003	4.39E-23	23	8812	0.19	0.105	0.046	2.26E-02	0%	3.31E-04
rs1965529	7:77825707	A/G	0.77	0.018	0.003	4.22E-08	23	8812	0.79	-0.007	0.043	8.70E-01	24%	1.08E-04
rs1701829	7:113033426	A/G	0.34	0.021	0.003	6.76E-16	23	8812	0.34	-0.002	0.037	9.65E-01	0%	2.04E-04

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs13228237	7:138780222	G/C	0.79	0.016	0.003	4.59E-08	23	8812	0.80	0.026	0.043	5.47E-01	0%	9.02E-05
rs4841504	8:11024663	C/A	0.50	0.019	0.002	4.24E-16	23	8812	0.52	0.033	0.035	3.49E-01	24%	1.86E-04
rs4123853	8:14091025	T/C	0.37	0.017	0.003	1.10E-10	23	8812	0.36	0.034	0.056	5.42E-01	51%	1.29E-04
rs354510	8:15534749	T/C	0.87	0.024	0.004	1.98E-08	23	8812	0.85	-0.034	0.050	4.98E-01	5%	1.30E-04
rs7827210	8:30871656	A/G	0.40	0.018	0.003	2.34E-12	23	8812	0.41	-0.048	0.036	1.81E-01	0%	1.53E-04
rs7012923	8:33630937	A/C	0.44	0.016	0.003	4.92E-11	23	8812	0.47	0.026	0.049	5.91E-01	37%	1.31E-04
rs35957544	8:73440371	G/T	0.44	0.018	0.003	4.14E-10	23	8812	0.44	0.009	0.049	8.51E-01	38%	1.60E-04
rs2588785	8:76636191	G/A	0.72	0.021	0.003	1.74E-15	23	8812	0.72	-0.006	0.038	8.70E-01	22%	1.81E-04
rs957447	8:95541223	C/A	0.76	0.023	0.003	8.56E-14	23	8812	0.73	0.012	0.061	8.44E-01	50%	1.84E-04
rs2960151	8:116718620	A/C	0.76	0.023	0.003	3.22E-11	21	8485	0.75	0.016	0.042	7.09E-01	22%	1.83E-04
rs72673947	8:118884379	G/A	0.11	0.028	0.005	1.76E-09	23	8812	0.12	-0.126	0.055	2.11E-02	10%	1.52E-04
rs7826388	8:128109776	C/T	0.96	0.037	0.007	1.40E-08	22	8712	0.97	0.074	0.146	6.13E-01	41%	9.84E-05
rs4740619	9:15634326	T/C	0.54	0.019	0.002	1.50E-15	23	8812	0.55	-0.009	0.035	7.95E-01	0%	1.74E-04
rs10738451	9:16713666	C/T	0.28	0.016	0.003	2.22E-09	23	8812	0.30	0.021	0.037	5.77E-01	0%	1.08E-04
rs10968114	9:27800007	A/C	0.53	0.015	0.003	8.70E-10	23	8812	0.55	0.014	0.037	7.04E-01	9%	1.17E-04
rs1412235	9:28410996	C/G	0.31	0.023	0.003	9.85E-21	23	8812	0.28	0.021	0.038	5.89E-01	0%	2.36E-04
rs10746862	9:73780912	G/T	0.42	0.016	0.003	8.63E-10	23	8812	0.40	-0.010	0.049	8.37E-01	38%	1.17E-04
rs1187351	9:87295077	C/A	0.60	0.014	0.003	4.51E-08	23	8812	0.59	-0.025	0.035	4.70E-01	0%	9.26E-05
rs6559921	9:88872039	A/T	0.77	0.018	0.003	1.19E-09	23	8812	0.79	0.043	0.044	3.32E-01	0%	1.16E-04
rs6477694	9:111932342	C/T	0.36	0.014	0.002	8.89E-09	23	8812	0.34	0.035	0.036	3.36E-01	0%	9.01E-05
rs7038943	9:120377178	T/C	0.66	0.015	0.003	6.54E-09	23	8812	0.64	0.027	0.036	4.58E-01	18%	1.04E-04
rs10760279	9:126105291	T/G	0.38	0.015	0.003	7.49E-09	23	8812	0.41	0.032	0.037	3.76E-01	0%	1.12E-04
rs3902840	9:129419025	A/G	0.09	0.031	0.004	2.49E-12	23	8812	0.07	0.068	0.065	2.99E-01	0%	1.50E-04
rs4740383	9:133783566	A/G	0.42	0.015	0.003	2.67E-09	23	8812	0.37	0.086	0.036	1.72E-02	0%	1.15E-04
rs11251291	10:2561766	C/A	0.53	0.014	0.003	1.65E-08	23	8812	0.52	0.036	0.034	2.92E-01	0%	9.90E-05
rs12251016	10:21821918	T/A	0.34	0.019	0.003	1.43E-10	22	8157	0.38	-0.018	0.037	6.28E-01	0%	1.70E-04
rs3758438	10:27400661	T/C	0.08	0.027	0.005	7.27E-09	22	8157	0.09	-0.083	0.064	1.90E-01	0%	1.08E-04
rs12761779	10:63782043	C/G	0.65	0.017	0.003	1.48E-08	23	8812	0.64	-0.005	0.037	8.92E-01	0%	1.36E-04
rs7072873	10:77210191	C/T	0.47	0.015	0.003	5.45E-09	23	8812	0.47	-0.060	0.046	1.94E-01	33%	1.08E-04
rs10788494	10:88110925	C/G	0.48	0.016	0.003	5.39E-10	22	8157	0.46	Excluded for MR				
rs10883026	10:99793865	C/T	0.48	0.019	0.003	6.23E-11	22	8157	0.49	-0.062	0.046	1.81E-01	27%	1.78E-04
rs17094222	10:102395440	C/T	0.21	0.026	0.003	1.14E-18	23	8812	0.20	0.017	0.043	6.88E-01	1%	2.15E-04
rs11191356	10:104393489	G/A	0.11	0.026	0.004	2.48E-10	22	8708	0.09	0.007	0.059	9.08E-01	0%	1.28E-04
rs79780963	10:104952499	T/C	0.08	0.037	0.005	1.55E-12	22	8708	0.09	-0.021	0.060	7.22E-01	0%	2.04E-04
rs7903146	10:114758349	C/T	0.72	0.023	0.003	3.57E-19	23	8812	0.69	0.114	0.058	4.98E-02	45%	2.14E-04
rs845084	10:125220036	A/G	0.27	0.016	0.003	3.85E-08	23	8812	0.29	-0.007	0.038	8.62E-01	1%	9.69E-05
rs7113874	11:8688016	C/T	0.67	0.014	0.002	3.30E-09	23	8812	0.63	0.003	0.035	9.26E-01	0%	9.13E-05
rs900144	11:13294268	T/C	0.58	0.015	0.003	5.54E-10	23	8812	0.55	0.047	0.036	1.90E-01	0%	1.15E-04
rs6265	11:27679916	C/T	0.82	0.048	0.003	6.25E-58	23	8812	0.80	0.002	0.042	9.68E-01	0%	6.84E-04
rs1765139	11:30353725	T/C	0.77	0.022	0.003	1.80E-13	23	8812	0.78	0.035	0.042	4.02E-01	0%	1.75E-04
rs2862996	11:43653833	G/T	0.30	0.020	0.003	2.49E-15	23	8812	0.31	0.072	0.039	6.06E-02	5%	1.65E-04

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs7124681	11:47529947	A/C	0.42	0.028	0.002	5.10E-31	23	8812	0.40	0.084	0.035	1.72E-02	3%	3.68E-04
rs7102454	11:65594820	C/T	0.36	0.018	0.003	1.29E-11	23	8812	0.35	-0.056	0.048	2.46E-01	34%	1.44E-04
rs11228371	11:68594174	A/C	0.41	0.017	0.003	1.31E-08	23	8812	0.45	-0.007	0.035	8.42E-01	8%	1.31E-04
rs349071	11:84776849	G/A	0.50	0.018	0.003	7.53E-10	23	8812	0.51	-0.050	0.034	1.45E-01	17%	1.57E-04
rs647248	11:89917699	A/G	0.54	0.016	0.003	2.59E-10	23	8812	0.52	0.039	0.035	2.65E-01	5%	1.29E-04
rs12286929	11:115022404	G/A	0.49	0.018	0.002	2.34E-14	23	8812	0.54	-0.014	0.043	7.52E-01	29%	1.58E-04
rs7933085	11:130796248	G/A	0.51	0.017	0.003	1.62E-09	23	8812	0.51	-0.057	0.035	1.04E-01	3%	1.51E-04
rs10894670	11:133221987	C/A	0.44	0.014	0.002	1.65E-09	11	3498	Excluded for MR					
rs11611246	12:939480	T/G	0.20	0.025	0.003	7.99E-17	23	8812	0.19	-0.028	0.045	5.34E-01	0%	1.91E-04
rs76895963	12:4384844	G/T	0.02	0.077	0.011	1.07E-11	NA in Courage-PD							
rs10772983	12:17141582	C/T	0.46	0.014	0.002	2.04E-09	20	6270	0.48	0.055	0.044	2.08E-01	5%	9.72E-05
rs10842240	12:24060075	C/G	0.13	0.026	0.004	4.56E-12	23	8812	0.14	-0.053	0.050	2.87E-01	0%	1.46E-04
rs11170468	12:39430048	A/C	0.78	0.016	0.003	7.84E-09	23	8812	0.77	-0.009	0.041	8.23E-01	0%	8.77E-05
rs11181001	12:41948196	A/G	0.48	0.014	0.002	1.25E-09	23	8812	0.46	0.092	0.035	8.32E-03	0%	1.04E-04
rs7132908	12:50263148	A/G	0.39	0.035	0.003	1.35E-38	23	8812	0.37	0.057	0.036	1.12E-01	18%	5.71E-04
rs705704	12:56435412	G/A	0.68	0.016	0.003	1.52E-10	23	8812	0.69	-0.003	0.037	9.27E-01	0%	1.16E-04
rs1689437	12:89758046	G/A	0.05	0.030	0.005	2.04E-09	23	8812	0.06	-0.025	0.074	7.33E-01	0%	8.78E-05
rs7488867	12:103699685	C/T	0.74	0.022	0.003	5.69E-14	23	8812	0.73	0.004	0.038	9.16E-01	0%	1.85E-04
rs10850184	12:114064977	T/G	0.32	0.017	0.003	3.53E-10	23	8812	0.33	0.020	0.037	5.91E-01	0%	1.22E-04
rs11067700	12:116083562	C/T	0.44	0.017	0.003	8.28E-09	23	8812	0.44	-0.076	0.035	2.68E-02	0%	1.37E-04
rs12369179	12:122963550	C/T	0.92	0.035	0.005	1.37E-14	22	8709	0.93	-0.054	0.070	4.34E-01	0%	1.90E-04
rs10902480	12:132414769	T/G	0.82	0.022	0.004	5.60E-09	18	6670	0.80	0.040	0.053	4.52E-01	0%	1.41E-04
rs2012835	13:27987643	G/T	0.73	0.021	0.003	3.06E-10	23	8812	0.75	-0.064	0.056	2.53E-01	39%	1.65E-04
rs2504236	13:28613298	C/T	0.41	0.015	0.003	1.94E-09	23	8812	0.47	-0.027	0.035	4.42E-01	0%	1.11E-04
rs9595893	13:33175793	G/T	0.64	0.020	0.003	1.24E-14	23	8812	0.63	-0.035	0.036	3.22E-01	0%	1.82E-04
rs9603697	13:40783323	T/C	0.32	0.020	0.003	1.34E-13	23	8812	0.33	-0.007	0.036	8.46E-01	0%	1.68E-04
rs12429545	13:54102206	A/G	0.12	0.034	0.004	2.03E-21	23	8812	0.12	-0.066	0.051	1.99E-01	0%	2.39E-04
rs7338127	13:59260511	A/T	0.33	0.020	0.003	1.39E-13	23	8812	0.34	0.021	0.036	5.58E-01	0%	1.72E-04
rs1441264	13:79580919	A/G	0.58	0.018	0.002	1.35E-13	23	8812	0.62	-0.052	0.035	1.34E-01	0%	1.59E-04
rs912690	13:97020705	G/C	0.44	0.017	0.003	6.92E-12	23	8812	0.48	Excluded for MR				
rs9168	13:99101583	C/A	0.73	0.015	0.003	4.62E-08	23	8812	0.72	-0.022	0.038	5.68E-01	0%	8.93E-05
rs9522279	13:112221296	T/C	0.42	0.022	0.003	1.65E-14	23	8812	0.41	-0.031	0.048	5.14E-01	37%	2.44E-04
rs10132280	14:25928179	C/A	0.69	0.030	0.003	1.38E-31	23	8812	0.71	-0.050	0.039	2.03E-01	0%	3.84E-04
rs1811859	14:29677727	C/T	0.78	0.020	0.004	6.48E-09	23	8812	0.79	0.010	0.044	8.20E-01	0%	1.41E-04
rs1955540	14:40801751	C/T	0.81	0.020	0.003	2.89E-10	23	8812	0.82	-0.019	0.044	6.72E-01	0%	1.25E-04
rs4900714	14:47302219	T/G	0.47	0.020	0.003	1.17E-15	23	8812	0.53	-0.032	0.034	3.49E-01	17%	1.99E-04
rs217672	14:62361021	C/A	0.28	0.020	0.003	4.40E-10	23	8812	0.24	0.001	0.054	9.90E-01	33%	1.61E-04
rs3902951	14:69789755	G/T	0.23	0.015	0.003	4.40E-08	20	8231	0.24	-0.060	0.043	1.68E-01	0%	8.05E-05
rs17109256	14:79939993	A/G	0.24	0.031	0.003	2.81E-27	23	8812	0.19	-0.021	0.044	6.31E-01	0%	3.43E-04
rs34918753	14:88312341	A/G	0.23	0.020	0.003	1.77E-09	23	8812	0.22	-0.065	0.041	1.13E-01	11%	1.49E-04
rs11160119	14:93932258	G/A	0.59	0.022	0.003	2.85E-14	23	8812	0.59	0.027	0.035	4.41E-01	1%	2.39E-04

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R²	
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I² (%)		
rs7161194	14:101529005	A/G	0.34	0.022	0.003	3.32E-15									
rs7143963	14:103304425	T/C	0.16	0.021	0.003	3.35E-12	23	8812	0.17	-0.054	0.048	2.63E-01	7%	1.22E-04	
rs11636536	15:36391772	T/C	0.50	0.015	0.003	2.80E-09	23	8812	0.48	-0.017	0.035	6.37E-01	0%	1.10E-04	
rs10851458	15:47939956	A/G	0.58	0.015	0.003	5.95E-09	23	8812	0.58	0.016	0.035	6.54E-01	17%	1.07E-04	
rs4776970	15:68080886	A/T	0.64	0.028	0.002	1.52E-30	23	8810	0.62	0.043	0.035	2.22E-01	0%	3.58E-04	
rs58429335	15:70199927	C/T	0.07	0.031	0.006	4.85E-08	23	8812	0.07	0.088	0.067	1.84E-01	0%	1.24E-04	
rs4777541	15:73082240	T/C	0.78	0.021	0.003	1.15E-12	23	8812	0.80	0.008	0.049	8.64E-01	17%	1.49E-04	
rs8041222	15:79465549	G/A	0.59	0.019	0.003	3.28E-11	23	8812	0.61	-0.004	0.036	9.04E-01	0%	1.82E-04	
rs8036171	15:95266810	A/C	0.37	0.015	0.003	4.26E-10	23	8812	0.35	0.004	0.040	9.14E-01	12%	1.10E-04	
rs12448257	16:3599655	A/G	0.22	0.019	0.003	1.17E-10	23	8812	0.21	-0.116	0.043	7.26E-03	0%	1.18E-04	
rs879620	16:4015729	T/C	0.60	0.021	0.003	3.11E-16	23	8811	0.61	-0.007	0.046	8.79E-01	33%	2.10E-04	
rs9926784	16:19941968	T/C	0.80	0.022	0.003	5.74E-14	23	8812	0.82	0.017	0.045	6.99E-01	0%	1.60E-04	
rs3888190	16:28889486	A/C	0.38	0.032	0.002	6.96E-40	23	8812	0.35	-0.018	0.035	6.13E-01	0%	4.68E-04	
rs57149692	16:30142021	G/C	0.60	0.027	0.003	1.11E-19	23	8812	0.57	Excluded for MR					
rs9937053	16:53799507	A/G	0.44	0.078	0.002	1.00E-200	23	8812	0.43	-0.011	0.034	7.60E-01	0%	3.01E-03	
rs889398	16:69556715	C/T	0.58	0.021	0.002	1.54E-18	18	6700	0.59	0.011	0.053	8.36E-01	26%	2.13E-04	
rs75950518	16:70378917	C/T	0.88	0.027	0.005	3.51E-09	23	8812	0.88	-0.032	0.053	5.50E-01	0%	1.44E-04	
rs28483459	16:71998398	C/T	0.67	0.018	0.003	2.92E-09	23	8812	0.69	-0.015	0.039	7.04E-01	14%	1.50E-04	
rs7206608	16:82872628	G/C	0.33	0.015	0.003	1.85E-08	23	8812	0.29	-0.029	0.038	4.41E-01	0%	9.88E-05	
rs3923783	17:1843189	C/A	0.82	0.023	0.003	7.47E-12	23	8812	0.82	0.053	0.046	2.50E-01	0%	1.49E-04	
rs12450045	17:4742112	A/G	0.46	0.014	0.003	1.68E-08	23	8812	0.45	-0.002	0.035	9.46E-01	0%	1.02E-04	
rs4986044	17:21261560	C/T	0.55	0.018	0.002	1.45E-14	23	8812	0.53	-0.022	0.033	5.02E-01	0%	1.62E-04	
rs8065172	17:31456969	G/A	0.76	0.017	0.003	1.23E-08	23	8812	0.74	0.067	0.039	8.96E-02	1%	1.01E-04	
rs12150665	17:34914787	T/C	0.59	0.018	0.002	3.43E-14	23	8812	0.59	0.025	0.035	4.83E-01	0%	1.58E-04	
rs676387	17:40706273	A/C	0.30	0.016	0.003	4.10E-09	23	8812	0.26	-0.069	0.040	8.60E-02	0%	1.11E-04	
rs208015	17:46252346	T/C	0.07	0.037	0.005	8.72E-14	22	8708	0.09	0.006	0.064	9.30E-01	0%	1.74E-04	
rs78369934	17:61739101	T/C	0.95	0.037	0.007	1.47E-08	7	2205	Excluded for MR						
rs12939549	17:78611724	A/G	0.56	0.020	0.002	1.29E-17	23	8812	0.55	0.027	0.035	4.29E-01	0%	1.97E-04	
rs7226371	18:1850771	G/A	0.16	0.019	0.003	7.73E-09	23	8812	0.15	-0.084	0.049	8.53E-02	0%	9.13E-05	
rs891387	18:21103909	T/C	0.50	0.023	0.003	6.81E-20	23	8812	0.53	0.011	0.035	7.46E-01	14%	2.58E-04	
rs11874191	18:36164084	C/T	0.27	0.017	0.003	3.06E-09	23	8812	0.28	-0.024	0.039	5.37E-01	0%	1.13E-04	
rs2612575	18:42967340	G/A	0.72	0.016	0.003	1.45E-08	23	8812	0.73	-0.046	0.039	2.41E-01	8%	1.02E-04	
rs9951619	18:56882326	G/T	0.78	0.019	0.003	1.75E-11	23	8812	0.74	0.049	0.066	4.55E-01	52%	1.20E-04	
rs6567160	18:57829135	C/T	0.25	0.053	0.003	2.11E-82	23	8812	0.24	-0.019	0.040	6.33E-01	10%	1.07E-03	
rs17066856	18:58049656	T/C	0.89	0.030	0.004	2.65E-14	23	8812	0.91	0.078	0.061	2.00E-01	0%	1.78E-04	
rs17710386	18:63461201	C/T	0.34	0.016	0.003	3.75E-11	23	8812	0.36	-0.016	0.037	6.62E-01	2%	1.20E-04	
rs1787267	18:76742544	G/C	0.94	0.033	0.005	2.49E-10	23	8812	0.95	0.052	0.078	5.07E-01	0%	1.26E-04	
rs45486197	19:2244849	A/G	0.06	0.035	0.006	3.49E-09	3	837	Excluded for MR						
rs7258309	19:4016005	T/G	0.78	0.023	0.003	6.54E-14	23	8812	0.79	-0.047	0.044	2.95E-01	13%	1.84E-04	
rs273496	19:18241857	T/C	0.39	0.020	0.003	2.50E-11	23	8812	0.41	-0.058	0.035	9.99E-02	0%	1.84E-04	
rs7258722	19:18808915	T/A	0.59	0.020	0.003	8.61E-15	23	8812	0.61	0.071	0.035	4.24E-02	20%	1.92E-04	

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure (BMI)				PD (Courage-PD)							R ²
			EAF	Beta	SE	P	n studies	n sample	EAF	Beta	SE	P	I ² (%)	
rs17513613	19:30286822	C/T	0.31	0.018	0.003	1.50E-12	23	8812	0.30	0.021	0.038	5.79E-01	25%	1.36E-04
rs11084553	19:31019780	A/G	0.85	0.024	0.004	9.41E-12	23	8812	0.87	-0.079	0.051	1.24E-01	11%	1.44E-04
rs769449	19:45410002	G/A	0.90	0.024	0.004	1.58E-09	23	8812	0.91	-0.033	0.058	5.67E-01	0%	1.07E-04
rs1800437	19:46181392	G/C	0.81	0.037	0.003	1.73E-33	23	8812	0.79	-0.029	0.043	4.94E-01	24%	4.04E-04
rs9304665	19:47602577	A/T	0.74	0.027	0.003	4.78E-21	3	1221	Excluded for MR					
rs7249149	19:51774538	A/G	0.70	0.015	0.003	4.41E-08	23	8812	0.75	0.002	0.040	9.54E-01	16%	9.78E-05
rs2145270	20:6621685	T/C	0.62	0.021	0.002	6.97E-18	18	6659	0.61	0.033	0.044	4.51E-01	15%	2.05E-04
rs8123881	20:15819495	G/A	0.14	0.019	0.003	2.53E-08	23	8812	0.12	0.026	0.053	6.27E-01	6%	8.65E-05
rs7272093	20:49810724	G/A	0.30	0.017	0.003	1.10E-09	23	8812	0.29	0.018	0.039	6.54E-01	9%	1.24E-04
rs35388084	20:50960490	G/A	0.82	0.028	0.004	1.12E-13	23	8812	0.81	0.044	0.044	3.14E-01	0%	2.28E-04
rs6092143	20:54181875	T/C	0.37	0.015	0.003	1.10E-08	23	8812	0.37	-0.010	0.036	7.89E-01	0%	1.03E-04
rs13047416	21:40309436	C/G	0.63	0.016	0.003	9.84E-10	23	8812	0.64	0.001	0.036	9.79E-01	11%	1.15E-04
rs427943	21:46570896	C/A	0.57	0.018	0.003	2.19E-12	23	8812	0.55	-0.046	0.035	1.87E-01	0%	1.50E-04
rs138383	22:38799861	C/T	0.49	0.016	0.003	1.39E-09	23	8812	0.51	-0.035	0.046	4.45E-01	27%	1.20E-04
rs733381	22:40669648	A/G	0.77	0.021	0.003	5.20E-13	23	8812	0.81	-0.002	0.044	9.64E-01	7%	1.52E-04

^aProxy SNP of rs6050446 used in Courage-PD

^bProxy SNP of rs9638713 used in Courage-PD

NA, not available; EA/BA, effect allele/base allele; SE, standard error. R², proportion of the variance of the exposure explained by the SNP: $2 \times \text{Beta}_{\text{exposure}}^2 \times \text{EAF}_{\text{exposure}} \times (1 - \text{EAF}_{\text{exposure}})$

Bold coefficient with their corresponding SE and p-values are significant at $p \leq 0.05$; those underlined with a solid line are negative and those underlined with a dashed line are positive.

eTable 5: SNPs used for Mendelian randomisation analyses: individual associations with PD (Courage-PD) stratified by age and disease duration.

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
BMI (per 1SD=4.8kg/m²)													
rs79113395	G/A	0.041	0.045	3.66E-01	0.044	0.046	3.40E-01	0.062	0.035	7.61E-02	0.055	0.038	1.47E-01
rs10909880	C/T	-0.002	0.060	9.74E-01	0.017	0.040	6.66E-01	0.015	0.031	6.32E-01	0.040	0.041	3.32E-01
rs11121210	C/T	0.012	0.039	7.57E-01	-0.113	0.040	4.42E-03	-0.032	0.030	2.84E-01	-0.066	0.033	4.23E-02
rs10779751	A/G	0.077	0.042	6.93E-02	-0.023	0.044	6.09E-01	0.029	0.033	3.84E-01	0.033	0.036	3.66E-01
rs61740466	G/A	-0.054	0.042	1.99E-01	Excluded for MR			-0.003	0.033	9.18E-01	-0.016	0.036	6.65E-01
rs4655141	C/T	0.040	0.080	6.11E-01	0.039	0.060	5.18E-01	0.037	0.048	4.38E-01	0.077	0.067	2.45E-01
rs2228552	T/G	-0.038	0.040	3.32E-01	-0.008	0.040	8.34E-01	-0.028	0.031	3.64E-01	-0.021	0.033	5.21E-01
rs4653017	T/C	0.001	0.040	9.80E-01	-0.003	0.041	9.50E-01	-0.027	0.031	3.83E-01	0.008	0.034	8.21E-01
rs7512146	G/T	0.070	0.039	7.52E-02	0.012	0.040	7.57E-01	-0.001	0.031	9.65E-01	0.082	0.032	1.09E-02
rs11577094	T/C	0.025	0.081	7.55E-01	0.105	0.081	1.94E-01	0.034	0.063	5.93E-01	0.130	0.062	3.67E-02
rs112646560	T/C	-0.011	0.060	8.61E-01	-0.038	0.045	4.07E-01	-0.005	0.034	8.89E-01	-0.016	0.037	6.73E-01
rs2984618	T/G	0.035	0.039	3.63E-01	0.094	0.040	1.99E-02	0.061	0.030	4.43E-02	0.045	0.032	1.60E-01
rs657452	A/G	0.015	0.039	7.00E-01	0.036	0.041	3.72E-01	0.015	0.030	6.20E-01	0.034	0.042	4.12E-01
rs587271	T/C	Excluded for MR											
rs79906980	T/C	0.050	0.053	3.43E-01	-0.074	0.054	1.72E-01	-0.017	0.041	6.80E-01	0.003	0.044	9.52E-01
rs12140153	G/T	-0.007	0.077	9.31E-01	0.062	0.074	4.05E-01	-0.013	0.059	8.27E-01	0.036	0.059	5.44E-01
rs2503185	A/G	-0.004	0.037	9.19E-01	-0.020	0.038	6.08E-01	-0.002	0.029	9.51E-01	-0.014	0.031	6.63E-01
rs3101336	C/T	-0.008	0.040	8.34E-01	-0.072	0.041	8.08E-02	-0.053	0.031	9.20E-02	-0.053	0.033	1.09E-01
rs6656785	G/A	-0.016	0.039	6.84E-01	-0.023	0.040	5.66E-01	0.002	0.031	9.60E-01	-0.012	0.033	7.11E-01
rs34517439	A/C	0.006	0.071	9.33E-01	-0.006	0.075	9.37E-01	0.021	0.056	7.08E-01	0.047	0.057	4.14E-01
rs6696828	C/G	0.012	0.042	7.76E-01	-0.011	0.043	8.05E-01	0.027	0.032	3.98E-01	-0.013	0.035	7.21E-01
rs321237	A/G	-0.080	0.042	5.88E-02	-0.024	0.044	5.87E-01	-0.061	0.033	6.60E-02	-0.090	0.036	1.13E-02
rs11165643	T/C	-0.017	0.038	6.50E-01	-0.058	0.039	1.35E-01	-0.051	0.029	8.53E-02	-0.043	0.032	1.78E-01
rs12072739	G/A	0.032	0.048	5.12E-01	-0.094	0.049	5.42E-02	-0.018	0.037	6.26E-01	-0.028	0.040	4.77E-01
rs17024393	C/T	-0.048	0.132	7.18E-01	0.019	0.134	8.88E-01	0.114	0.098	2.43E-01	-0.052	0.101	6.07E-01
rs197374	T/C	0.011	0.038	7.64E-01	-0.003	0.039	9.39E-01	0.027	0.030	3.64E-01	-0.009	0.032	7.73E-01
rs17544384	C/T	-0.068	0.046	1.38E-01	0.020	0.047	6.69E-01	-0.029	0.036	4.23E-01	-0.045	0.038	2.34E-01
rs7534091	G/A	-0.045	0.044	3.04E-01	0.028	0.045	5.40E-01	-0.009	0.034	7.93E-01	-0.007	0.037	8.56E-01
rs74887628	A/G	Excluded for MR											
rs4970991	T/C	0.061	0.046	1.81E-01	0.020	0.062	7.45E-01	0.071	0.036	4.82E-02	0.009	0.039	8.13E-01
rs61813324	T/C	Excluded for MR											
rs1750307	A/T	0.009	0.039	8.13E-01	0.037	0.041	3.59E-01	0.006	0.031	8.56E-01	0.018	0.033	5.90E-01
rs10733051	A/G	-0.031	0.054	5.66E-01	-0.027	0.041	5.05E-01	-0.019	0.031	5.35E-01	-0.039	0.033	2.40E-01
rs61828641	A/G	-0.082	0.056	1.45E-01	-0.005	0.059	9.32E-01	-0.044	0.045	3.24E-01	-0.032	0.048	5.04E-01
rs543874	G/A	-0.062	0.062	3.13E-01	-0.093	0.055	8.90E-02	-0.106	0.048	2.88E-02	-0.080	0.050	1.07E-01
rs10920678	A/G	-0.023	0.053	6.64E-01	0.034	0.039	3.82E-01	0.044	0.029	1.33E-01	-0.026	0.032	4.09E-01
rs2400414	C/T	0.027	0.039	4.90E-01	-0.031	0.040	4.46E-01	-0.013	0.030	6.62E-01	0.000	0.033	9.88E-01
rs2820295	A/G	-0.008	0.042	8.45E-01	-0.030	0.049	5.44E-01	-0.009	0.045	8.36E-01	-0.019	0.034	5.86E-01
rs10920336	G/A	-0.045	0.038	2.39E-01	-0.015	0.040	7.14E-01	-0.022	0.030	4.59E-01	-0.046	0.032	1.48E-01
rs1006317	T/G	-0.101	0.074	1.72E-01	-0.022	0.056	6.99E-01	-0.028	0.043	5.08E-01	-0.047	0.061	4.46E-01
rs6661316	T/C	-0.010	0.037	7.84E-01	-0.066	0.039	9.12E-02	-0.058	0.029	4.98E-02	-0.024	0.032	4.53E-01
rs10864728	A/G	-0.002	0.039	9.67E-01	0.001	0.040	9.75E-01	0.021	0.031	4.89E-01	-0.007	0.033	8.33E-01
rs946824	T/C	-0.002	0.067	9.72E-01	0.091	0.068	1.81E-01	0.035	0.053	5.05E-01	0.018	0.054	7.45E-01
rs6710091	C/G	-0.012	0.041	7.62E-01	-0.018	0.052	7.24E-01	-0.056	0.032	7.67E-02	0.028	0.034	4.11E-01

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs77165542	C/T							Excluded for MR					
rs13021737	G/A	-0.059	0.048	2.15E-01	0.081	0.072	2.65E-01	-0.016	0.037	6.76E-01	0.013	0.041	7.47E-01
rs10929925	C/A	0.037	0.038	3.21E-01	0.014	0.039	7.27E-01	0.024	0.029	4.18E-01	0.065	0.031	3.82E-02
rs11902450	T/C	-0.072	0.061	2.39E-01	-0.050	0.063	4.25E-01	-0.051	0.063	4.15E-01	-0.061	0.067	3.63E-01
rs10182181	G/A	0.044	0.038	2.37E-01	0.012	0.039	7.55E-01	0.031	0.029	2.88E-01	0.026	0.032	4.08E-01
rs935166	G/A	0.020	0.038	5.92E-01	-0.025	0.040	5.20E-01	-0.018	0.030	5.37E-01	0.039	0.039	3.24E-01
rs10168563	A/G	0.018	0.042	6.67E-01	-0.003	0.042	9.42E-01	-0.009	0.032	7.84E-01	0.006	0.035	8.72E-01
rs3770890	G/T							Excluded for MR					
rs10185199	G/A	0.031	0.061	6.07E-01	0.000	0.045	9.97E-01	0.004	0.046	9.36E-01	-0.039	0.046	3.94E-01
rs10169594	C/T	-0.016	0.040	6.99E-01	-0.059	0.053	2.66E-01	-0.013	0.031	6.76E-01	0.020	0.033	5.40E-01
rs7561278	T/C	-0.005	0.064	9.43E-01	0.002	0.049	9.62E-01	-0.042	0.037	2.49E-01	0.027	0.040	4.97E-01
rs930295	A/C	-0.037	0.051	4.72E-01	-0.016	0.053	7.67E-01	-0.015	0.040	7.07E-01	-0.004	0.054	9.48E-01
rs805412	G/A	0.004	0.038	9.20E-01	-0.038	0.039	3.39E-01	-0.014	0.030	6.31E-01	0.000	0.032	9.99E-01
rs4671328	T/G	-0.092	0.039	1.66E-02	0.016	0.043	7.11E-01	-0.048	0.034	1.53E-01	0.021	0.032	4.96E-01
rs6545714	G/A	0.033	0.054	5.36E-01	0.029	0.040	4.66E-01	-0.003	0.030	9.11E-01	0.058	0.032	6.94E-02
rs2861685	T/C	-0.052	0.038	1.75E-01	0.025	0.039	5.28E-01	-0.025	0.030	3.98E-01	0.034	0.032	2.92E-01
rs17020497	A/G	-0.027	0.070	7.01E-01	-0.003	0.054	9.50E-01	-0.026	0.056	6.44E-01	-0.041	0.044	3.60E-01
rs12714199	C/T	0.045	0.039	2.45E-01	-0.024	0.040	5.45E-01	-0.005	0.031	8.73E-01	0.005	0.033	8.88E-01
rs4303732	T/C	0.058	0.039	1.36E-01	0.001	0.040	9.84E-01	0.039	0.030	2.05E-01	-0.021	0.033	5.24E-01
rs264941	C/A	-0.047	0.038	2.08E-01	0.048	0.050	3.33E-01	-0.026	0.041	5.24E-01	0.030	0.050	5.54E-01
rs10197031	C/T	-0.007	0.043	8.62E-01	0.045	0.063	4.71E-01	-0.001	0.033	9.79E-01	0.059	0.048	2.19E-01
rs13033310	A/G	-0.012	0.055	8.22E-01	0.035	0.044	4.24E-01	0.012	0.033	7.27E-01	-0.009	0.048	8.50E-01
rs4988235	A/G	0.110	0.043	1.09E-02	0.052	0.048	2.77E-01	0.071	0.038	6.02E-02	0.087	0.045	5.12E-02
rs17814208	G/A	-0.016	0.045	7.17E-01	0.038	0.047	4.15E-01	0.013	0.048	7.82E-01	0.030	0.038	4.37E-01
rs1451077	G/A	-0.021	0.039	5.89E-01	-0.013	0.053	7.99E-01	-0.029	0.030	3.40E-01	0.014	0.033	6.59E-01
rs2119753	A/G	-0.026	0.040	5.10E-01	-0.051	0.041	2.14E-01	-0.059	0.031	5.90E-02	-0.030	0.033	3.65E-01
rs11695013	C/T	-0.018	0.039	6.45E-01	0.000	0.041	9.93E-01	-0.023	0.031	4.65E-01	0.008	0.033	8.01E-01
rs3764835	G/A	0.029	0.070	6.81E-01	-0.014	0.070	8.45E-01	-0.018	0.042	6.64E-01	-0.001	0.045	9.86E-01
rs12692596	T/C	-0.058	0.039	1.39E-01	0.006	0.040	8.89E-01	-0.017	0.031	5.83E-01	-0.032	0.033	3.32E-01
rs62176243	A/T	0.054	0.044	2.21E-01	-0.019	0.073	7.90E-01	0.008	0.049	8.68E-01	0.026	0.037	4.87E-01
rs56133507	G/T	-0.133	0.047	5.13E-03	-0.041	0.049	4.04E-01	-0.090	0.037	1.65E-02	-0.050	0.040	2.15E-01
rs34234296	G/A							Excluded for MR					
rs7588437	G/A	0.018	0.039	6.50E-01	-0.041	0.041	3.15E-01	0.012	0.031	6.97E-01	-0.014	0.033	6.68E-01
rs6716898	A/G	-0.023	0.038	5.47E-01	0.083	0.051	1.06E-01	0.006	0.030	8.49E-01	0.057	0.032	7.00E-02
rs7593917	G/A	-0.060	0.038	1.13E-01	0.024	0.039	5.41E-01	0.004	0.030	8.98E-01	-0.054	0.032	8.90E-02
rs4482463	C/A							NA in COURAGE PD					
rs11692326	T/C	0.082	0.047	8.47E-02	-0.019	0.048	6.96E-01	0.037	0.037	3.11E-01	-0.020	0.052	6.97E-01
rs73985439	C/A	-0.002	0.041	9.56E-01	0.025	0.042	5.58E-01	-0.023	0.032	4.64E-01	0.040	0.034	2.37E-01
rs7599312	G/A	0.016	0.052	7.62E-01	0.051	0.047	2.80E-01	0.039	0.034	2.47E-01	0.015	0.045	7.34E-01
rs12987009	T/A	Excluded for MR			0.018	0.052	7.33E-01	Excluded for MR					
rs6725931	T/C							Excluded for MR					
rs4973618	G/A	-0.050	0.039	2.04E-01	-0.063	0.040	1.18E-01	-0.028	0.031	3.63E-01	-0.022	0.048	6.45E-01
rs6720868	T/C	-0.064	0.053	2.26E-01	-0.005	0.041	9.08E-01	-0.047	0.031	1.29E-01	-0.051	0.033	1.23E-01
rs7568228	G/C							Excluded for MR					
rs59302296	A/T	-0.061	0.097	5.30E-01	-0.009	0.066	8.95E-01	-0.032	0.076	6.72E-01	-0.094	0.055	8.77E-02
rs6783054	A/C	-0.026	0.038	4.91E-01	-0.050	0.039	2.00E-01	-0.017	0.029	5.67E-01	-0.023	0.032	4.71E-01
rs10510419	G/T	0.009	0.052	8.60E-01	-0.036	0.080	6.50E-01	0.008	0.041	8.38E-01	-0.025	0.045	5.82E-01

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs2600226	C/T	-0.016	0.045	7.24E-01	0.059	0.054	2.69E-01	0.014	0.031	6.46E-01	0.013	0.033	6.87E-01
rs1048637	G/T	0.014	0.038	7.09E-01	-0.040	0.039	3.07E-01	-0.009	0.030	7.71E-01	-0.033	0.032	3.05E-01
rs4858193	T/C	0.047	0.044	2.93E-01	0.013	0.069	8.55E-01	0.035	0.035	3.09E-01	0.009	0.037	8.05E-01
rs6804842	G/A	-0.014	0.058	8.06E-01	0.024	0.039	5.42E-01	-0.002	0.030	9.34E-01	0.013	0.032	6.92E-01
rs11921432	C/T	-0.008	0.063	9.00E-01	0.033	0.064	6.10E-01	-0.001	0.049	9.81E-01	0.038	0.052	4.68E-01
rs1799923	G/A	-0.028	0.063	6.56E-01	-0.045	0.065	4.90E-01	-0.041	0.049	4.02E-01	-0.021	0.051	6.82E-01
rs28350	A/G	Excluded for MR											
rs4017425	C/T	0.040	0.037	2.78E-01	-0.022	0.039	5.76E-01	0.032	0.029	2.72E-01	-0.006	0.031	8.52E-01
rs11919665	A/T	-0.031	0.041	4.44E-01	0.043	0.042	3.04E-01	0.016	0.032	6.25E-01	0.028	0.034	4.12E-01
rs11713193	A/G	-0.002	0.049	9.60E-01	0.002	0.039	9.53E-01	0.019	0.029	5.13E-01	-0.019	0.031	5.47E-01
rs2365389	C/T	-0.008	0.038	8.25E-01	-0.015	0.050	7.61E-01	0.003	0.030	9.22E-01	-0.013	0.040	7.56E-01
rs6445258	T/C	Excluded for MR											
rs925018	G/C	-0.018	0.040	6.48E-01	-0.018	0.041	6.59E-01	0.007	0.031	8.24E-01	-0.043	0.034	1.96E-01
rs11915371	C/A	-0.043	0.047	3.56E-01	-0.020	0.048	6.80E-01	-0.046	0.037	2.08E-01	-0.043	0.039	2.64E-01
rs12636480	T/G	0.019	0.039	6.26E-01	-0.096	0.040	1.66E-02	-0.067	0.032	3.52E-02	-0.036	0.033	2.75E-01
rs9827823	T/C	0.083	0.052	1.13E-01	-0.107	0.078	1.67E-01	-0.022	0.041	5.89E-01	-0.047	0.044	2.87E-01
rs9818122	C/T	-0.011	0.046	8.14E-01	-0.044	0.046	3.43E-01	-0.021	0.036	5.64E-01	0.001	0.038	9.77E-01
rs34184235	C/T	-0.062	0.037	9.71E-02	-0.042	0.039	2.81E-01	-0.086	0.029	3.58E-03	-0.006	0.032	8.53E-01
rs11128021	G/A	0.020	0.054	7.13E-01	0.097	0.055	8.06E-02	0.083	0.043	5.03E-02	-0.020	0.045	6.54E-01
rs1492014	C/T	-0.017	0.039	6.56E-01	-0.099	0.040	1.41E-02	-0.055	0.030	7.24E-02	-0.044	0.033	1.74E-01
rs1436344	C/G	Excluded for MR											
rs7640424	C/T	-0.104	0.042	1.45E-02	-0.001	0.043	9.84E-01	-0.056	0.033	8.79E-02	-0.071	0.035	4.08E-02
rs17681451	G/A	-0.031	0.071	6.61E-01	0.126	0.072	7.80E-02	0.031	0.055	5.73E-01	0.088	0.059	1.35E-01
rs6808814	T/C	0.011	0.043	7.95E-01	-0.042	0.044	3.38E-01	-0.011	0.033	7.44E-01	0.006	0.045	9.02E-01
rs7631156	A/G	0.074	0.040	6.44E-02	-0.044	0.058	4.48E-01	0.014	0.031	6.59E-01	0.027	0.034	4.15E-01
rs687339	T/C	0.053	0.069	4.44E-01	0.007	0.045	8.69E-01	-0.002	0.044	9.59E-01	0.077	0.038	4.09E-02
rs16851483	T/G	-0.104	0.083	2.07E-01	-0.104	0.080	1.93E-01	-0.118	0.064	6.28E-02	-0.007	0.066	9.18E-01
rs355777	C/G	0.039	0.039	3.17E-01	0.056	0.039	1.50E-01	0.031	0.030	2.94E-01	0.058	0.032	6.60E-02
rs9826775	A/G	-0.021	0.053	6.94E-01	-0.037	0.057	5.24E-01	-0.068	0.042	1.07E-01	-0.013	0.046	7.68E-01
rs2047648	T/A	0.069	0.042	1.03E-01	0.036	0.044	4.13E-01	0.086	0.033	9.00E-03	-0.024	0.036	5.00E-01
rs3732927	T/C	0.009	0.040	8.16E-01	-0.008	0.041	8.46E-01	0.004	0.031	8.91E-01	-0.011	0.033	7.43E-01
rs12635553	A/T	Excluded for MR											
rs39654	G/A	0.031	0.039	4.34E-01	0.090	0.057	1.13E-01	0.032	0.031	3.04E-01	0.029	0.047	5.30E-01
rs6443750	C/T	NA in COURAGE PD											
rs865809	A/G	0.031	0.046	5.08E-01	-0.045	0.049	3.60E-01	0.017	0.037	6.48E-01	-0.001	0.039	9.70E-01
rs9816226	T/A	0.019	0.050	7.03E-01	0.001	0.051	9.88E-01	0.005	0.043	9.06E-01	0.032	0.052	5.35E-01
rs7616009	G/A	-0.070	0.074	3.41E-01	0.001	0.073	9.92E-01	-0.023	0.056	6.87E-01	-0.077	0.045	8.50E-02
rs6803161	T/C	-0.001	0.040	9.80E-01	-0.032	0.056	5.74E-01	-0.007	0.031	8.26E-01	-0.057	0.033	8.72E-02
rs2051559	C/T	0.000	0.057	9.98E-01	0.054	0.060	3.69E-01	0.028	0.045	5.32E-01	0.026	0.049	5.96E-01
rs12642970	G/C	Excluded for MR											
rs994596	T/C	0.086	0.040	3.10E-02	-0.045	0.041	2.71E-01	0.032	0.031	2.99E-01	-0.012	0.034	7.13E-01
rs34811474	G/A	NA in COURAGE PD											
rs73213484	A/T	-0.086	0.049	7.67E-02	-0.040	0.051	4.32E-01	-0.059	0.039	1.25E-01	-0.079	0.042	5.78E-02
rs337637	G/A	-0.044	0.042	2.90E-01	0.079	0.041	5.63E-02	0.024	0.038	5.36E-01	-0.009	0.034	7.86E-01
rs10938397	G/A	0.001	0.038	9.72E-01	-0.004	0.039	9.20E-01	-0.033	0.030	2.73E-01	0.006	0.042	8.93E-01
rs2271046	T/A	-0.013	0.042	7.60E-01	-0.007	0.045	8.68E-01	-0.011	0.034	7.42E-01	-0.016	0.037	6.65E-01
rs1492767	T/C	-0.013	0.038	7.42E-01	0.028	0.039	4.73E-01	0.025	0.030	4.01E-01	-0.012	0.032	6.97E-01

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs2192158	A/G	0.007	0.038	8.63E-01	0.001	0.039	9.87E-01	0.035	0.030	2.40E-01	-0.030	0.039	4.41E-01
rs1346841	G/A	-0.059	0.039	1.26E-01	0.056	0.047	2.35E-01	-0.021	0.034	5.35E-01	0.011	0.032	7.40E-01
rs10002111	A/G	0.063	0.045	1.59E-01	0.002	0.047	9.57E-01	0.047	0.035	1.75E-01	-0.012	0.038	7.52E-01
rs10033843	A/G	-0.030	0.061	6.26E-01	-0.028	0.046	5.47E-01	-0.024	0.049	6.29E-01	-0.085	0.038	2.39E-02
rs72649373	C/T	0.009	0.055	8.69E-01	0.018	0.056	7.53E-01	0.053	0.042	2.05E-01	-0.008	0.046	8.57E-01
rs4148155	A/G	0.004	0.064	9.44E-01	0.118	0.066	7.16E-02	0.015	0.050	7.73E-01	0.078	0.054	1.48E-01
rs4286488	A/G	-0.008	0.045	8.63E-01	0.004	0.047	9.24E-01	-0.015	0.035	6.64E-01	0.013	0.038	7.41E-01
rs7678054	G/A	0.056	0.038	1.40E-01	0.012	0.039	7.54E-01	0.025	0.030	3.89E-01	0.040	0.032	2.02E-01
rs3796432	G/T	-0.009	0.054	8.72E-01	0.031	0.040	4.41E-01	0.009	0.039	8.07E-01	-0.050	0.033	1.26E-01
rs13107325	T/C	-0.195	0.074	8.14E-03	0.012	0.074	8.67E-01	-0.110	0.057	5.30E-02	-0.048	0.063	4.51E-01
rs326893	T/C	-0.018	0.039	6.43E-01	-0.022	0.040	5.87E-01	-0.021	0.031	4.87E-01	0.026	0.033	4.20E-01
rs7696649	A/G	-0.008	0.054	8.90E-01	0.024	0.043	5.79E-01	-0.046	0.045	3.05E-01	0.012	0.034	7.29E-01
rs4864201	T/C	0.032	0.040	4.27E-01	0.002	0.040	9.55E-01	0.006	0.032	8.41E-01	0.008	0.033	8.07E-01
rs1296328	A/C	0.015	0.038	7.01E-01	0.075	0.055	1.74E-01	-0.019	0.030	5.38E-01	0.072	0.032	2.59E-02
rs17367750	C/T	0.060	0.058	3.03E-01	-0.025	0.042	5.49E-01	0.029	0.044	5.04E-01	-0.041	0.034	2.30E-01
rs9992189	G/C	0.030	0.051	5.56E-01	Excluded for MR						0.031	0.032	3.36E-01
rs3914628	T/C	-0.056	0.053	2.87E-01	-0.019	0.055	7.34E-01	-0.075	0.041	6.87E-02	-0.033	0.045	4.62E-01
rs750090	T/C	-0.104	0.040	1.03E-02	-0.056	0.041	1.76E-01	-0.049	0.032	1.22E-01	-0.083	0.033	1.32E-02
rs13110266	G/A	0.057	0.038	1.39E-01	-0.056	0.040	1.65E-01	-0.004	0.030	8.83E-01	0.014	0.040	7.24E-01
rs7685628	A/T	-0.055	0.038	1.45E-01	0.008	0.052	8.84E-01	-0.043	0.030	1.52E-01	0.010	0.032	7.59E-01
rs1522569	T/G	-0.113	0.047	1.62E-02	0.083	0.049	9.05E-02	-0.012	0.037	7.49E-01	-0.040	0.040	3.08E-01
rs1437842	G/A	0.012	0.038	7.46E-01	-0.012	0.057	8.35E-01	-0.027	0.030	3.74E-01	-0.007	0.032	8.25E-01
rs6850421	A/G	0.070	0.038	6.56E-02	0.029	0.039	4.55E-01	0.044	0.029	1.39E-01	0.047	0.032	1.39E-01
rs35408866	A/G	0.063	0.057	2.67E-01	-0.089	0.060	1.40E-01	-0.013	0.045	7.74E-01	0.048	0.048	3.15E-01
rs698147	A/G	0.019	0.045	6.71E-01	0.047	0.043	2.80E-01	0.046	0.035	1.86E-01	0.004	0.032	9.00E-01
rs6890310	G/A	0.090	0.041	2.81E-02	0.096	0.043	2.55E-02	0.074	0.032	2.20E-02	0.066	0.035	5.69E-02
rs7730004	T/C	-0.014	0.041	7.31E-01	-0.041	0.043	3.31E-01	-0.021	0.032	5.12E-01	-0.022	0.034	5.12E-01
rs116374395	A/G	-0.008	0.094	9.36E-01	-0.085	0.129	5.10E-01	0.027	0.072	7.08E-01	-0.035	0.079	6.53E-01
rs150215901	T/A	Excluded for MR											
rs4865796	G/A	0.003	0.040	9.40E-01	0.011	0.041	7.94E-01	0.000	0.031	9.92E-01	0.013	0.034	7.03E-01
rs13186194	T/C	-0.020	0.039	6.06E-01	-0.014	0.041	7.22E-01	-0.018	0.031	5.61E-01	-0.017	0.033	6.04E-01
rs4700608	C/T	0.037	0.054	4.96E-01	-0.012	0.039	7.61E-01	-0.001	0.041	9.71E-01	0.015	0.040	7.10E-01
rs10050620	C/T	0.003	0.040	9.37E-01	-0.079	0.041	5.70E-02	-0.035	0.041	3.93E-01	-0.043	0.034	2.00E-01
rs1159692	A/C	-0.028	0.038	4.68E-01	-0.015	0.057	8.00E-01	-0.014	0.038	7.04E-01	-0.018	0.032	5.62E-01
rs2112347	T/G	0.041	0.039	2.87E-01	-0.019	0.040	6.26E-01	0.019	0.030	5.24E-01	-0.005	0.032	8.83E-01
rs10942267	A/G	-0.042	0.041	3.01E-01	0.004	0.043	9.32E-01	-0.030	0.032	3.57E-01	-0.046	0.035	1.90E-01
rs2962334	T/G	0.095	0.128	4.56E-01	0.038	0.130	7.69E-01	0.084	0.097	3.88E-01	0.108	0.104	2.97E-01
rs1501673	A/G	-0.040	0.069	5.65E-01	-0.013	0.054	8.15E-01	0.016	0.056	7.70E-01	-0.055	0.062	3.70E-01
rs12652212	G/A	0.037	0.039	3.45E-01	0.001	0.039	9.85E-01	0.021	0.030	4.89E-01	0.030	0.032	3.47E-01
rs7713317	G/A	0.008	0.042	8.54E-01	-0.003	0.043	9.47E-01	-0.005	0.047	9.13E-01	0.016	0.035	6.39E-01
rs6882366	C/T	-0.026	0.039	5.02E-01	-0.015	0.040	7.11E-01	-0.002	0.030	9.42E-01	-0.006	0.033	8.57E-01
rs11739877	T/C	0.036	0.039	3.57E-01	0.007	0.045	8.76E-01	0.005	0.030	8.71E-01	0.013	0.039	7.49E-01
rs6888194	C/T	-0.054	0.056	3.39E-01	0.045	0.056	4.29E-01	-0.006	0.043	8.83E-01	0.001	0.046	9.75E-01
rs40067	G/A	-0.086	0.068	2.09E-01	-0.002	0.051	9.72E-01	-0.030	0.039	4.35E-01	0.009	0.042	8.36E-01
rs459552	T/A	-0.039	0.059	5.05E-01	0.014	0.057	8.09E-01	-0.019	0.046	6.80E-01	-0.036	0.069	6.03E-01
rs6893539	C/A	-0.007	0.041	8.72E-01	-0.029	0.055	5.96E-01	0.012	0.032	7.20E-01	-0.047	0.035	1.73E-01
rs6864049	G/A	0.020	0.038	5.93E-01	-0.044	0.056	4.39E-01	-0.015	0.029	6.11E-01	0.021	0.032	5.14E-01

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs6886072	C/T	-0.013	0.037	7.26E-01	-0.016	0.052	7.51E-01	-0.025	0.029	3.93E-01	-0.012	0.031	6.99E-01
rs13174863	G/A	-0.034	0.053	5.14E-01	0.006	0.053	9.05E-01	-0.019	0.040	6.34E-01	-0.022	0.043	6.06E-01
rs17405603	T/A	-0.027	0.044	5.35E-01	0.056	0.045	2.10E-01	0.029	0.034	3.91E-01	0.017	0.036	6.43E-01
rs2910026	C/T	-0.022	0.042	6.06E-01	-0.007	0.044	8.64E-01	-0.009	0.033	7.85E-01	-0.026	0.035	4.61E-01
rs7715256	G/T	0.082	0.056	1.47E-01	0.014	0.039	7.18E-01	0.027	0.029	3.64E-01	0.027	0.039	4.88E-01
rs7734385	G/A	-0.052	0.057	3.60E-01	-0.016	0.040	6.79E-01	-0.052	0.030	8.60E-02	-0.042	0.040	2.92E-01
rs4921301	C/T	0.086	0.062	1.68E-01	0.048	0.074	5.16E-01	0.011	0.037	7.66E-01	0.067	0.040	9.21E-02
rs2861089	A/T	0.102	0.038	7.54E-03	Excluded for MR			0.030	0.030	3.22E-01	0.028	0.032	3.84E-01
rs7727781	T/C	0.011	0.038	7.79E-01	0.021	0.039	5.87E-01	0.016	0.037	6.72E-01	0.068	0.032	3.20E-02
rs2053682	A/C	-0.046	0.040	2.56E-01	-0.046	0.042	2.72E-01	-0.082	0.042	5.24E-02	-0.032	0.043	4.50E-01
rs6556301	G/T	-0.032	0.041	4.32E-01	-0.011	0.049	8.28E-01	-0.015	0.042	7.26E-01	-0.058	0.033	7.97E-02
rs2228213	G/A	0.031	0.039	4.33E-01	-0.003	0.040	9.49E-01	0.026	0.031	4.03E-01	-0.023	0.033	4.84E-01
rs11757278	T/C	0.012	0.041	7.80E-01	0.011	0.042	7.88E-01	-0.003	0.032	9.27E-01	0.001	0.034	9.76E-01
rs3806114	G/A	0.047	0.042	2.66E-01	-0.009	0.043	8.38E-01	0.023	0.033	4.89E-01	0.022	0.035	5.30E-01
rs2066295	A/G	0.015	0.059	7.96E-01	0.022	0.046	6.25E-01	-0.005	0.044	9.16E-01	0.025	0.037	4.94E-01
rs3115667	C/T	-0.004	0.059	9.47E-01	-0.132	0.046	4.05E-03	-0.078	0.035	2.40E-02	-0.085	0.036	1.95E-02
rs2281819	T/A	-0.003	0.059	9.53E-01	0.064	0.046	1.67E-01	0.008	0.044	8.55E-01	0.041	0.038	2.79E-01
rs2744974	T/C	-0.054	0.039	1.66E-01	-0.006	0.041	8.90E-01	-0.029	0.031	3.51E-01	0.013	0.033	7.03E-01
rs2436728	A/G	-0.017	0.042	6.82E-01	-0.021	0.040	6.04E-01	-0.014	0.030	6.34E-01	-0.025	0.037	4.99E-01
rs1358980	C/T	0.059	0.042	1.60E-01	-0.045	0.057	4.25E-01	0.028	0.038	4.70E-01	0.001	0.032	9.64E-01
rs2206277	T/C	-0.115	0.048	1.79E-02	-0.011	0.049	8.21E-01	-0.061	0.038	1.04E-01	-0.025	0.040	5.31E-01
rs1327259	A/G	-0.098	0.039	1.13E-02	0.012	0.040	7.58E-01	-0.062	0.030	3.85E-02	-0.025	0.032	4.35E-01
rs6915002	T/C	-0.016	0.040	6.99E-01	-0.027	0.041	5.07E-01	-0.030	0.031	3.40E-01	0.035	0.033	2.90E-01
rs9370410	A/G	-0.032	0.043	4.56E-01	0.063	0.045	1.64E-01	0.012	0.039	7.61E-01	-0.002	0.035	9.50E-01
rs2622274	G/T	-0.009	0.038	8.21E-01	0.042	0.040	2.85E-01	-0.025	0.042	5.41E-01	0.048	0.032	1.37E-01
rs1293037	T/C	0.031	0.044	4.76E-01	0.037	0.045	4.05E-01	0.011	0.034	7.45E-01	0.041	0.037	2.69E-01
rs6921533	T/C	-0.010	0.042	8.09E-01	-0.020	0.043	6.38E-01	-0.021	0.033	5.19E-01	-0.038	0.035	2.75E-01
rs9294260	A/G	0.002	0.038	9.61E-01	0.034	0.049	4.86E-01	-0.034	0.029	2.42E-01	0.039	0.031	2.10E-01
rs6909685	C/T	-0.076	0.041	6.10E-02	-0.033	0.042	4.26E-01	-0.068	0.032	3.26E-02	-0.026	0.034	4.46E-01
rs9320823	C/T	-0.045	0.038	2.41E-01	0.013	0.040	7.44E-01	-0.031	0.030	3.00E-01	0.002	0.032	9.54E-01
rs57989773	C/T	0.018	0.045	6.83E-01	0.095	0.046	4.03E-02	0.069	0.035	4.91E-02	0.073	0.038	5.54E-02
rs156201	C/G	-0.066	0.044	1.34E-01	0.020	0.046	6.60E-01	-0.029	0.034	3.98E-01	0.002	0.037	9.51E-01
rs768023	A/G	0.073	0.039	5.92E-02	-0.003	0.051	9.61E-01	0.014	0.030	6.51E-01	0.025	0.033	4.40E-01
rs2357760	A/G	-0.027	0.046	5.59E-01	0.069	0.049	1.58E-01	-0.027	0.031	3.78E-01	0.060	0.034	7.25E-02
rs2875762	C/G	-0.024	0.043	5.74E-01	0.004	0.058	9.41E-01	-0.061	0.034	7.25E-02	0.014	0.036	7.04E-01
rs1268065	G/A	0.068	0.056	2.23E-01	-0.009	0.050	8.53E-01	0.021	0.030	4.79E-01	0.062	0.032	5.19E-02
rs9375702	C/T	0.006	0.041	8.82E-01	0.010	0.042	8.02E-01	0.024	0.032	4.58E-01	0.024	0.034	4.89E-01
rs2246012	C/T	-0.024	0.055	6.65E-01	Excluded for MR			-0.012	0.042	7.84E-01	0.013	0.044	7.62E-01
rs6922607	G/A	0.022	0.046	6.29E-01	-0.015	0.062	8.16E-01	-0.023	0.047	6.33E-01	-0.012	0.039	7.62E-01
rs765875	C/T	-0.010	0.038	7.96E-01	0.033	0.038	3.86E-01	0.031	0.029	2.86E-01	-0.026	0.031	4.03E-01
rs7760482	G/A	-0.064	0.039	9.69E-02	-0.075	0.040	5.99E-02	-0.062	0.030	3.99E-02	-0.026	0.032	4.31E-01
rs12527426	A/G	-0.021	0.041	6.06E-01	0.027	0.053	6.18E-01	0.015	0.042	7.22E-01	-0.055	0.035	1.14E-01
rs9478496	C/T	-0.011	0.050	8.30E-01	-0.015	0.053	7.86E-01	0.009	0.040	8.20E-01	-0.073	0.043	9.10E-02
rs13191362	A/G	-0.029	0.058	6.17E-01	0.029	0.070	6.82E-01	-0.021	0.045	6.48E-01	-0.023	0.048	6.40E-01
rs9458814	C/T	0.071	0.045	1.16E-01	0.012	0.062	8.51E-01	0.079	0.047	9.67E-02	-0.001	0.049	9.80E-01
rs6950388	A/G	-0.098	0.046	3.40E-02	0.000	0.065	9.99E-01	-0.028	0.036	4.33E-01	-0.037	0.039	3.45E-01
rs4721089	T/C	-0.026	0.044	5.55E-01	0.051	0.045	2.55E-01	0.021	0.034	5.44E-01	-0.014	0.037	6.97E-01

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs6463489	T/C							Excluded for MR					
rs4307239	G/A	-0.071	0.038	5.96E-02	0.072	0.039	6.42E-02	-0.012	0.029	6.72E-01	0.010	0.032	7.59E-01
rs213518	C/T	0.012	0.054	8.26E-01	-0.196	0.056	5.21E-04	-0.061	0.043	1.52E-01	-0.076	0.046	1.01E-01
rs215669	G/A	-0.031	0.050	5.36E-01	-0.015	0.040	7.04E-01	-0.017	0.047	7.13E-01	-0.010	0.033	7.69E-01
rs2108719	A/G	-0.049	0.059	4.11E-01	0.049	0.044	2.70E-01	-0.002	0.045	9.64E-01	-0.005	0.036	8.89E-01
rs2177433	C/T	0.024	0.048	6.13E-01	0.099	0.049	4.42E-02	0.067	0.037	7.25E-02	0.006	0.040	8.80E-01
rs2289379	C/T	-0.039	0.039	3.11E-01	0.012	0.040	7.59E-01	-0.034	0.030	2.60E-01	-0.009	0.033	7.85E-01
rs10499694	A/G	0.052	0.047	2.61E-01	-0.023	0.039	5.56E-01	0.037	0.038	3.24E-01	0.042	0.042	3.13E-01
rs11772246	T/C	-0.056	0.047	2.32E-01	0.050	0.049	3.11E-01	-0.009	0.037	8.10E-01	0.012	0.049	8.13E-01
rs17207196	C/T	0.037	0.042	3.77E-01	-0.046	0.043	2.86E-01	0.008	0.033	8.08E-01	-0.010	0.035	7.64E-01
rs17149254	T/C	0.033	0.061	5.82E-01	0.005	0.061	9.35E-01	0.002	0.047	9.66E-01	0.024	0.048	6.14E-01
rs6973656	G/A	0.089	0.050	7.45E-02	0.004	0.053	9.37E-01	0.066	0.038	8.70E-02	0.006	0.032	8.60E-01
rs1965529	A/G	-0.050	0.045	2.75E-01	-0.005	0.048	9.15E-01	0.000	0.036	9.94E-01	-0.046	0.039	2.33E-01
rs274628	C/A	0.013	0.039	7.49E-01	-0.018	0.041	6.61E-01	0.024	0.031	4.32E-01	-0.003	0.044	9.39E-01
rs2283006	A/G	-0.012	0.054	8.30E-01	-0.023	0.065	7.25E-01	-0.056	0.043	1.95E-01	0.010	0.049	8.47E-01
rs13240600	A/G	-0.051	0.052	3.26E-01	-0.039	0.054	4.73E-01	-0.074	0.041	6.99E-02	-0.032	0.044	4.63E-01
rs1721447	G/T	0.077	0.038	4.42E-02	0.019	0.049	7.00E-01	0.033	0.033	3.10E-01	0.046	0.037	2.08E-01
rs2396625	T/A	Excluded for MR			-0.037	0.039	3.50E-01	Excluded for MR					
rs13245051	A/G	0.052	0.040	2.00E-01	-0.004	0.042	9.19E-01	0.012	0.032	7.05E-01	0.061	0.034	7.15E-02
rs10261050	T/C	0.035	0.038	3.55E-01	0.035	0.039	3.70E-01	0.010	0.030	7.27E-01	0.015	0.032	6.36E-01
rs2283093	T/C	0.034	0.046	4.62E-01	0.020	0.047	6.76E-01	0.022	0.036	5.47E-01	0.039	0.038	3.04E-01
rs7802342	G/T	-0.029	0.042	4.84E-01	0.031	0.044	4.74E-01	-0.020	0.033	5.40E-01	-0.001	0.035	9.73E-01
rs11525873	T/C	-0.046	0.068	4.97E-01	Excluded for MR			-0.070	0.053	1.86E-01	-0.058	0.056	2.99E-01
rs11773362	C/T	-0.008	0.041	8.40E-01	-0.044	0.042	2.90E-01	-0.040	0.035	2.45E-01	-0.020	0.034	5.65E-01
rs2907948	G/A	-0.091	0.043	3.43E-02	0.031	0.045	4.92E-01	-0.043	0.046	3.50E-01	-0.039	0.036	2.81E-01
rs56211164	G/A	0.006	0.045	8.86E-01	0.001	0.047	9.91E-01	0.050	0.052	3.33E-01	0.050	0.052	3.36E-01
rs1700082	C/G	0.003	0.041	9.40E-01	0.019	0.043	6.60E-01	-0.027	0.032	4.04E-01	0.051	0.035	1.37E-01
rs4240673	T/C	0.030	0.038	4.31E-01	0.040	0.060	5.05E-01	0.026	0.029	3.68E-01	0.029	0.032	3.66E-01
rs13263601	C/A	0.029	0.039	4.56E-01	-0.021	0.041	6.09E-01	0.000	0.039	9.93E-01	0.020	0.042	6.33E-01
rs10110189	C/T	Excluded for MR											
rs10101364	T/C	-0.014	0.041	7.34E-01	0.034	0.043	4.24E-01	-0.014	0.032	6.66E-01	0.057	0.035	9.66E-02
rs73225274	G/A	-0.099	0.054	6.91E-02	0.023	0.081	7.75E-01	-0.022	0.043	6.05E-01	0.007	0.046	8.72E-01
rs13249650	A/T	Excluded for MR											
rs1421334	A/C	-0.029	0.038	4.40E-01	-0.023	0.039	5.64E-01	-0.005	0.030	8.65E-01	0.014	0.032	6.70E-01
rs2466103	G/T	-0.062	0.040	1.22E-01	0.008	0.056	8.85E-01	-0.037	0.031	2.45E-01	-0.011	0.034	7.49E-01
rs6468266	T/A	0.010	0.039	7.88E-01	-0.018	0.054	7.43E-01	0.022	0.031	4.68E-01	-0.006	0.033	8.49E-01
rs12681792	A/C	0.005	0.066	9.41E-01	-0.022	0.052	6.67E-01	-0.016	0.040	6.90E-01	0.033	0.041	4.28E-01
rs12334877	G/A	0.033	0.054	5.45E-01	0.068	0.072	3.47E-01	0.030	0.051	5.55E-01	0.027	0.039	4.86E-01
rs1808629	G/A	0.043	0.041	2.92E-01	-0.045	0.054	4.04E-01	0.033	0.041	4.26E-01	-0.032	0.035	3.52E-01
rs17405819	T/C	-0.061	0.041	1.33E-01	0.023	0.062	7.06E-01	-0.023	0.032	4.72E-01	-0.009	0.043	8.31E-01
rs2196618	G/A	0.052	0.060	3.85E-01	-0.035	0.045	4.31E-01	-0.007	0.034	8.46E-01	0.018	0.036	6.27E-01
rs12386885	T/C	-0.056	0.073	4.42E-01	0.040	0.055	4.70E-01	-0.036	0.058	5.36E-01	-0.001	0.044	9.84E-01
rs2120710	A/G	-0.017	0.040	6.76E-01	0.011	0.042	7.86E-01	0.025	0.032	4.23E-01	-0.027	0.034	4.29E-01
rs12680842	A/G	0.059	0.039	1.34E-01	-0.025	0.041	5.34E-01	0.003	0.031	9.31E-01	-0.018	0.033	5.98E-01
rs1383592	A/G	0.016	0.045	7.14E-01	-0.005	0.047	9.14E-01	0.007	0.036	8.43E-01	0.028	0.053	5.96E-01
rs3808477	C/T	-0.029	0.044	5.17E-01	-0.037	0.056	5.08E-01	0.032	0.035	3.51E-01	-0.058	0.043	1.82E-01
rs72673947	G/A	-0.083	0.059	1.61E-01	-0.100	0.062	1.07E-01	-0.097	0.047	3.95E-02	-0.061	0.050	2.23E-01

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs6470144	T/G	-0.078	0.040	5.24E-02	0.053	0.041	2.00E-01	-0.012	0.031	7.05E-01	-0.008	0.033	8.19E-01
rs7842934	C/T	-0.091	0.074	2.18E-01	0.008	0.079	9.19E-01	-0.049	0.060	4.14E-01	0.031	0.063	6.19E-01
rs305256	C/T	-0.030	0.059	6.17E-01	0.017	0.065	7.91E-01	-0.025	0.048	6.00E-01	0.006	0.046	9.03E-01
rs16906838	C/T	0.035	0.079	6.53E-01	-0.001	0.085	9.95E-01	-0.022	0.062	7.18E-01	0.107	0.071	1.31E-01
rs11782074	T/G	0.018	0.040	6.57E-01	-0.021	0.042	6.14E-01	-0.024	0.032	4.54E-01	0.005	0.034	8.75E-01
rs10099330	G/A	-0.088	0.055	1.12E-01	0.009	0.039	8.16E-01	-0.044	0.029	1.35E-01	0.004	0.041	9.20E-01
rs10975933	C/G	0.031	0.040	4.35E-01	-0.036	0.041	3.76E-01	0.011	0.031	7.36E-01	-0.030	0.034	3.67E-01
rs1948080	T/G	-0.035	0.039	3.59E-01	-0.013	0.039	7.48E-01	-0.024	0.046	6.07E-01	0.061	0.033	6.00E-02
rs10961649	T/C	-0.001	0.039	9.78E-01	-0.010	0.042	8.13E-01	-0.005	0.041	9.02E-01	0.041	0.033	2.22E-01
rs4740619	T/C	-0.013	0.038	7.23E-01	-0.029	0.039	4.65E-01	-0.022	0.030	4.70E-01	-0.033	0.032	3.09E-01
rs10962550	C/G	0.004	0.048	9.36E-01	-0.056	0.072	4.36E-01	-0.061	0.038	1.12E-01	0.042	0.040	2.98E-01
rs10811868	G/A	-0.020	0.040	6.05E-01	-0.020	0.041	6.23E-01	-0.032	0.031	3.05E-01	-0.003	0.033	9.18E-01
rs10968114	A/C	0.002	0.039	9.53E-01	0.058	0.039	1.38E-01	0.011	0.030	7.20E-01	0.054	0.032	8.89E-02
rs1412235	C/G	0.045	0.042	2.87E-01	0.058	0.044	1.80E-01	0.044	0.033	1.82E-01	0.055	0.035	1.20E-01
rs10121187	C/G	Excluded for MR											
rs2275003	A/G	-0.052	0.038	1.77E-01	0.022	0.056	6.92E-01	0.005	0.030	8.61E-01	-0.027	0.045	5.49E-01
rs13296413	C/T	-0.031	0.038	4.11E-01	-0.068	0.059	2.49E-01	-0.093	0.047	4.58E-02	-0.044	0.032	1.69E-01
rs2134858	C/T	0.039	0.038	3.02E-01	-0.051	0.054	3.51E-01	0.003	0.040	9.48E-01	-0.034	0.032	2.81E-01
rs7861160	T/C	-0.003	0.063	9.61E-01	-0.050	0.040	2.09E-01	-0.015	0.030	6.12E-01	0.010	0.032	7.64E-01
rs1999433	C/T	0.004	0.038	9.18E-01	0.006	0.039	8.75E-01	0.003	0.030	9.12E-01	0.001	0.032	9.87E-01
rs2777768	A/G	0.028	0.043	5.14E-01	-0.059	0.044	1.83E-01	-0.031	0.034	3.51E-01	0.003	0.036	9.39E-01
rs7357754	G/A	0.054	0.049	2.72E-01	-0.065	0.039	9.88E-02	-0.006	0.030	8.48E-01	-0.011	0.032	7.32E-01
rs10992867	A/G	0.017	0.065	7.98E-01	0.011	0.043	7.94E-01	-0.012	0.036	7.34E-01	-0.023	0.046	6.22E-01
rs7025938	G/C	-0.016	0.039	6.87E-01	0.023	0.041	5.71E-01	0.018	0.031	5.67E-01	0.011	0.034	7.51E-01
rs7024334	T/G	-0.131	0.045	4.03E-03	-0.011	0.058	8.53E-01	-0.060	0.049	2.21E-01	-0.042	0.038	2.65E-01
rs1928295	T/C	0.036	0.044	4.11E-01	0.059	0.039	1.29E-01	0.053	0.034	1.14E-01	0.030	0.032	3.42E-01
rs1877875	C/T	-0.011	0.038	7.76E-01	-0.065	0.039	9.86E-02	0.000	0.030	9.87E-01	-0.001	0.032	9.77E-01
rs13298487	T/C	Excluded for MR											
rs10733682	A/G	0.015	0.052	7.68E-01	0.061	0.040	1.26E-01	0.026	0.031	3.98E-01	0.001	0.033	9.84E-01
rs2267958	G/A	Excluded for MR											
rs4740383	A/G	0.040	0.040	3.10E-01	0.101	0.041	1.31E-02	0.046	0.031	1.36E-01	0.075	0.033	2.25E-02
rs10858334	G/C	-0.041	0.056	4.68E-01	-0.123	0.074	9.47E-02	-0.040	0.059	4.99E-01	-0.065	0.061	2.86E-01
rs7907470 ^a	G/A	0.110	0.130	4.00E-01	-0.024	0.069	7.29E-01	0.019	0.061	7.57E-01	0.021	0.076	7.78E-01
rs7893571	T/G	-0.070	0.040	8.34E-02	-0.010	0.042	8.17E-01	-0.037	0.032	2.42E-01	-0.041	0.034	2.21E-01
rs76638898	G/A	Excluded for MR											
rs7084454	A/G	0.028	0.042	5.00E-01	-0.011	0.042	7.90E-01	-0.014	0.033	6.57E-01	0.048	0.035	1.67E-01
rs10829164	T/C	-0.056	0.055	3.08E-01	-0.069	0.055	2.06E-01	-0.013	0.042	7.57E-01	-0.074	0.047	1.17E-01
rs4097319	T/G	-0.023	0.056	6.85E-01	0.031	0.040	4.43E-01	-0.009	0.031	7.60E-01	-0.003	0.033	9.24E-01
rs12765914	T/C	0.002	0.073	9.81E-01	-0.040	0.070	5.61E-01	-0.028	0.055	6.06E-01	-0.062	0.058	2.87E-01
rs1624134	C/G	-0.005	0.041	9.01E-01	0.035	0.041	3.88E-01	0.008	0.031	7.89E-01	0.018	0.034	5.84E-01
rs12259464	A/G	0.024	0.040	5.51E-01	0.013	0.057	8.22E-01	0.073	0.040	6.59E-02	0.018	0.032	5.76E-01
rs7070670	C/T	0.023	0.041	5.73E-01	0.026	0.043	5.41E-01	0.036	0.032	2.70E-01	0.003	0.034	9.34E-01
rs10761785	G/T	-0.056	0.038	1.40E-01	-0.061	0.039	1.25E-01	-0.050	0.041	2.20E-01	-0.078	0.032	1.48E-02
rs12098284	T/C	-0.044	0.056	4.30E-01	-0.007	0.057	8.97E-01	-0.032	0.044	4.58E-01	-0.002	0.048	9.75E-01
rs11001259	T/A	NA in COURAGE PD											
rs7899106	G/A	-0.054	0.127	6.67E-01	Excluded for MR			-0.046	0.073	5.32E-01	0.027	0.077	7.27E-01
rs10788494	C/G	Excluded for MR											

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs147568678	T/C	0.010	0.074	8.93E-01	-0.046	0.051	3.66E-01	-0.015	0.039	7.09E-01	-0.028	0.042	4.93E-01
rs2439823	G/A	-0.034	0.041	4.08E-01	0.009	0.063	8.89E-01	0.004	0.032	8.93E-01	-0.029	0.034	3.97E-01
rs17094222	C/T	0.056	0.047	2.33E-01	0.036	0.048	4.47E-01	0.088	0.036	1.52E-02	-0.010	0.039	7.94E-01
rs11594179	C/T	0.061	0.046	1.81E-01	-0.006	0.048	8.94E-01	0.006	0.053	9.03E-01	0.047	0.039	2.38E-01
rs79780963	T/C	-0.041	0.066	5.37E-01	-0.024	0.068	7.27E-01	0.010	0.051	8.51E-01	-0.089	0.056	1.11E-01
rs7903146	C/T	0.054	0.062	3.84E-01	-0.012	0.055	8.34E-01	-0.019	0.033	5.66E-01	0.033	0.035	3.47E-01
rs2257791	G/A	-0.045	0.044	3.09E-01	0.039	0.046	4.05E-01	-0.026	0.045	5.67E-01	-0.002	0.038	9.63E-01
rs845084	A/G	-0.027	0.042	5.13E-01	-0.009	0.043	8.39E-01	-0.029	0.033	3.83E-01	-0.001	0.035	9.89E-01
rs17636031	C/T	Excluded for MR											
rs4880341	C/T	-0.041	0.038	2.82E-01	0.018	0.039	6.39E-01	-0.022	0.030	4.58E-01	0.021	0.041	6.06E-01
rs11246136	C/A	Excluded for MR											
rs12421848	G/A	0.009	0.042	8.22E-01	0.026	0.041	5.20E-01	0.024	0.033	4.60E-01	-0.002	0.039	9.68E-01
rs4256980	G/C	-0.001	0.038	9.72E-01	0.012	0.040	7.60E-01	0.006	0.030	8.47E-01	-0.010	0.032	7.52E-01
rs900144	T/C	0.050	0.039	2.00E-01	0.034	0.040	3.97E-01	0.067	0.030	2.67E-02	0.011	0.032	7.30E-01
rs2074314	T/C	-0.042	0.040	2.98E-01	-0.024	0.040	5.58E-01	-0.013	0.031	6.73E-01	-0.046	0.036	2.03E-01
rs6265	C/T	0.044	0.047	3.54E-01	-0.006	0.048	9.05E-01	0.022	0.037	5.56E-01	0.031	0.040	4.41E-01
rs570463	C/A	-0.047	0.040	2.36E-01	-0.053	0.041	1.96E-01	-0.047	0.031	1.36E-01	0.026	0.046	5.73E-01
rs11030618	T/C	0.006	0.038	8.82E-01	0.024	0.054	6.50E-01	0.002	0.030	9.56E-01	0.002	0.032	9.62E-01
rs2065418	T/G	-0.020	0.045	6.64E-01	-0.017	0.040	6.68E-01	0.006	0.031	8.42E-01	-0.019	0.033	5.59E-01
rs2862996	G/T	0.050	0.042	2.32E-01	0.114	0.067	8.89E-02	0.061	0.043	1.51E-01	0.042	0.045	3.46E-01
rs10742752	C/T	0.030	0.038	4.26E-01	-0.024	0.040	5.51E-01	0.009	0.030	7.70E-01	0.019	0.032	5.48E-01
rs118081010	T/C	-0.065	0.156	6.78E-01	-0.188	0.163	2.49E-01	-0.017	0.117	8.85E-01	-0.005	0.139	9.72E-01
rs7124681	A/C	0.048	0.039	2.18E-01	0.010	0.039	7.89E-01	0.025	0.030	4.11E-01	0.067	0.032	3.64E-02
rs6591407	C/A	-0.114	0.047	1.57E-02	0.051	0.048	2.89E-01	-0.010	0.037	7.97E-01	-0.065	0.039	9.97E-02
rs562664	C/T	-0.031	0.049	5.32E-01	-0.007	0.069	9.13E-01	-0.049	0.049	3.15E-01	-0.011	0.041	7.93E-01
rs7102454	C/T	0.017	0.040	6.72E-01	0.056	0.041	1.70E-01	0.017	0.037	6.41E-01	0.017	0.040	6.63E-01
rs592483	C/T	0.064	0.039	1.01E-01	-0.048	0.040	2.28E-01	0.034	0.031	2.59E-01	-0.003	0.033	9.18E-01
rs12282785	C/A	-0.086	0.044	4.76E-02	0.024	0.045	6.01E-01	-0.034	0.034	3.14E-01	-0.037	0.037	3.14E-01
rs349088	C/A	-0.040	0.040	3.23E-01	-0.084	0.044	5.57E-02	-0.053	0.030	7.96E-02	-0.033	0.031	2.92E-01
rs10741329	A/G	-0.008	0.040	8.44E-01	-0.041	0.041	3.16E-01	-0.014	0.031	6.49E-01	-0.012	0.034	7.26E-01
rs3019466	C/T	-0.017	0.051	7.46E-01	0.170	0.054	1.66E-03	0.061	0.041	1.37E-01	0.061	0.044	1.62E-01
rs2605603	G/A	-0.021	0.037	5.69E-01	-0.006	0.039	8.79E-01	0.004	0.029	8.78E-01	-0.064	0.031	4.25E-02
rs2513999	G/A	-0.075	0.053	1.60E-01	-0.036	0.055	5.14E-01	-0.050	0.042	2.31E-01	-0.048	0.045	2.86E-01
rs12286929	G/A	0.016	0.041	7.01E-01	-0.113	0.039	3.75E-03	-0.056	0.029	5.63E-02	-0.014	0.037	6.97E-01
rs76942203	A/G	-0.089	0.079	2.61E-01	-0.211	0.081	9.00E-03	-0.169	0.063	7.01E-03	-0.042	0.066	5.29E-01
rs3825061	T/C	0.058	0.039	1.38E-01	-0.003	0.041	9.39E-01	0.033	0.031	2.84E-01	-0.008	0.033	8.06E-01
rs11218510	G/A	-0.023	0.039	5.60E-01	0.018	0.040	6.50E-01	-0.002	0.030	9.54E-01	0.029	0.033	3.75E-01
rs35483388	T/C	0.016	0.039	6.90E-01	-0.027	0.040	4.92E-01	0.022	0.030	4.62E-01	-0.022	0.032	4.98E-01
rs7944782	G/T	0.045	0.061	4.65E-01	-0.023	0.039	5.59E-01	-0.006	0.030	8.51E-01	-0.004	0.032	8.98E-01
rs2007518	G/A	0.004	0.038	9.18E-01	0.004	0.060	9.52E-01	-0.002	0.030	9.54E-01	-0.040	0.032	2.16E-01
rs1941213	A/C	-0.017	0.050	7.39E-01	0.002	0.050	9.66E-01	0.004	0.043	9.19E-01	-0.001	0.040	9.76E-01
rs329651	T/G	-0.065	0.046	1.61E-01	-0.089	0.048	6.13E-02	-0.096	0.036	7.93E-03	-0.058	0.039	1.41E-01
rs12364470	G/T	Excluded for MR											
rs11611246	T/G	0.010	0.049	8.43E-01	-0.057	0.050	2.51E-01	-0.040	0.038	2.97E-01	-0.023	0.040	5.63E-01
rs765125	C/T	-0.017	0.039	6.65E-01	-0.024	0.039	5.32E-01	-0.023	0.030	4.31E-01	0.006	0.032	8.52E-01
rs10772983	C/T	0.145	0.064	2.36E-02	-0.011	0.045	8.15E-01	0.059	0.036	1.06E-01	0.035	0.039	3.75E-01
rs11044430	A/T	-0.012	0.076	8.73E-01	0.067	0.054	2.15E-01	0.014	0.054	7.98E-01	0.075	0.044	8.75E-02

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs11046972	T/C	-0.110	0.065	9.25E-02	0.050	0.069	4.66E-01	-0.033	0.052	5.19E-01	-0.032	0.056	5.63E-01
rs10842240	C/G	0.025	0.054	6.43E-01	-0.086	0.057	1.30E-01	-0.014	0.043	7.41E-01	-0.023	0.046	6.23E-01
rs11170468	A/C	-0.025	0.044	5.77E-01	-0.044	0.046	3.33E-01	-0.023	0.034	5.03E-01	-0.017	0.037	6.43E-01
rs1350430	C/T	-0.019	0.038	6.22E-01	0.073	0.039	5.90E-02	0.006	0.030	8.34E-01	0.052	0.031	9.45E-02
rs1126930	C/G	Excluded for MR											
rs7138803	A/G	0.085	0.043	4.77E-02	0.047	0.040	2.38E-01	0.053	0.030	8.00E-02	0.080	0.032	1.37E-02
rs2271189	G/A	0.007	0.053	8.89E-01	0.019	0.040	6.41E-01	0.003	0.031	9.10E-01	0.011	0.033	7.44E-01
rs7975187	G/A	0.056	0.046	2.25E-01	0.068	0.047	1.52E-01	0.052	0.036	1.49E-01	0.083	0.039	3.09E-02
rs650198	C/T	0.013	0.040	7.52E-01	-0.043	0.042	3.00E-01	-0.041	0.032	2.00E-01	0.047	0.034	1.69E-01
rs11115176	T/C	-0.004	0.044	9.35E-01	0.001	0.045	9.74E-01	-0.003	0.034	9.29E-01	-0.054	0.036	1.39E-01
rs10506971	G/A	0.037	0.039	3.42E-01	0.074	0.040	6.38E-02	0.042	0.030	1.65E-01	0.012	0.033	7.02E-01
rs11105839	T/A	-0.005	0.070	9.45E-01	0.010	0.040	8.10E-01	0.006	0.030	8.33E-01	-0.025	0.043	5.63E-01
rs2712665	C/T	0.013	0.041	7.57E-01	0.077	0.042	6.78E-02	0.038	0.032	2.37E-01	0.001	0.034	9.86E-01
rs6539064	C/G	0.031	0.042	4.51E-01	0.013	0.043	7.71E-01	0.029	0.032	3.73E-01	0.002	0.035	9.64E-01
rs1860561	A/G	0.033	0.049	4.95E-01	-0.068	0.049	1.69E-01	-0.016	0.038	6.67E-01	0.008	0.040	8.42E-01
rs11066188	G/A	0.068	0.042	1.02E-01	0.056	0.044	2.04E-01	0.030	0.033	3.65E-01	0.068	0.035	5.63E-02
rs2707183	G/T	-0.039	0.039	3.15E-01	0.042	0.040	2.96E-01	0.019	0.030	5.28E-01	-0.028	0.033	3.88E-01
rs11615578	T/C	-0.051	0.083	5.39E-01	-0.060	0.058	3.04E-01	0.005	0.059	9.30E-01	-0.049	0.046	2.86E-01
rs12369179	C/T	0.074	0.077	3.36E-01	0.035	0.078	6.54E-01	0.040	0.060	5.02E-01	0.014	0.062	8.25E-01
rs11060853	G/A	0.108	0.038	4.54E-03	0.054	0.039	1.66E-01	0.087	0.039	2.73E-02	0.100	0.047	3.29E-02
rs11614340	C/T	0.026	0.043	5.41E-01	0.029	0.044	5.07E-01	0.022	0.033	5.15E-01	0.028	0.035	4.24E-01
rs9512648	A/G	-0.001	0.038	9.82E-01	-0.015	0.040	7.14E-01	-0.035	0.043	4.09E-01	-0.036	0.032	2.66E-01
rs7323	G/C	-0.091	0.043	3.55E-02	0.048	0.045	2.82E-01	-0.036	0.034	2.89E-01	-0.080	0.035	2.40E-02
rs4771218	G/A	-0.065	0.039	9.80E-02	0.013	0.050	8.00E-01	-0.045	0.030	1.35E-01	-0.024	0.035	4.91E-01
rs9595908	T/C	0.002	0.052	9.66E-01	-0.018	0.040	6.48E-01	-0.020	0.030	5.02E-01	0.024	0.032	4.68E-01
rs9603697	T/C	-0.007	0.041	8.65E-01	-0.050	0.054	3.53E-01	-0.023	0.033	4.85E-01	-0.003	0.034	9.36E-01
rs12429545	A/G	-0.036	0.059	5.45E-01	-0.125	0.065	5.33E-02	-0.042	0.052	4.22E-01	-0.028	0.048	5.52E-01
rs962796	T/C	0.002	0.053	9.74E-01	-0.034	0.049	4.80E-01	-0.023	0.041	5.81E-01	0.040	0.039	3.06E-01
rs9569777	G/T	0.023	0.051	6.56E-01	-0.045	0.053	3.95E-01	-0.044	0.039	2.68E-01	0.001	0.042	9.90E-01
rs9527895	C/T	-0.054	0.049	2.71E-01	0.073	0.052	1.60E-01	-0.033	0.039	3.99E-01	0.047	0.042	2.58E-01
rs8181823	C/A	-0.036	0.045	4.22E-01	-0.044	0.045	3.31E-01	-0.006	0.035	8.56E-01	-0.035	0.051	4.88E-01
rs9599161	T/C	-0.005	0.038	9.02E-01	0.073	0.040	6.82E-02	0.038	0.030	2.04E-01	0.019	0.032	5.44E-01
rs1441264	A/G	-0.010	0.045	8.26E-01	-0.038	0.048	4.28E-01	-0.025	0.030	4.03E-01	-0.055	0.043	1.95E-01
rs9531786	G/C	0.029	0.051	5.71E-01	0.020	0.040	6.13E-01	-0.026	0.031	4.00E-01	0.058	0.033	8.13E-02
rs77432547	G/A	-0.098	0.043	2.24E-02	0.045	0.044	3.10E-01	-0.037	0.033	2.69E-01	0.037	0.036	3.07E-01
rs1927790	C/T	-0.024	0.054	6.62E-01	-0.035	0.050	4.86E-01	-0.042	0.030	1.55E-01	-0.023	0.032	4.75E-01
rs9168	C/A	-0.049	0.042	2.40E-01	0.029	0.043	5.02E-01	-0.023	0.033	4.84E-01	0.012	0.045	7.81E-01
rs9888533	T/C	Excluded for MR											
rs9522183	G/T	0.017	0.039	6.58E-01	0.056	0.040	1.60E-01	0.071	0.030	2.07E-02	0.006	0.032	8.42E-01
rs12868881	A/T	-0.006	0.038	8.80E-01	0.030	0.039	4.52E-01	-0.013	0.030	6.55E-01	0.024	0.032	4.59E-01
rs10132280	C/A	0.090	0.068	1.83E-01	-0.066	0.044	1.33E-01	-0.014	0.033	6.74E-01	-0.022	0.047	6.34E-01
rs4981693	A/G	0.082	0.047	8.04E-02	-0.003	0.047	9.54E-01	0.014	0.038	7.03E-01	0.036	0.038	3.42E-01
rs225882	T/C	-0.017	0.061	7.77E-01	-0.030	0.042	4.78E-01	-0.001	0.044	9.89E-01	-0.001	0.043	9.82E-01
rs1958898	G/C	-0.027	0.047	5.71E-01	-0.035	0.049	4.79E-01	-0.011	0.037	7.77E-01	0.032	0.039	4.11E-01
rs61983990	A/G	-0.121	0.072	9.58E-02	-0.107	0.114	3.46E-01	-0.100	0.057	7.86E-02	-0.013	0.076	8.66E-01
rs4900714	T/G	-0.001	0.037	9.83E-01	0.012	0.039	7.53E-01	-0.026	0.044	5.61E-01	-0.012	0.031	6.95E-01
rs217669	C/T	-0.021	0.044	6.38E-01	0.007	0.045	8.83E-01	-0.023	0.047	6.21E-01	-0.011	0.045	8.01E-01

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs4430672	T/C	-0.065	0.047	1.66E-01	0.061	0.049	2.10E-01	0.016	0.048	7.37E-01	-0.021	0.040	5.89E-01
rs3902951	G/T	0.006	0.049	9.04E-01	-0.003	0.051	9.57E-01	-0.011	0.038	7.83E-01	0.003	0.041	9.44E-01
rs17182027	G/A	-0.016	0.052	7.59E-01	-0.008	0.040	8.36E-01	-0.008	0.030	7.89E-01	0.001	0.032	9.84E-01
rs7144011	T/G	-0.024	0.049	6.18E-01	-0.035	0.050	4.79E-01	-0.025	0.054	6.47E-01	0.026	0.040	5.10E-01
rs4517716	G/C	-0.005	0.045	9.11E-01	0.058	0.065	3.66E-01	-0.001	0.036	9.80E-01	0.052	0.038	1.73E-01
rs12888545	G/A	-0.038	0.045	4.01E-01	-0.027	0.058	6.39E-01	-0.035	0.035	3.18E-01	0.019	0.049	6.96E-01
rs1951455	C/T	0.014	0.042	7.35E-01	-0.046	0.043	2.85E-01	-0.005	0.033	8.71E-01	0.000	0.035	9.93E-01
rs942066	G/A	0.043	0.040	2.80E-01	-0.017	0.040	6.82E-01	0.034	0.031	2.75E-01	-0.025	0.033	4.54E-01
rs7161194	A/G	NA in COURAGE PD											
rs10145749	T/C	0.029	0.055	6.06E-01	-0.021	0.057	7.16E-01	-0.006	0.043	8.84E-01	-0.059	0.059	3.19E-01
rs4906263	G/C	-0.076	0.040	5.50E-02	0.026	0.041	5.33E-01	-0.002	0.031	9.40E-01	-0.042	0.034	2.08E-01
rs2273175	C/T	-0.012	0.064	8.47E-01	0.047	0.043	2.74E-01	0.023	0.046	6.07E-01	0.019	0.044	6.71E-01
rs12594043	C/G	Excluded for MR											
rs7172627	G/A	0.036	0.038	3.43E-01	-0.012	0.039	7.52E-01	0.020	0.029	5.04E-01	0.012	0.032	7.13E-01
rs11636611	T/C	-0.003	0.038	9.47E-01	-0.020	0.040	6.13E-01	-0.001	0.030	9.67E-01	-0.026	0.032	4.19E-01
rs9944219	G/A	-0.078	0.057	1.72E-01	0.033	0.051	5.26E-01	-0.068	0.045	1.34E-01	-0.010	0.032	7.47E-01
rs12912198	C/T	0.015	0.043	7.30E-01	0.017	0.044	7.05E-01	-0.002	0.033	9.46E-01	0.006	0.036	8.59E-01
rs6493498	T/C	-0.021	0.038	5.74E-01	-0.011	0.039	7.83E-01	-0.014	0.030	6.46E-01	-0.005	0.032	8.76E-01
rs10518694	A/C	-0.080	0.057	1.57E-01	0.015	0.059	7.93E-01	-0.001	0.044	9.75E-01	-0.069	0.049	1.56E-01
rs12439632	C/G	-0.165	0.060	6.28E-03	-0.012	0.059	8.44E-01	-0.075	0.046	1.03E-01	-0.055	0.048	2.56E-01
rs339991	G/A	0.018	0.038	6.42E-01	-0.053	0.039	1.77E-01	-0.010	0.030	7.29E-01	-0.033	0.043	4.39E-01
rs1559673	A/C	0.117	0.132	3.78E-01	0.176	0.131	1.81E-01	0.141	0.102	1.67E-01	-0.007	0.108	9.51E-01
rs2241423	G/A	-0.024	0.045	6.04E-01	0.071	0.046	1.23E-01	0.029	0.042	4.95E-01	0.001	0.038	9.78E-01
rs7171864	A/G	-0.094	0.042	2.45E-02	0.025	0.059	6.68E-01	-0.072	0.032	2.73E-02	0.017	0.035	6.28E-01
rs2470893	T/C	0.006	0.059	9.19E-01	0.038	0.067	5.72E-01	0.050	0.040	2.16E-01	0.027	0.049	5.86E-01
rs56151256	A/C	-0.089	0.043	4.10E-02	0.003	0.045	9.55E-01	-0.042	0.034	2.24E-01	-0.056	0.036	1.20E-01
rs12914623	G/C	-0.042	0.043	3.26E-01	-0.045	0.044	3.05E-01	-0.034	0.033	3.13E-01	-0.047	0.047	3.14E-01
rs72757415	G/T	0.005	0.050	9.19E-01	0.000	0.051	9.97E-01	-0.009	0.039	8.25E-01	0.030	0.041	4.61E-01
rs11633626	C/A	-0.006	0.055	9.12E-01	0.027	0.042	5.21E-01	0.012	0.032	7.11E-01	-0.012	0.034	7.15E-01
rs6496248	A/T	-0.001	0.039	9.81E-01	-0.003	0.041	9.33E-01	-0.013	0.030	6.65E-01	0.019	0.033	5.60E-01
rs12591120	T/C	-0.057	0.045	2.03E-01	0.038	0.062	5.34E-01	-0.001	0.044	9.77E-01	-0.010	0.052	8.51E-01
rs2715423	G/A	0.044	0.048	3.63E-01	-0.018	0.049	7.17E-01	0.020	0.038	5.93E-01	0.017	0.039	6.57E-01
rs214249	T/G	-0.071	0.040	7.17E-02	-0.025	0.040	5.37E-01	-0.031	0.030	3.08E-01	-0.040	0.033	2.14E-01
rs12448257	A/G	-0.065	0.047	1.72E-01	-0.072	0.049	1.40E-01	-0.055	0.037	1.37E-01	-0.090	0.040	2.47E-02
rs879620	T/C	-0.045	0.043	2.93E-01	0.020	0.045	6.60E-01	0.001	0.030	9.77E-01	-0.054	0.033	9.45E-02
rs2058527	G/T	0.033	0.060	5.84E-01	-0.013	0.044	7.66E-01	0.006	0.034	8.56E-01	-0.007	0.037	8.52E-01
rs9926784	T/C	0.003	0.060	9.55E-01	0.028	0.050	5.73E-01	0.038	0.039	3.35E-01	-0.027	0.049	5.81E-01
rs194809	A/G	0.033	0.063	6.05E-01	-0.065	0.049	1.82E-01	-0.004	0.038	9.19E-01	0.003	0.040	9.36E-01
rs2342892	T/G	-0.006	0.038	8.83E-01	0.035	0.049	4.74E-01	0.017	0.030	5.68E-01	0.025	0.031	4.32E-01
rs7498665	G/A	-0.056	0.040	1.61E-01	0.013	0.041	7.43E-01	-0.043	0.031	1.69E-01	-0.028	0.033	4.00E-01
rs3814883	T/C	-0.001	0.058	9.90E-01	0.072	0.040	7.31E-02	0.036	0.030	2.39E-01	-0.006	0.032	8.45E-01
rs6500208	A/G	-0.076	0.051	1.38E-01	-0.006	0.050	9.11E-01	-0.039	0.039	3.16E-01	-0.012	0.041	7.68E-01
rs1477199	G/A	0.034	0.058	5.58E-01	0.015	0.061	8.09E-01	0.023	0.046	6.18E-01	0.071	0.048	1.39E-01
rs7206790	G/C	Excluded for MR											
rs8057911	T/C	0.001	0.046	9.89E-01	0.039	0.069	5.70E-01	0.011	0.036	7.57E-01	0.032	0.038	4.06E-01
rs889398	C/T	-0.029	0.064	6.50E-01	-0.101	0.071	1.57E-01	0.001	0.056	9.79E-01	0.013	0.055	8.11E-01
rs35949039	G/T	0.015	0.063	8.14E-01	Excluded for MR			-0.029	0.048	5.52E-01	0.003	0.052	9.58E-01

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs12926250	T/G	-0.043	0.062	4.88E-01	Excluded for MR			-0.033	0.049	5.04E-01	-0.080	0.052	1.26E-01
rs756717	G/A	-0.026	0.043	5.38E-01	-0.025	0.046	5.84E-01	-0.050	0.034	1.45E-01	0.007	0.036	8.35E-01
rs4390583	C/A	0.042	0.040	2.86E-01	-0.028	0.052	5.94E-01	-0.007	0.041	8.71E-01	-0.018	0.033	5.93E-01
rs12922346	C/G	-0.085	0.043	5.02E-02	-0.016	0.046	7.31E-01	-0.068	0.034	5.00E-02	-0.022	0.037	5.47E-01
rs7206608	G/C	-0.018	0.055	7.43E-01	0.005	0.042	8.99E-01	-0.002	0.032	9.45E-01	-0.030	0.034	3.78E-01
rs3923783	C/A	-0.024	0.051	6.36E-01	0.004	0.052	9.33E-01	-0.003	0.040	9.31E-01	-0.004	0.042	9.32E-01
rs11078883	G/C	0.006	0.040	8.86E-01	-0.009	0.058	8.71E-01	0.002	0.049	9.71E-01	0.034	0.034	3.05E-01
rs7774	A/C	0.027	0.042	5.23E-01	-0.037	0.043	3.84E-01	-0.020	0.032	5.33E-01	0.035	0.035	3.15E-01
rs1075901	C/T	-0.072	0.039	6.69E-02	-0.045	0.040	2.50E-01	-0.067	0.030	2.64E-02	-0.035	0.032	2.76E-01
rs4986044	C/T	-0.049	0.045	2.80E-01	0.030	0.039	4.29E-01	-0.024	0.029	4.20E-01	0.000	0.032	9.92E-01
rs8065172	G/A	0.049	0.044	2.59E-01	0.015	0.044	7.33E-01	0.045	0.034	1.79E-01	0.064	0.048	1.77E-01
rs12150665	T/C	0.039	0.038	3.08E-01	0.039	0.039	3.20E-01	0.037	0.030	2.08E-01	0.042	0.032	1.84E-01
rs6607337	C/T	-0.105	0.041	1.03E-02	0.030	0.041	4.69E-01	-0.059	0.032	6.02E-02	-0.016	0.034	6.34E-01
rs56161855	T/A	-0.001	0.053	9.86E-01	0.043	0.054	4.30E-01	0.021	0.053	6.85E-01	0.018	0.058	7.60E-01
rs9299	T/C	-0.017	0.040	6.73E-01	-0.010	0.043	8.10E-01	0.003	0.031	9.10E-01	0.000	0.033	9.89E-01
rs11655587	C/T	-0.012	0.041	7.73E-01	-0.113	0.042	7.75E-03	-0.055	0.045	2.21E-01	-0.036	0.034	2.95E-01
rs11649864	A/G	-0.018	0.067	7.85E-01	0.090	0.069	1.96E-01	0.017	0.052	7.48E-01	0.070	0.054	1.99E-01
rs12602912	T/C	0.032	0.047	4.97E-01	Excluded for MR			0.007	0.037	8.50E-01	0.015	0.040	7.12E-01
rs312750	A/G	-0.028	0.063	6.60E-01	0.018	0.039	6.48E-01	0.028	0.038	4.63E-01	-0.013	0.042	7.55E-01
rs12939549	A/G	-0.033	0.037	3.82E-01	0.024	0.050	6.33E-01	-0.012	0.029	6.85E-01	-0.002	0.032	9.62E-01
rs35867081	A/G	0.021	0.039	5.84E-01	0.001	0.040	9.87E-01	0.022	0.031	4.76E-01	0.034	0.032	3.01E-01
rs8097672	T/A	0.079	0.053	1.38E-01	-0.091	0.070	1.94E-01	0.000	0.042	9.93E-01	-0.020	0.044	6.51E-01
rs478707	C/T	0.037	0.046	4.19E-01	-0.006	0.048	8.99E-01	0.014	0.036	6.94E-01	0.010	0.039	8.05E-01
rs891387	T/C	-0.053	0.049	2.77E-01	-0.005	0.051	9.26E-01	-0.029	0.030	3.32E-01	-0.009	0.032	7.82E-01
rs1945160	G/A	0.057	0.039	1.38E-01	-0.004	0.040	9.15E-01	0.020	0.030	5.13E-01	0.044	0.032	1.73E-01
rs1941696	A/G	0.042	0.038	2.61E-01	-0.020	0.038	6.07E-01	0.020	0.029	4.87E-01	-0.009	0.031	7.78E-01
rs474605	G/A	0.055	0.056	3.32E-01	-0.017	0.043	6.84E-01	0.004	0.032	8.90E-01	-0.015	0.047	7.54E-01
rs1356506	T/C	-0.094	0.039	1.59E-02	-0.103	0.041	1.13E-02	-0.127	0.044	4.23E-03	-0.118	0.042	5.16E-03
rs2612576	T/A	-0.097	0.042	2.14E-02	0.079	0.043	6.93E-02	0.003	0.033	9.21E-01	-0.015	0.035	6.67E-01
rs9951619	G/T	0.072	0.069	2.94E-01	-0.021	0.059	7.24E-01	0.020	0.048	6.71E-01	0.022	0.051	6.72E-01
rs6567160	C/T	0.032	0.045	4.71E-01	-0.027	0.046	5.60E-01	0.042	0.035	2.29E-01	-0.049	0.038	1.92E-01
rs17066856	T/C	0.008	0.067	9.04E-01	0.018	0.069	7.96E-01	-0.017	0.072	8.09E-01	0.014	0.055	7.99E-01
rs66595146	A/C	0.066	0.038	8.24E-02	0.042	0.039	2.83E-01	0.039	0.030	1.97E-01	0.059	0.032	6.62E-02
rs17783165	C/T	-0.027	0.041	5.18E-01	0.013	0.043	7.58E-01	-0.007	0.032	8.35E-01	-0.021	0.035	5.40E-01
rs11150911	A/C	0.053	0.041	1.93E-01	-0.026	0.043	5.42E-01	0.000	0.041	9.91E-01	-0.008	0.034	8.15E-01
rs12981256	A/G	-0.026	0.039	5.08E-01	0.022	0.040	5.72E-01	0.012	0.030	6.89E-01	0.006	0.032	8.64E-01
rs45486197	A/G	Excluded for MR											
rs895330	C/G	-0.032	0.048	5.03E-01	-0.082	0.050	9.66E-02	-0.028	0.038	4.49E-01	-0.081	0.040	4.32E-02
rs273512	T/C	-0.026	0.038	4.94E-01	-0.033	0.039	3.96E-01	-0.048	0.030	1.02E-01	0.000	0.032	9.88E-01
rs17724992	A/G	0.008	0.044	8.56E-01	0.074	0.043	8.48E-02	0.022	0.033	5.14E-01	0.028	0.036	4.27E-01
rs7258722	T/A	0.056	0.039	1.56E-01	0.044	0.039	2.59E-01	0.063	0.030	3.83E-02	0.063	0.041	1.30E-01
rs12611148	C/A	-0.014	0.052	7.88E-01	-0.080	0.053	1.27E-01	-0.029	0.041	4.69E-01	-0.093	0.043	2.98E-02
rs12462975	A/G	0.007	0.041	8.73E-01	0.005	0.042	9.07E-01	0.013	0.032	6.93E-01	0.013	0.034	7.04E-01
rs7245985	T/G	0.007	0.046	8.81E-01	0.007	0.061	9.13E-01	-0.002	0.036	9.62E-01	-0.039	0.039	3.10E-01
rs11882409	A/C	-0.035	0.062	5.69E-01	0.030	0.044	4.94E-01	0.004	0.033	8.98E-01	0.000	0.049	9.98E-01
rs185350	T/C	-0.010	0.038	7.96E-01	-0.057	0.039	1.43E-01	-0.023	0.030	4.43E-01	-0.077	0.032	1.56E-02
rs429358	T/C	0.003	0.057	9.53E-01	-0.015	0.062	8.05E-01	-0.035	0.045	4.38E-01	0.011	0.047	8.22E-01

SNP	EA/BA	Age ≤67 years			Age >67 years			Disease duration ≤7 years			Disease duration >7 years		
		Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs11672660	C/T	-0.027	0.048	5.65E-01	-0.028	0.049	5.73E-01	-0.066	0.037	7.74E-02	0.012	0.039	7.56E-01
rs9304665	A/T	Excluded for MR											
rs3764625	T/G	0.037	0.039	3.38E-01	0.035	0.041	3.95E-01	0.032	0.031	2.99E-01	0.033	0.033	3.06E-01
rs1884389	C/T	0.019	0.039	6.25E-01	0.009	0.040	8.24E-01	0.028	0.031	3.58E-01	0.032	0.033	3.28E-01
rs4813619	G/T	0.036	0.038	3.48E-01	0.056	0.039	1.49E-01	0.069	0.030	2.06E-02	0.021	0.032	5.15E-01
rs1884897	G/A	-0.012	0.039	7.62E-01	0.002	0.040	9.51E-01	0.029	0.036	4.15E-01	-0.022	0.032	4.96E-01
rs2423668	T/C	0.019	0.054	7.29E-01	0.007	0.041	8.73E-01	0.027	0.031	3.85E-01	0.002	0.044	9.72E-01
rs852056	T/C	-0.007	0.044	8.65E-01	0.012	0.046	7.87E-01	0.007	0.034	8.46E-01	-0.025	0.037	5.05E-01
rs1409818	T/C	-0.028	0.061	6.38E-01	0.041	0.064	5.25E-01	-0.027	0.048	5.80E-01	0.032	0.050	5.29E-01
rs8122855	A/G	0.027	0.041	5.19E-01	-0.016	0.060	7.87E-01	0.088	0.043	4.14E-02	-0.015	0.034	6.61E-01
rs4812405	C/A	Excluded for MR											
rs742748	C/T	-0.023	0.039	5.56E-01	0.084	0.040	3.76E-02	0.019	0.030	5.36E-01	0.030	0.033	3.62E-01
rs79186842	A/G	-0.022	0.062	7.18E-01	0.100	0.077	1.91E-01	-0.012	0.047	7.93E-01	0.062	0.050	2.16E-01
rs17806224	G/A	0.028	0.049	5.71E-01	0.084	0.050	9.20E-02	0.051	0.038	1.84E-01	0.027	0.055	6.27E-01
rs1304549	G/A	-0.030	0.045	5.09E-01	-0.098	0.047	3.64E-02	-0.061	0.036	8.56E-02	-0.073	0.038	5.64E-02
rs6010784	T/C	-0.076	0.038	4.89E-02	0.015	0.048	7.46E-01	-0.028	0.034	4.15E-01	-0.056	0.032	7.77E-02
rs6512302	C/G	-0.046	0.070	5.08E-01	0.021	0.051	6.77E-01	0.021	0.053	6.91E-01	0.002	0.040	9.58E-01
rs2064044	C/A	Excluded for MR											
rs2832283	A/G	-0.100	0.048	3.69E-02	-0.082	0.049	8.94E-02	-0.109	0.037	3.47E-03	-0.030	0.039	4.39E-01
rs13047416	C/G	0.044	0.057	4.43E-01	-0.013	0.040	7.40E-01	0.064	0.042	1.32E-01	0.026	0.033	4.31E-01
rs8134638	C/T	0.094	0.039	1.54E-02	0.026	0.040	5.11E-01	0.057	0.030	5.82E-02	0.052	0.032	1.09E-01
rs8126575	T/G	-0.009	0.072	9.03E-01	-0.024	0.073	7.42E-01	-0.005	0.055	9.33E-01	-0.124	0.055	2.51E-02
rs427943	C/A	-0.028	0.038	4.62E-01	-0.069	0.054	2.05E-01	-0.031	0.030	2.98E-01	-0.070	0.042	9.65E-02
rs11538	G/A	0.075	0.064	2.41E-01	-0.066	0.053	2.17E-01	-0.019	0.041	6.35E-01	0.046	0.047	3.24E-01
rs2238799	A/G	0.047	0.039	2.23E-01	-0.009	0.040	8.22E-01	0.020	0.031	5.13E-01	0.021	0.033	5.27E-01
rs12628891	C/T	0.038	0.044	3.84E-01	0.014	0.045	7.51E-01	-0.015	0.034	6.69E-01	0.068	0.037	6.53E-02
rs12628051	T/C	-0.097	0.063	1.22E-01	-0.042	0.046	3.62E-01	-0.037	0.037	3.26E-01	-0.068	0.034	4.21E-02
rs28489620	G/A	0.003	0.043	9.51E-01	-0.061	0.044	1.60E-01	-0.065	0.033	4.84E-02	-0.009	0.036	8.08E-01
rs9615337	G/C	Excluded for MR											

^a In Courage-PD, we used the proxy rs7079940 for rs7907470.

NA, not available; EA/BA, effect allele/base allele; SE, standard error.

Bold coefficient with their corresponding SE and p-values are significant at p≤0.05.

eTable 6: Forward MR analysis: Leave-one-out analysis

SNP removed	OR _{I_{IVW}} (95% CI)	P	SNP removed	OR _{I_{IVW}} (95% CI)	P	SNP removed	OR _{I_{IVW}} (95% CI)	P
rs10002111	0.78 (0.62-0.99)	0.039	rs1721447	0.78 (0.62-0.98)	0.036	rs4988235	0.78 (0.62-0.98)	0.034
rs10033843	0.79 (0.63-1.00)	0.046	rs17367750	0.79 (0.63-0.99)	0.043	rs543874	0.80 (0.63-1.00)	0.053
rs10050620	0.79 (0.63-0.99)	0.045	rs17405603	0.78 (0.62-0.99)	0.039	rs56133507	0.79 (0.63-0.99)	0.043
rs1006317	0.79 (0.63-0.99)	0.043	rs17405819	0.78 (0.62-0.98)	0.036	rs56151256	0.79 (0.62-0.99)	0.041
rs10099330	0.79 (0.63-1.00)	0.046	rs1750307	0.78 (0.62-0.99)	0.038	rs56161855	0.79 (0.63-0.99)	0.044
rs10101364	0.79 (0.62-0.99)	0.042	rs17544384	0.79 (0.63-1.00)	0.049	rs56211164	0.78 (0.62-0.99)	0.038
rs10110189	0.79 (0.63-0.99)	0.043	rs17636031	0.79 (0.62-0.99)	0.041	rs562664	0.79 (0.62-0.99)	0.042
rs10132280	0.79 (0.63-1.00)	0.049	rs17681451	0.78 (0.62-0.98)	0.035	rs570463	0.79 (0.63-0.99)	0.044
rs10145749	0.79 (0.63-0.99)	0.045	rs17724992	0.78 (0.62-0.98)	0.033	rs57989773	0.78 (0.62-0.99)	0.038
rs10168563	0.79 (0.63-1.00)	0.046	rs17783165	0.79 (0.63-0.99)	0.044	rs587271	0.79 (0.62-0.99)	0.042
rs10169594	0.79 (0.62-0.99)	0.042	rs17806224	0.78 (0.62-0.98)	0.036	rs592483	0.79 (0.63-0.99)	0.044
rs10182181	0.78 (0.62-0.99)	0.039	rs17814208	0.79 (0.62-0.99)	0.041	rs59302296	0.79 (0.62-0.99)	0.042
rs10185199	0.78 (0.62-0.98)	0.036	rs1799923	0.79 (0.62-0.99)	0.041	rs6010784	0.79 (0.63-1.00)	0.047
rs10197031	0.79 (0.62-0.99)	0.041	rs1808629	0.79 (0.62-0.99)	0.042	rs61740466	0.78 (0.62-0.99)	0.037
rs10261050	0.79 (0.62-0.99)	0.041	rs185350	0.79 (0.63-1.00)	0.049	rs61813324	0.79 (0.62-0.99)	0.042
rs1048637	0.79 (0.63-0.99)	0.044	rs1860561	0.79 (0.63-0.99)	0.044	rs61828641	0.79 (0.63-1.00)	0.046
rs10499694	0.78 (0.62-0.99)	0.037	rs1877875	0.79 (0.62-0.99)	0.042	rs61983990	0.79 (0.62-0.99)	0.042
rs10506971	0.78 (0.62-0.99)	0.039	rs1884389	0.78 (0.62-0.98)	0.036	rs62176243	0.79 (0.62-0.99)	0.041
rs10510419	0.79 (0.63-0.99)	0.043	rs1884897	0.78 (0.62-0.99)	0.038	rs6265	0.78 (0.62-0.99)	0.04
rs10518694	0.79 (0.62-0.99)	0.043	rs1927790	0.79 (0.63-1.00)	0.048	rs6445258	0.79 (0.62-0.99)	0.042
rs10733051	0.79 (0.63-0.99)	0.043	rs1928295	0.78 (0.62-0.99)	0.039	rs6463489	0.79 (0.62-0.99)	0.042
rs10733682	0.78 (0.62-0.98)	0.035	rs1941213	0.79 (0.63-0.99)	0.043	rs6468266	0.79 (0.62-0.99)	0.042
rs10741329	0.78 (0.62-0.99)	0.039	rs1941696	0.79 (0.63-0.99)	0.044	rs6470144	0.79 (0.63-0.99)	0.043
rs10742752	0.78 (0.62-0.99)	0.039	rs1945160	0.78 (0.62-0.99)	0.039	rs6493498	0.79 (0.62-0.99)	0.042
rs1075901	0.79 (0.63-1.00)	0.048	rs1948080	0.79 (0.62-0.99)	0.042	rs6496248	0.79 (0.62-0.99)	0.043
rs10761785	0.79 (0.63-1.00)	0.049	rs194809	0.79 (0.62-0.99)	0.043	rs6500208	0.79 (0.63-0.99)	0.043
rs10772983	0.78 (0.62-0.99)	0.038	rs1951455	0.78 (0.62-0.99)	0.039	rs650198	0.79 (0.63-0.99)	0.043
rs10779751	0.79 (0.63-0.99)	0.043	rs1958898	0.79 (0.63-0.99)	0.043	rs6512302	0.79 (0.62-0.99)	0.041
rs10811868	0.79 (0.62-0.99)	0.04	rs1965529	0.79 (0.62-0.99)	0.042	rs6539064	0.79 (0.62-0.99)	0.041
rs10829164	0.79 (0.63-0.99)	0.044	rs197374	0.78 (0.62-0.98)	0.036	rs6545714	0.78 (0.62-0.98)	0.036
rs10842240	0.79 (0.63-1.00)	0.046	rs1999433	0.78 (0.62-0.99)	0.039	rs6556301	0.79 (0.62-0.99)	0.043
rs10858334	0.79 (0.63-1.00)	0.05	rs2007518	0.79 (0.63-1.00)	0.045	rs6567160	0.79 (0.62-1.00)	0.047
rs10864728	0.79 (0.62-0.99)	0.041	rs2047648	0.78 (0.62-0.99)	0.039	rs657452	0.78 (0.62-0.99)	0.04
rs10909880	0.78 (0.62-0.99)	0.037	rs2051559	0.79 (0.63-0.99)	0.045	rs6591407	0.79 (0.62-0.99)	0.041
rs10920336	0.79 (0.63-1.00)	0.046	rs2053682	0.79 (0.63-1.00)	0.051	rs6607337	0.79 (0.63-1.00)	0.046
rs10920678	0.78 (0.62-0.99)	0.04	rs2058527	0.79 (0.62-0.99)	0.041	rs6656785	0.79 (0.62-0.99)	0.043
rs10929925	0.78 (0.62-0.98)	0.037	rs2064044	0.78 (0.62-0.99)	0.039	rs66595146	0.78 (0.62-0.98)	0.033
rs10938397	0.79 (0.63-1.00)	0.052	rs2065418	0.79 (0.62-0.99)	0.04	rs6661316	0.79 (0.63-1.00)	0.047
rs10942267	0.79 (0.63-1.00)	0.047	rs2066295	0.78 (0.62-0.98)	0.036	rs6696828	0.79 (0.62-0.99)	0.041
rs10961649	0.78 (0.62-0.99)	0.04	rs2074314	0.79 (0.62-0.99)	0.042	rs6710091	0.79 (0.63-1.00)	0.047
rs10962550	0.78 (0.62-0.99)	0.037	rs2108719	0.79 (0.62-0.99)	0.041	rs6716898	0.78 (0.62-0.98)	0.035
rs10968114	0.79 (0.62-0.99)	0.04	rs2112347	0.78 (0.62-0.99)	0.039	rs6720868	0.79 (0.63-1.00)	0.047
rs10975933	0.79 (0.63-1.00)	0.049	rs2119753	0.79 (0.63-1.00)	0.046	rs6725931	0.79 (0.62-0.99)	0.042
rs10992867	0.79 (0.62-0.99)	0.042	rs2120710	0.79 (0.62-0.99)	0.042	rs6783054	0.79 (0.63-0.99)	0.043
rs11030618	0.79 (0.63-0.99)	0.043	rs2134858	0.79 (0.62-0.99)	0.043	rs6803161	0.79 (0.63-1.00)	0.046
rs11044430	0.79 (0.63-1.00)	0.046	rs213518	0.79 (0.63-0.99)	0.045	rs6804842	0.79 (0.63-1.00)	0.046
rs11046972	0.79 (0.62-0.99)	0.04	rs214249	0.78 (0.62-0.99)	0.04	rs6808814	0.79 (0.62-0.99)	0.043
rs11060853	0.78 (0.62-0.98)	0.031	rs215669	0.79 (0.63-0.99)	0.043	rs6850421	0.78 (0.62-0.99)	0.039

SNP removed	OR _{IW} (95% CI)	P	SNP removed	OR _{IW} (95% CI)	P	SNP removed	OR _{IW} (95% CI)	P
rs11066188	0.79 (0.62-0.99)	0.04	rs217433	0.78 (0.62-0.99)	0.039	rs6864049	0.78 (0.62-0.99)	0.038
rs11078883	0.79 (0.62-0.99)	0.042	rs217669	0.79 (0.62-0.99)	0.042	rs687339	0.78 (0.62-0.98)	0.037
rs11105839	0.79 (0.62-0.99)	0.042	rs2192158	0.79 (0.62-0.99)	0.043	rs6882366	0.79 (0.62-0.99)	0.04
rs11115176	0.79 (0.62-0.99)	0.041	rs2196618	0.78 (0.62-0.99)	0.039	rs6886072	0.79 (0.63-0.99)	0.044
rs11121210	0.79 (0.63-1.00)	0.046	rs2206277	0.80 (0.63-1.01)	0.058	rs6888194	0.79 (0.62-0.99)	0.041
rs11128021	0.78 (0.62-0.99)	0.038	rs2228213	0.79 (0.62-0.99)	0.043	rs6890310	0.78 (0.62-0.98)	0.035
rs11150911	0.79 (0.62-0.99)	0.042	rs2228552	0.79 (0.63-0.99)	0.044	rs6893539	0.79 (0.63-0.99)	0.043
rs11165643	0.80 (0.63-1.00)	0.052	rs2238799	0.78 (0.62-0.99)	0.04	rs6909685	0.79 (0.63-1.00)	0.048
rs11170468	0.79 (0.62-0.99)	0.042	rs2241423	0.78 (0.62-0.98)	0.037	rs6915002	0.79 (0.63-0.99)	0.043
rs11218510	0.78 (0.62-0.99)	0.04	rs2246012	0.79 (0.63-0.99)	0.044	rs6921533	0.79 (0.63-1.00)	0.049
rs11246136	0.79 (0.62-0.99)	0.042	rs2257791	0.78 (0.62-0.99)	0.039	rs6922607	0.79 (0.63-0.99)	0.043
rs112646560	0.79 (0.62-0.99)	0.041	rs225882	0.78 (0.62-0.99)	0.04	rs6950388	0.79 (0.63-1.00)	0.048
rs1126930	0.79 (0.62-0.99)	0.042	rs2267958	0.79 (0.62-0.99)	0.042	rs6973656	0.78 (0.62-0.98)	0.034
rs11525873	0.79 (0.63-0.99)	0.043	rs2271046	0.79 (0.63-0.99)	0.044	rs698147	0.79 (0.62-0.99)	0.042
rs11538	0.79 (0.62-0.99)	0.042	rs2271189	0.79 (0.63-0.99)	0.044	rs7024334	0.79 (0.63-0.99)	0.045
rs11577094	0.79 (0.62-0.99)	0.041	rs2273175	0.79 (0.62-0.99)	0.041	rs7025938	0.79 (0.63-0.99)	0.045
rs11594179	0.78 (0.62-0.99)	0.04	rs2275003	0.78 (0.62-0.99)	0.04	rs7070670	0.79 (0.62-0.99)	0.041
rs1159692	0.79 (0.63-0.99)	0.043	rs2281819	0.78 (0.62-0.99)	0.039	rs7079940	0.78 (0.62-0.99)	0.04
rs11611246	0.79 (0.63-0.99)	0.045	rs2283006	0.79 (0.63-1.00)	0.046	rs7084454	0.79 (0.63-1.00)	0.045
rs11614340	0.78 (0.62-0.99)	0.039	rs2283093	0.79 (0.62-0.99)	0.041	rs7102454	0.79 (0.63-1.00)	0.046
rs11615578	0.79 (0.62-0.99)	0.042	rs2289379	0.79 (0.62-0.99)	0.042	rs7124681	0.77 (0.61-0.97)	0.025
rs11633626	0.79 (0.62-0.99)	0.042	rs2342892	0.79 (0.62-0.99)	0.041	rs7138803	0.77 (0.61-0.97)	0.026
rs11636611	0.79 (0.63-0.99)	0.043	rs2357760	0.78 (0.62-0.99)	0.039	rs7144011	0.79 (0.63-0.99)	0.045
rs116374395	0.79 (0.62-0.99)	0.043	rs2365389	0.79 (0.63-1.00)	0.048	rs7171864	0.79 (0.63-0.99)	0.045
rs11649864	0.79 (0.62-0.99)	0.041	rs2400414	0.79 (0.62-0.99)	0.043	rs7172627	0.78 (0.62-0.99)	0.038
rs11655587	0.79 (0.63-0.99)	0.044	rs2423668	0.79 (0.63-1.00)	0.046	rs7206608	0.79 (0.63-0.99)	0.045
rs11672660	0.79 (0.63-1.00)	0.047	rs2436728	0.79 (0.63-0.99)	0.044	rs7245985	0.79 (0.62-0.99)	0.041
rs11692326	0.78 (0.62-0.99)	0.039	rs2439823	0.79 (0.63-1.00)	0.051	rs7258722	0.77 (0.61-0.98)	0.03
rs11695013	0.79 (0.63-1.00)	0.046	rs2466103	0.79 (0.63-0.99)	0.044	rs72649373	0.78 (0.62-0.99)	0.039
rs11713193	0.79 (0.63-0.99)	0.045	rs2470893	0.78 (0.62-0.99)	0.038	rs72673947	0.80 (0.63-1.00)	0.052
rs11739877	0.78 (0.62-0.99)	0.04	rs2503185	0.78 (0.62-0.99)	0.04	rs72757415	0.78 (0.62-0.99)	0.04
rs11757278	0.78 (0.62-0.99)	0.04	rs2513999	0.79 (0.63-1.00)	0.045	rs73213484	0.79 (0.63-1.00)	0.046
rs11772246	0.79 (0.62-0.99)	0.041	rs2600226	0.79 (0.62-0.99)	0.041	rs73225274	0.79 (0.62-0.99)	0.041
rs11773362	0.79 (0.63-1.00)	0.047	rs2605603	0.78 (0.62-0.99)	0.039	rs7323	0.79 (0.63-1.00)	0.046
rs11782074	0.79 (0.62-0.99)	0.041	rs2612576	0.79 (0.63-0.99)	0.044	rs7357754	0.78 (0.62-0.99)	0.037
rs118081010	0.79 (0.63-0.99)	0.044	rs2622274	0.79 (0.62-0.99)	0.04	rs73985439	0.78 (0.62-0.99)	0.038
rs11882409	0.78 (0.62-0.99)	0.039	rs264941	0.79 (0.62-0.99)	0.04	rs742748	0.78 (0.62-0.99)	0.039
rs11902450	0.79 (0.63-1.00)	0.046	rs2707183	0.79 (0.63-0.99)	0.044	rs74887628	0.79 (0.62-0.99)	0.041
rs11915371	0.79 (0.63-1.00)	0.049	rs2712665	0.78 (0.62-0.99)	0.039	rs7498665	0.79 (0.63-1.00)	0.046
rs11919665	0.79 (0.63-1.00)	0.046	rs2715423	0.79 (0.62-0.99)	0.041	rs750090	0.79 (0.63-1.00)	0.049
rs11921432	0.78 (0.62-0.99)	0.039	rs273512	0.80 (0.63-1.00)	0.051	rs7512146	0.79 (0.62-0.99)	0.042
rs12072739	0.79 (0.63-1.00)	0.045	rs2744974	0.79 (0.62-0.99)	0.041	rs7534091	0.79 (0.63-1.00)	0.046
rs12098284	0.79 (0.62-0.99)	0.041	rs274628	0.79 (0.62-0.99)	0.042	rs7561278	0.79 (0.62-0.99)	0.04
rs12140153	0.78 (0.62-0.98)	0.035	rs2777768	0.78 (0.62-0.99)	0.04	rs756717	0.79 (0.63-0.99)	0.045
rs12150665	0.78 (0.62-0.99)	0.038	rs2820295	0.79 (0.62-0.99)	0.041	rs7588437	0.79 (0.62-0.99)	0.041
rs12259464	0.78 (0.62-0.99)	0.038	rs2832283	0.79 (0.63-1.00)	0.048	rs7593917	0.79 (0.63-0.99)	0.044
rs12282785	0.79 (0.62-0.99)	0.042	rs28350	0.78 (0.62-0.99)	0.039	rs7599312	0.78 (0.62-0.99)	0.04
rs12286929	0.79 (0.62-0.99)	0.043	rs28489620	0.79 (0.63-1.00)	0.046	rs7616009	0.79 (0.63-0.99)	0.043
rs12334877	0.78 (0.62-0.98)	0.036	rs2861089	0.78 (0.62-0.99)	0.038	rs7631156	0.79 (0.62-0.99)	0.041

SNP removed	OR _{IW} (95% CI)	P	SNP removed	OR _{IW} (95% CI)	P	SNP removed	OR _{IW} (95% CI)	P
rs12364470	0.79 (0.63-0.99)	0.045	rs2861685	0.79 (0.62-0.99)	0.043	rs7640424	0.80 (0.63-1.00)	0.052
rs12369179	0.79 (0.63-1.00)	0.046	rs2862996	0.78 (0.62-0.98)	0.031	rs765125	0.79 (0.63-0.99)	0.043
rs12386885	0.79 (0.63-0.99)	0.043	rs2875762	0.80 (0.63-1.00)	0.051	rs765875	0.78 (0.62-0.99)	0.04
rs12421848	0.78 (0.62-0.98)	0.036	rs2907948	0.79 (0.63-0.99)	0.043	rs76638898	0.79 (0.62-0.99)	0.041
rs12429545	0.79 (0.63-1.00)	0.05	rs2910026	0.79 (0.63-1.00)	0.048	rs7678054	0.79 (0.62-0.99)	0.041
rs12439632	0.79 (0.63-1.00)	0.048	rs2962334	0.78 (0.62-0.98)	0.037	rs768023	0.78 (0.62-0.98)	0.036
rs12448257	0.80 (0.63-1.00)	0.052	rs2984618	0.78 (0.62-0.98)	0.035	rs7685628	0.79 (0.63-0.99)	0.044
rs12462975	0.78 (0.62-0.99)	0.039	rs3019466	0.79 (0.62-0.99)	0.042	rs76942203	0.80 (0.63-1.00)	0.051
rs12527426	0.79 (0.63-1.00)	0.047	rs305256	0.79 (0.63-0.99)	0.043	rs7696649	0.79 (0.63-0.99)	0.043
rs12591120	0.79 (0.62-0.99)	0.042	rs3101336	0.80 (0.63-1.01)	0.056	rs7713317	0.78 (0.62-0.99)	0.039
rs12602912	0.78 (0.62-0.99)	0.037	rs3115667	0.79 (0.63-1.00)	0.049	rs7715256	0.79 (0.62-0.99)	0.042
rs12611148	0.79 (0.62-0.99)	0.041	rs312750	0.79 (0.62-0.99)	0.041	rs77165542	0.79 (0.62-0.99)	0.04
rs12628051	0.79 (0.62-0.99)	0.042	rs321237	0.79 (0.63-1.00)	0.048	rs7727781	0.79 (0.62-0.99)	0.042
rs12628891	0.78 (0.62-0.99)	0.04	rs326893	0.78 (0.62-0.99)	0.037	rs7730004	0.79 (0.63-1.00)	0.047
rs12636480	0.79 (0.63-1.00)	0.047	rs329651	0.79 (0.63-1.00)	0.05	rs7734385	0.79 (0.62-0.99)	0.042
rs12652212	0.78 (0.62-0.98)	0.035	rs337637	0.78 (0.62-0.99)	0.039	rs77432547	0.79 (0.62-0.99)	0.04
rs1268065	0.78 (0.62-0.99)	0.037	rs339991	0.79 (0.62-0.99)	0.042	rs7760482	0.79 (0.63-1.00)	0.046
rs12680842	0.79 (0.63-0.99)	0.043	rs34184235	0.79 (0.63-1.00)	0.047	rs7774	0.79 (0.62-0.99)	0.042
rs12681792	0.78 (0.62-0.99)	0.039	rs34234296	0.79 (0.62-0.99)	0.042	rs7802342	0.79 (0.62-0.99)	0.042
rs12692596	0.79 (0.63-1.00)	0.047	rs34517439	0.79 (0.63-0.99)	0.045	rs7861160	0.78 (0.62-0.99)	0.039
rs12714199	0.79 (0.63-0.99)	0.045	rs349088	0.79 (0.63-1.00)	0.046	rs7893571	0.79 (0.63-0.99)	0.043
rs12765914	0.79 (0.63-1.00)	0.046	rs35408866	0.79 (0.62-0.99)	0.042	rs7899106	0.79 (0.62-0.99)	0.042
rs12868881	0.79 (0.63-0.99)	0.044	rs35483388	0.79 (0.62-0.99)	0.043	rs7903146	0.78 (0.62-0.98)	0.035
rs12888545	0.79 (0.63-1.00)	0.047	rs355777	0.78 (0.62-0.98)	0.035	rs79113395	0.78 (0.62-0.98)	0.035
rs12912198	0.79 (0.62-0.99)	0.042	rs35867081	0.78 (0.62-0.98)	0.034	rs79186842	0.79 (0.62-0.99)	0.04
rs12914623	0.79 (0.62-0.99)	0.043	rs35949039	0.79 (0.62-0.99)	0.042	rs7944782	0.79 (0.63-1.00)	0.049
rs12922346	0.79 (0.62-0.99)	0.043	rs3732927	0.79 (0.63-0.99)	0.044	rs7975187	0.78 (0.62-0.98)	0.034
rs12926250	0.79 (0.63-1.00)	0.049	rs3764625	0.78 (0.62-0.98)	0.037	rs79780963	0.79 (0.63-0.99)	0.043
rs1293037	0.79 (0.62-0.99)	0.041	rs3764835	0.79 (0.62-0.99)	0.041	rs79906980	0.79 (0.62-0.99)	0.042
rs12939549	0.78 (0.62-0.99)	0.037	rs3770890	0.79 (0.63-0.99)	0.043	rs805412	0.79 (0.62-0.99)	0.042
rs1296328	0.78 (0.62-0.99)	0.038	rs3796432	0.79 (0.62-0.99)	0.042	rs8057911	0.79 (0.62-0.99)	0.042
rs12981256	0.78 (0.62-0.99)	0.04	rs3806114	0.79 (0.62-0.99)	0.041	rs8065172	0.78 (0.62-0.98)	0.036
rs13021737	0.80 (0.63-1.01)	0.057	rs3808477	0.78 (0.62-0.99)	0.039	rs8097672	0.80 (0.63-1.00)	0.052
rs13033310	0.78 (0.62-0.98)	0.034	rs3814883	0.79 (0.63-1.00)	0.047	rs8122855	0.78 (0.62-0.99)	0.04
rs1304549	0.79 (0.63-1.00)	0.047	rs3825061	0.79 (0.62-0.99)	0.041	rs8126575	0.79 (0.63-1.00)	0.045
rs13047416	0.79 (0.62-0.99)	0.041	rs3902951	0.79 (0.63-1.00)	0.046	rs8134638	0.78 (0.62-0.99)	0.037
rs13107325	0.79 (0.63-1.00)	0.046	rs3914628	0.79 (0.63-0.99)	0.043	rs8181823	0.79 (0.62-0.99)	0.042
rs13110266	0.78 (0.62-0.99)	0.04	rs3923783	0.78 (0.62-0.98)	0.036	rs845084	0.79 (0.62-0.99)	0.042
rs13174863	0.78 (0.62-0.99)	0.039	rs39654	0.78 (0.62-0.98)	0.037	rs852056	0.79 (0.62-0.99)	0.043
rs13186194	0.79 (0.62-0.99)	0.042	rs40067	0.79 (0.62-0.99)	0.043	rs865809	0.78 (0.62-0.99)	0.039
rs13191362	0.78 (0.62-0.98)	0.036	rs4017425	0.79 (0.63-0.99)	0.044	rs879620	0.79 (0.62-0.99)	0.042
rs13240600	0.79 (0.62-0.99)	0.041	rs4097319	0.79 (0.63-0.99)	0.045	rs889398	0.79 (0.62-0.99)	0.041
rs13245051	0.78 (0.62-0.98)	0.03	rs4148155	0.78 (0.62-0.99)	0.037	rs891387	0.78 (0.62-0.99)	0.039
rs13263601	0.79 (0.62-0.99)	0.041	rs4240673	0.78 (0.62-0.98)	0.037	rs895330	0.79 (0.63-1.00)	0.048
rs1327259	0.79 (0.63-1.00)	0.048	rs4256980	0.79 (0.62-0.99)	0.04	rs900144	0.78 (0.62-0.98)	0.036
rs13296413	0.80 (0.63-1.00)	0.053	rs427943	0.79 (0.63-1.00)	0.049	rs9168	0.79 (0.63-0.99)	0.044
rs13298487	0.79 (0.62-0.99)	0.042	rs4286488	0.78 (0.62-0.99)	0.039	rs925018	0.79 (0.62-0.99)	0.04
rs1346841	0.79 (0.62-0.99)	0.042	rs429358	0.79 (0.62-0.99)	0.041	rs9294260	0.79 (0.63-0.99)	0.045
rs1350430	0.77 (0.62-0.97)	0.029	rs4303732	0.78 (0.62-0.99)	0.038	rs9299	0.79 (0.62-0.99)	0.042

SNP removed	OR _{IVW} (95% CI)	P	SNP removed	OR _{IVW} (95% CI)	P	SNP removed	OR _{IVW} (95% CI)	P
rs1356506	0.80 (0.63-1.00)	0.051	rs4307239	0.78 (0.62-0.99)	0.038	rs930295	0.79 (0.62-0.99)	0.041
rs1358980	0.79 (0.63-0.99)	0.043	rs4390583	0.79 (0.63-0.99)	0.044	rs9304665	0.79 (0.63-0.99)	0.043
rs1383592	0.79 (0.63-0.99)	0.044	rs4430672	0.79 (0.63-1.00)	0.046	rs9320823	0.79 (0.62-0.99)	0.043
rs1409818	0.79 (0.63-0.99)	0.044	rs4517716	0.79 (0.63-0.99)	0.043	rs935166	0.79 (0.63-0.99)	0.044
rs1412235	0.78 (0.62-0.99)	0.038	rs45486197	0.79 (0.62-0.99)	0.041	rs9370410	0.78 (0.62-0.99)	0.038
rs1421334	0.79 (0.63-1.00)	0.051	rs459552	0.79 (0.62-0.99)	0.04	rs9375702	0.78 (0.62-0.99)	0.038
rs1437842	0.79 (0.62-0.99)	0.042	rs4653017	0.78 (0.62-0.99)	0.039	rs942066	0.79 (0.63-0.99)	0.045
rs1441264	0.79 (0.63-1.00)	0.05	rs4655141	0.78 (0.62-0.99)	0.038	rs9458814	0.79 (0.62-0.99)	0.043
rs1451077	0.79 (0.62-0.99)	0.042	rs4671328	0.79 (0.63-1.00)	0.052	rs946824	0.79 (0.62-0.99)	0.042
rs147568678	0.79 (0.63-0.99)	0.045	rs4700608	0.78 (0.62-0.99)	0.039	rs9478496	0.79 (0.63-0.99)	0.043
rs1477199	0.79 (0.62-0.99)	0.043	rs4721089	0.79 (0.63-0.99)	0.044	rs9512648	0.79 (0.63-0.99)	0.045
rs1492014	0.79 (0.63-1.00)	0.049	rs4740383	0.78 (0.62-0.98)	0.032	rs9522183	0.78 (0.62-0.98)	0.035
rs1492767	0.79 (0.62-0.99)	0.04	rs4740619	0.79 (0.62-0.99)	0.043	rs9527895	0.78 (0.62-0.99)	0.04
rs1501673	0.79 (0.62-0.99)	0.043	rs474605	0.78 (0.62-0.98)	0.036	rs9531786	0.79 (0.62-0.99)	0.042
rs150215901	0.78 (0.62-0.99)	0.04	rs4771218	0.79 (0.63-0.99)	0.045	rs9569777	0.79 (0.63-0.99)	0.045
rs1522569	0.79 (0.62-0.99)	0.043	rs478707	0.79 (0.62-0.99)	0.042	rs9595908	0.79 (0.63-1.00)	0.046
rs1559673	0.79 (0.62-0.99)	0.041	rs4812405	0.79 (0.62-0.99)	0.04	rs9599161	0.78 (0.62-0.99)	0.038
rs156201	0.79 (0.63-0.99)	0.045	rs4813619	0.78 (0.62-0.98)	0.033	rs9603697	0.79 (0.62-0.99)	0.042
rs1624134	0.79 (0.63-0.99)	0.043	rs4858193	0.79 (0.62-0.99)	0.041	rs962796	0.78 (0.62-0.99)	0.038
rs16851483	0.80 (0.64-1.01)	0.058	rs4864201	0.79 (0.62-0.99)	0.043	rs9816226	0.78 (0.62-0.99)	0.038
rs16906838	0.78 (0.62-0.98)	0.035	rs4865796	0.79 (0.63-0.99)	0.044	rs9818122	0.79 (0.63-1.00)	0.05
rs1700082	0.79 (0.63-0.99)	0.043	rs4880341	0.78 (0.62-0.99)	0.039	rs9826775	0.78 (0.62-0.99)	0.038
rs17020497	0.79 (0.63-0.99)	0.045	rs4900714	0.79 (0.63-1.00)	0.046	rs9827823	0.78 (0.62-0.99)	0.038
rs17024393	0.79 (0.63-0.99)	0.044	rs4906263	0.79 (0.63-1.00)	0.051	rs9888533	0.79 (0.63-0.99)	0.043
rs17066856	0.78 (0.62-0.98)	0.034	rs4921301	0.78 (0.62-0.98)	0.037	rs9926784	0.78 (0.62-0.99)	0.039
rs17094222	0.78 (0.62-0.99)	0.04	rs4970991	0.79 (0.62-0.99)	0.04	rs9944219	0.79 (0.63-1.00)	0.046
rs17149254	0.78 (0.62-0.98)	0.03	rs4973618	0.79 (0.62-0.99)	0.042	rs994596	0.79 (0.62-0.99)	0.041
rs17182027	0.79 (0.63-1.00)	0.046	rs4981693	0.79 (0.62-0.99)	0.041	rs9951619	0.78 (0.62-0.99)	0.04
rs17207196	0.79 (0.62-0.99)	0.042	rs4986044	0.79 (0.63-1.00)	0.045			

OR, odds ratio per 1SD=4.8kg/m²; IVW, inverse-variance weighted; CI, confidence interval.

eTable 7: Mendelian randomisation analyses stratified by age at study, disease duration in PD cases, and sex.

Characteristic	Study	Strata	OR _{IVW} (95% CI)	<i>P</i>	<i>P</i> -heterogeneity	<i>P</i> -Interaction
Age	Courage-PD	≤ 67y (3502 cases; 3306 controls)	0.71 (0.55-0.92)	0.009	0.23	
	Courage-PD	> 67y (3822 cases; 2904 controls)	0.89 (0.69-1.15)	0.39	0.91	0.22
Disease duration	Courage-PD	≤ 7y (4358 cases; 7416 controls)	0.75 (0.62-0.91)	0.003	0.54	
	Courage-PD	> 7y (3917 cases; 7416 controls)	0.92 (0.75-1.13)	0.45	0.57	--
Sex	Courage-PD	Women (3554 cases; 4153 controls)	0.81 (0.64-1.03)	0.087	0.41	
		Men (5365 cases; 3447 controls)	0.95 (0.75-1.21)	0.67	0.28	0.36
	iPDGC	Women (7384 cases; 12389 controls)	0.88 (0.73-1.05)	0.17	<0.001	
		Men (12054 cases; 11999 controls)	0.90 (0.77-1.05)	0.18	0.002	0.86
	Pooled^a	Women (10938 cases; 16542 controls)	0.85 (0.74-0.99)	0.032	0.59 ^a	
		Men (17419 cases; 15446 controls)	0.92 (0.80-1.04)	0.18	0.71 ^a	0.48

OR, odds ratio per 1SD=4.8kg/m²; IVW, inverse-variance weighted; CI, confidence interval.

Summary statistics from sex-stratified analyses in iPDGC with exclusion of UK Biobank participants (Blauwendraat et al. Investigation of Autosomal Genetic Sex Differences in Parkinson's Disease. 2021).

^a Meta-analysis of Courage-PD and iPDGC.

^b p-value from the Cochran's Q statistic for heterogeneity between iPDGC and Courage-PD.

eTable 8: Association between IVs used for BMI and other traits related to PD using the PhenoScanner V2 database at genome-wide significant threshold (5×10^{-8}).

Author, date	SNP	EA	BA	Beta	SE	P	n	Unit
Parkinson's disease								
Nalls M., 2014	rs4988235	A	G	0.117	0.020	7.41E-09	108990	log OR
HDL cholesterol								
Willer C.J., 2013	rs11066188	A	G	-0.021	0.004	1.20E-08	185469	IVNT
	rs13107325	T	C	-0.071	0.008	1.07E-15	179316	IVNT
	rs1358980	C	T	0.025	0.004	6.77E-11	187057	IVNT
	rs2744974	T	C	-0.024	0.004	3.25E-11	185464	IVNT
	rs6567160	C	T	-0.026	0.004	2.92E-09	185608	IVNT
	rs687339	C	T	0.032	0.004	7.11E-13	187105	IVNT
	rs7124681	A	C	-0.034	0.004	6.16E-22	187053	IVNT
Surakka I., 2015	rs429358	C	T	-0.066	0.009	1.00E-14	62166	SD increase
LDL cholesterol								
Willer C.J., 2013	rs11066188	A	G	-0.026	0.004	7.99E-11	170278	IVNT
	rs2112347	G	T	0.044	0.004	4.43E-30	173034	IVNT
	rs4988235	A	G	-0.028	0.004	3.22E-11	169531	IVNT
	rs742748	T	C	0.024	0.004	8.25E-09	171470	IVNT
Prins B., 2017	rs429358	C	T	0.200	0.020	2.97E-24	9961	IVNT
Triglycerides								
Willer C.J., 2013	rs10761785	G	T	0.024	0.003	9.85E-14	177823	IVNT
	rs1358980	C	T	-0.026	0.004	6.02E-13	177761	IVNT
	rs687339	C	T	-0.029	0.004	2.51E-12	177800	IVNT
Surakka I., 2015	rs10864728	A	G	0.052	0.006	5.00E-16	62166	SD increase
	rs1358980	C	T	-0.039	0.007	4.00E-09	62166	SD increase
Uric acid								
Kottgen A., 2013	rs4148155	G	A	0.220	0.009	8.60E-116	110098	mg/dl
Smoking initiation								
TAG consortium, 2010	rs6265	T	C	-0.061	0.011	1.84E-08	143023	log OR
Neale B., 2017	rs264941	A	C	-0.007	0.001	2.21E-09	336067	risk diff.
	rs9818122	C	T	0.009	0.001	5.57E-09	336067	risk diff.
Alcohol consumption								
Neale B., 2017	rs11713193	A	G	0.021	0.004	1.64E-09	336965	-
	rs11782074	G	T	-0.023	0.004	3.42E-10	336965	-
	rs13107325	T	C	0.051	0.007	7.88E-14	336965	-
	rs2051559	T	C	-0.030	0.005	1.32E-08	336965	-
	rs3814883	T	C	0.020	0.004	1.34E-08	336965	-
	rs6567160	C	T	0.026	0.004	2.76E-10	336965	-
	rs7124681	A	C	0.024	0.004	1.92E-11	336965	-
	rs7498665	A	G	-0.033	0.004	2.02E-19	336965	-
	rs891387	T	C	0.029	0.004	1.52E-16	336965	-
	rs9320823	C	T	0.021	0.004	5.68E-09	336965	-
Coffee consumption								
Amin N., 2011	rs2470893	T	C	0.068	0.01	2.00E-11	26105	unit increase
Depression/Anxiety/Neuroticism								
<i>Seen doctor for nerves, anxiety, tension or depression</i>								
Neale B., 2017	rs3101336	T	C	-0.009	0.001	1.22E-13	335108	risk diff.
<i>Neuroticism</i>								
Neale B., 2017	rs4240673	C	T	0.081	0.009	2.44E-20	274108	Score
Okbayt A., 2016	rs4240673	C	T	0.025	0.003	7.46E-13	170911	SD increase
Turley P., 2018	rs4240673	C	T	0.018	0.002	5.63E-14	168105	SD increase
Neale B., 2017	rs900144	T	C	-0.051	0.009	5.37E-09	274108	Score
<i>Worrier or anxious feelings</i>								
Neale B., 2017	rs4240673	C	T	0.012	0.001	1.78E-23	328717	risk diff.
	rs6567160	C	T	-0.009	0.001	2.76E-10	328717	risk diff.

OR, odds ratio; SD, standard deviation; IVNT, inverse normal rank transformed phenotype; risk diff., risk difference.

eTable 9: SNPs used for reverse Mendelian randomisation analyses: individual associations with PD in iPDGC (Chang et al., 2017; Blauwendraat et al., 2021) and BMI.

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure: PD				Outcome: BMI				Exclusion
			EAF	Beta	SE	P	EAF	Beta	SE	P	
Chang et al. 2017											
rs35749011	1:155135036	A/G	0.01	0.545	0.044	2.59E-35	0.01	<u>0.017</u>	0.008	3.96E-02	-
rs823118	1:205723572	T/C	0.56	0.117	0.012	1.12E-23	0.54	<u>-0.006</u>	0.002	6.12E-04	-
rs4653767	1:226916078	T/C	0.69	0.083	0.013	1.63E-11	0.72	0.001	0.002	6.38E-01	-
rs10797576	1:232664611	T/C	0.14	0.113	0.016	8.41E-13	0.12	<u>-0.006</u>	0.003	3.23E-02	-
rs34043159	2:102413116	C/T	0.35	0.077	0.012	5.48E-11	0.34	0.002	0.002	3.30E-01	-
rs6430538	2:135539967	C/T	0.55	0.117	0.012	8.24E-24	0.60	<u>0.008</u>	0.002	6.57E-06	-
rs1474055	2:169110394	T/C	0.13	0.186	0.018	5.68E-26	0.12	<u>0.009</u>	0.003	2.90E-03	-
rs4073221	3:18277488	G/T	0.13	0.095	0.017	1.57E-08	0.12	<u>0.012</u>	0.003	5.98E-05	-
rs12497850	3:48748989	T/G	0.65	0.073	0.013	9.16E-09	0.63	0.001	0.002	4.88E-01	-
rs115185635	3:87520857	C/G	0.04	0.191	0.052	1.22E-04	0.04	-0.006	0.005	2.06E-01	-
rs12637471	3:182762437	G/A	0.80	0.163	0.014	2.11E-30	0.80	<u>0.008</u>	0.002	5.59E-04	-
rs34311866	4:951947	C/T	0.18	0.207	0.014	1.47E-50	0.18	-0.002	0.002	4.65E-01	-
rs11724635	4:15737101	A/C	0.55	0.105	0.012	1.22E-19	0.53	-0.003	0.002	7.34E-02	-
rs356182	4:90626111	G/A	0.35	0.285	0.012	5.21E-123	0.34	<u>-0.007</u>	0.002	4.25E-04	-
rs78738012	4:114360372	C/T	0.11	0.122	0.019	4.78E-11	0.10	0.003	0.003	3.83E-01	-
rs2694528	5:60273923	C/A	0.12	0.140	0.018	4.84E-15	0.08	-0.002	0.003	5.21E-01	-
rs9468199	6:27681215	A/G	0.17	0.104	0.015	1.46E-12	0.18	-0.002	0.002	3.13E-01	-
rs9275326	6:32666660	C/T	0.90	0.163	0.022	1.26E-13	0.90	0.004	0.003	2.17E-01	-
rs199347	7:23293746	A/G	0.59	0.094	0.011	3.51E-18	0.59	-0.003	0.002	6.61E-02	-
rs591323	8:16697091	G/A	0.73	0.094	0.014	2.38E-11	0.71	<u>0.005</u>	0.002	6.12E-03	-
rs2280104	8:22525980	T/C	0.37	0.068	0.012	2.53E-08	0.35	<u>-0.004</u>	0.002	2.41E-02	-
rs13294100	9:17579690	G/T	0.63	0.083	0.012	4.84E-13	0.64	-0.003	0.002	1.42E-01	-
rs10906923	10:15569598	A/C	0.69	0.073	0.013	1.35E-08	0.67	<0.001	0.002	7.60E-01	-
rs117896735	10:121536327	A/G	0.01	0.501	0.056	2.23E-19	0.02	-0.011	0.008	1.41E-01	-
rs3793947	11:83544472	G/A	0.56	0.073	0.013	3.72E-09	0.57	<u>-0.005</u>	0.002	4.76E-03	-
rs329648	11:133765367	T/C	0.35	0.086	0.012	1.11E-13	0.36	<u>-0.01</u>	0.002	1.02E-08	Excluded for reverse MR
rs11060180	12:123303586	A/G	0.55	0.105	0.011	2.05E-20	0.56	<u>0.012</u>	0.002	5.85E-12	Excluded for reverse MR
rs11158026	14:55348869	C/T	0.67	0.094	0.012	4.30E-16	0.65	<u>0.007</u>	0.002	9.84E-04	-
rs1555399	14:67984370	T/A	0.51	0.086	0.014	9.61E-11	0.51	<u>-0.007</u>	0.002	6.67E-04	Excluded for reverse MR
rs8005172	14:88472612	T/C	0.42	0.077	0.012	8.77E-11	0.42	-0.002	0.002	2.01E-01	-
rs2414739	15:61994134	A/G	0.73	0.094	0.013	3.94E-14	0.73	0.001	0.002	5.38E-01	-
rs11343	16:19279464	T/G	0.45	0.068	0.011	9.13E-11	0.44	<u>-0.006</u>	0.002	2.28E-04	-
rs14235	16:31121793	A/G	0.38	0.077	0.011	5.44E-12	0.36	<u>-0.021</u>	0.002	7.30E-35	Excluded for reverse MR
rs4784227	16:52599188	T/C	0.26	0.086	0.014	9.75E-11	0.24	0.003	0.002	1.65E-01	-
rs17649553	17:43994648	C/T	0.78	0.248	0.014	1.26E-68	0.79	<u>-0.004</u>	0.002	4.38E-02	-
rs12456492	18:40673380	G/A	0.32	0.095	0.012	5.56E-16	0.33	<u>-0.006</u>	0.002	4.30E-04	-
rs62120679	19:2363319	T/C	0.31	0.077	0.016	6.64E-07	0.31	<u>0.004</u>	0.002	3.81E-02	-
rs8118008	20:3168166	A/G	0.61	0.068	0.015	1.99E-06	NA in BMI GWAS				

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure: PD				Outcome: BMI				Exclusion
			EAF	Beta	SE	P	EAF	Beta	SE	P	
Blauwendraat et al. 2021 (women and men pooled)											
rs145330152	1:155371119	A/C	0.98	-0.701	0.064	3.07E-28	0.99	-0.015	0.009	7.46E-02	-
rs823116	1:205720483	A/G	0.58	0.103	0.015	7.65E-12	0.54	<u>-0.007</u>	0.002	6.17E-04	-
rs6741007	2:135537119	T/G	0.54	0.130	0.015	2.88E-17	0.60	<u>0.007</u>	0.002	1.53E-04	-
rs4613239	2:169119609	C/G	0.86	-0.188	0.022	1.05E-17	0.88	<u>-0.009</u>	0.003	3.03E-03	-
rs10513789	3:182760073	T/G	0.82	0.151	0.019	6.26E-15	0.81	<u>0.006</u>	0.002	2.50E-03	-
rs34311866	4:951947	T/C	0.80	-0.242	0.019	1.30E-37	0.82	0.002	0.003	4.65E-01	-
rs4698412	4:15737348	A/G	0.55	0.122	0.015	2.11E-16	0.53	-0.003	0.002	6.55E-02	-
rs7666265	4:77176281	A/G	0.19	0.108	0.019	9.41E-09	0.18	0.002	0.002	3.93E-01	-
rs356182	4:90626111	A/G	0.63	-0.270	0.017	1.72E-59	0.66	<u>0.007</u>	0.002	4.25E-04	-
rs10018362	4:90703753	T/C	0.89	-0.186	0.024	1.44E-14	0.89	<u>0.009</u>	0.003	3.86E-03	-
rs6863749	5:60457627	T/C	0.11	0.178	0.023	1.81E-14	0.10	-0.002	0.003	5.48E-01	-
rs2760985	6:32566398	A/G	0.15	-0.199	0.025	1.04E-15	0.18	0.002	0.003	3.53E-01	-
rs466225	7:23332403	T/G	0.41	-0.100	0.016	1.01E-09	0.40	<u>0.003</u>	0.002	4.71E-02	-
rs1692821	8:11699988	T/C	0.29	-0.121	0.016	2.23E-13	0.28	<u>-0.006</u>	0.002	2.60E-03	-
rs34096562	8:16701281	T/G	0.73	0.101	0.017	1.62E-09	0.71	<u>0.006</u>	0.002	8.83E-03	-
rs188789342	10:121372328	T/C	0.02	0.349	0.058	1.35E-09	0.02	-0.007	0.007	2.68E-01	-
rs10894767	11:133811531	A/G	0.29	0.110	0.016	1.66E-11	0.28	-0.011	0.002	6.83E-07	Excluded for reverse MR
rs28370649	12:40399149	A/G	0.97	-0.315	0.048	7.83E-11	0.98	0.004	0.007	5.70E-01	-
rs75505347	12:40885549	T/C	0.02	0.385	0.059	8.13E-11	0.02	<u>0.019</u>	0.008	1.82E-02	-
rs10847839	12:123322560	T/C	0.63	-0.126	0.016	1.22E-14	0.64	-0.004	0.002	5.38E-02	-
rs7155501	14:55347827	A/G	0.56	0.105	0.016	1.42E-10	0.56	<u>0.004</u>	0.002	3.83E-02	-
rs4774417	15:61993702	A/G	0.74	0.119	0.017	1.95E-12	0.72	0.000	0.002	9.32E-01	-
rs9972727	16:31149142	A/G	0.39	0.108	0.016	2.03E-11	0.35	-0.021	0.002	2.09E-26	Excluded for reverse MR
rs12929797	16:52632944	T/C	0.43	0.084	0.015	2.24E-08	0.41	0.009	0.002	1.74E-07	Excluded for reverse MR
rs3785884	17:44057595	A/G	0.23	-0.266	0.018	8.49E-49	0.22	0.004	0.002	9.57E-02	-
rs4588066	18:40672964	A/G	0.33	0.097	0.016	8.24E-10	0.31	<u>-0.007</u>	0.002	3.69E-04	-
rs2295549	20:3175556	C/G	0.64	0.086	0.016	4.20E-08	0.64	<u>0.005</u>	0.002	1.26E-02	-

NA, not available; EA/BA, effect allele/base allele; SE, standard error.

Bold coefficients with their corresponding SE and p-values are significant at $P \leq 0.05$; those underlined with a solid line are negative and those underlined with a dashed line are positive.

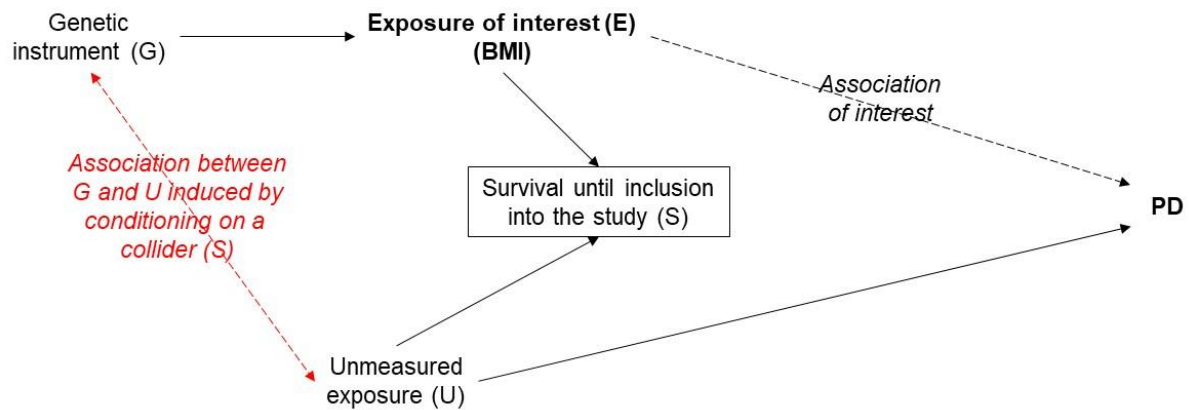
SNPs associated with BMI at $P < 5.0E-08$ are excluded.

eTable 10: Reverse MR analysis: Leave-one-out analysis.

SNP	Odds ratio (95% confidence interval)					
	IVW	P	Weighted median	p	Weighted mode	p
Chang et al., 2017						
rs10797576	1.00 (0.98-1.01)	0.57	0.98 (0.97-0.99)	0.002	0.98 (0.97-0.99)	0.001
rs10906923	1.00 (0.98-1.01)	0.49	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs11158026	0.99 (0.98-1.01)	0.36	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs111343	1.00 (0.98-1.01)	0.61	0.98 (0.97-0.99)	0.002	0.98 (0.97-0.99)	<0.001
rs115185635	1.00 (0.98-1.01)	0.54	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs11724635	1.00 (0.98-1.01)	0.58	0.98 (0.97-0.99)	0.002	0.98 (0.97-0.99)	0.001
rs117896735	1.00 (0.98-1.01)	0.57	0.98 (0.97-0.99)	0.003	0.98 (0.97-0.99)	0.001
rs12456492	1.00 (0.98-1.01)	0.65	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs12497850	0.99 (0.98-1.01)	0.48	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs12637471	0.99 (0.98-1.01)	0.31	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs13294100	1.00 (0.98-1.01)	0.55	0.98 (0.97-0.99)	0.002	0.98 (0.97-0.99)	<0.001
rs1474055	0.99 (0.98-1.01)	0.34	0.98 (0.97-0.99)	<0.001	0.98 (0.97-0.99)	<0.001
rs17649553	1.00 (0.98-1.01)	0.68	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	0.001
rs199347	1.00 (0.98-1.01)	0.58	0.98 (0.97-0.99)	0.002	0.98 (0.97-0.99)	<0.001
rs2280104	1.00 (0.98-1.01)	0.56	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	0.001
rs2414739	0.99 (0.98-1.01)	0.47	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs2694528	1.00 (0.98-1.01)	0.52	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs34043159	0.99 (0.98-1.01)	0.47	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs34311866	1.00 (0.98-1.01)	0.54	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs356182	1.00 (0.98-1.01)	0.97	0.99 (0.97-1.00)	0.015	0.98 (0.97-1.00)	0.036
rs35749011	0.99 (0.98-1.01)	0.38	0.98 (0.97-0.99)	<0.001	0.98 (0.97-0.99)	<0.001
rs3793947	1.00 (0.98-1.01)	0.58	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs4073221	0.99 (0.98-1.01)	0.38	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs4653767	0.99 (0.98-1.01)	0.48	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs4784227	0.99 (0.98-1.01)	0.45	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs591323	0.99 (0.98-1.01)	0.38	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	0.001
rs62120679	0.99 (0.98-1.01)	0.43	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	0.001
rs6430538	0.99 (0.98-1.01)	0.25	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	0.001
rs78738012	0.99 (0.98-1.01)	0.47	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001
rs8005172	1.00 (0.98-1.01)	0.54	0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	0.001
rs823118	1.00 (0.98-1.01)	0.67	0.98 (0.97-0.99)	0.003	0.98 (0.97-0.99)	<0.001
rs9275326	0.99 (0.98-1.01)	0.45	0.98 (0.97-0.99)	<0.001	0.98 (0.97-0.99)	<0.001
rs9468199	1.00 (0.98-1.01)	0.53	0.98 (0.97-0.99)	0.002	0.98 (0.97-0.99)	0.001

IVW, inverse variance weighted.

eFigure 1: Survival bias in Mendelian randomisation studies of diseases in elderly populations.



If both the exposure of interest (E) and an unmeasured exposure (U) influence survival (S), conditioning on survival up to the age at inclusion into the study creates an association between U and G (and E) (red dashed double arrow) because S is a collider. If U is not taken into account in the analysis, the association of G (and E) with PD is biased due to the association between U and G. The bias is more important for exposures that have an important effect on survival, and if there is an interaction between U and E in determining survival.

The importance and direction of the bias depends on the direction of the U-S and E-S associations (discordant or concordant) and of the U×E interaction for S. Depending on these parameters, the bias can go in any direction: it can distort associations towards the null (e.g., true associations that weaken as age increases), or it can create a false association between G and PD in situations where there is no true association (e.g., no association in younger subjects while there is one in older subjects) or make a true association seem stronger; in some extreme situations, it can even revert the direction of a true association (e.g., true positive association becomes negative as age increases).

MR estimates of the association between E and PD are based on the association between G and E, and the association between G and PD. In one-sample MR, both associations are estimated in the same sample and are likely to be similarly biased; therefore, taking the ratio of these associations cancels out much of the bias. Alternatively, in two-sample MR, only the association between G and PD is estimated in the study sample, and the bias of MR estimates equals the bias seen for the G and PD association (Smit RA et al., *Epidemiology* 2019;30(6):813-816).

eFigure 2: Bidirectional MR analyses between BMI and PD: (A) Plots relating the effects sizes of the SNPs-exposure (x-axis) and SNP-outcome (y-axis, log OR) associations with standard error bars: the slope of the lines corresponds to causal estimates using different methods; (B) funnel plots of individual variant effects plotted against the inverse of their standard error. For reverse MR, SNP-PD associations come from two GWAS using the iPDGC dataset.

