

Genome-wide analysis identifies genetic effects on reproductive success and ongoing natural selection at the *FADS* locus

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1958BC-T1DGC and 1958BC-WTCCC2

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BMES: The Blue Mountains Eye Study

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coLaus: Cohorte Lausannoise

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deCODE

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EGCUT: Estonian Genome Center, University of Tartu

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GENOA: Genetic Epidemiology Network of Arteriopathy

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INGI-FVG: Friuli Venezia Giulia Genetic Park

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NTR: Netherlands Twin Register

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RS-I (Rotterdam Study Baseline), RS-II (Rotterdam Study Extension of Baseline) and RS-III (Rotterdam Study Young)

The generation and management of GWAS genotype data for the Rotterdam Study is supported by the Netherlands Organisation of Scientific Research NWO Investments (nr. 175.010.2005.011, 911-03-012). This study is funded by the Research Institute for Diseases in the Elderly (014-93-015; RIDE2), the Netherlands Genomics Initiative (NGI)/Netherlands Organisation for Scientific Research (NWO) project nr. 050-060-810. We thank Pascal Arp, Mila Jhamai, Marijn Verkerk, Lizbeth Herrera and Marjolein Peters for their help in creating the GWAS database, and Karol Estrada and Maksim V. Struchalin for their support in creation and analysis of imputed data. The Rotterdam Study is funded by Erasmus Medical Center and Erasmus University, Rotterdam, Netherlands Organization for the Health Research and Development (ZonMw), the Research Institute for Diseases in the Elderly (RIDE), the Ministry of Education, Culture and Science, the Ministry for Health, Welfare and Sports, the European Commission (DG XII), and the Municipality of Rotterdam. The authors are grateful to the study participants, the staff from the Rotterdam Study and the participating general practitioners and pharmacists.

SHIP: Study of Health in Pomerania

SHIP is part of the Community Medicine Research net of the University of Greifswald, Germany, which is funded by the Federal Ministry of Education and Research (grants no. 01ZZ9603, 01ZZ0103, and 01ZZ0403), the Ministry of Cultural Affairs as well as the Social Ministry of the Federal State of Mecklenburg-West Pomerania, and the network 'Greifswald Approach to Individualized Medicine (GANI_MED)' funded by the Federal Ministry of Education and Research (grant 03IS2061A). Genome-wide data have been supported by the Federal Ministry of Education and Research (grant no. 03ZIK012) and a joint grant from Siemens Healthineers, Erlangen, Germany and the Federal State of Mecklenburg-West Pomerania. The University of Greifswald is a member of the Caché Campus program of the InterSystems GmbH. HJG has received travel grants and speakers honoraria from Fresenius Medical Care, Neuraxpharm, Servier and Janssen Cilag as well as research funding from Fresenius Medical Care.

STR: Swedish Twin Registry

The Jan Wallander and Tom Hedelius Foundation (P2015-0001:1), the Ragnar Soderberg Foundation (E9/11, E42/15), The Swedish Research Council (421-2013-1061). STR is financially supported by Karolinska Institutet. Researchers interested in using STR data must obtain approval from a Swedish Ethical Review Board and from the Steering Committee of the Swedish Twin Registry. Researchers using the data are required to follow the terms of an Assistance Agreement containing a number of clauses designed to ensure protection of privacy and compliance with relevant laws. For further information, contact Patrik Magnusson (Patrik.magnusson@ki.se).

TwinsUK: St Thomas' UK Adult Twin Registry

The Twins UK study was funded by the Wellcome Trust, European Community's Seventh Framework Program (FP7/2007-2013)/grant agreement HEALTH-F2-2008-201865-GEFOS and (FP7/2007-2013), ENGAGE project grant agreement HEALTH-F4-2007-201413, and the FP-5 GenomeUtwinn Project (QLG2-CT-2002-01254). The Twins UK study also receives support from the Department of Health via the National Institute for Health Research (NIHR) comprehensive Biomedical Research Centre award to Guy's and St. Thomas' NHS Foundation Trust in partnership with King's College London. TDS is an NIHR Senior Investigator. The Twins UK study also received support from a Biotechnology and Biological Sciences Research Council (BBSRC) project grant (G20234) and a U.S. National Institutes of Health (NIH)/National Eye Institute (NEI) grant (1RO1EY018246), and genotyping was supported by the

NIH Center for Inherited Disease Research. The Twins UK study also received support from the National Institute for Health Research (NIHR) comprehensive Biomedical Research Centre award to Guy's and St. Thomas' National Health Service Foundation Trust partnering with King's College London.

UKHLS: Understanding Society – The UK Household Longitudinal Study

The UK Household Longitudinal Study, led by the Institute for Social and Economic Research at the University of Essex is funded by the Economic and Social Research Council (Grant Number: ES/M008592/1). Data were collected by NatCen and the genome wide scan data were analysed by the Wellcome Trust Sanger Institute. Access the data at <https://www.understandingsociety.ac.uk/>

WGHS: Women's Genome Health Study

The WGHS is supported by the National Heart, Lung, and Blood Institute (HL043851, HL080467, HL09935) and the National Cancer Institute (CA047988 and UM1CA182913) with collaborative scientific support and funding for genotyping provided by Amgen.

WLS: Wisconsin Longitudinal Study

This research uses data from the Wisconsin Longitudinal Study (WLS) of the University of Wisconsin-Madison. Since 1991, the WLS has been supported principally by the National Institute on Aging (AG-9775, AG-21079, AG-033285, and AG-041868, R01 AG041868-01A1), with additional support from the Vilas Estate Trust, the National Science Foundation, the Spencer Foundation, and the Graduate School of the University of Wisconsin-Madison. Since 1992, data have been collected by the University of Wisconsin Survey Center. The opinions expressed herein are those of the authors. A public use file of data from the Wisconsin Longitudinal Study is available from the Wisconsin Longitudinal Study, University of Wisconsin-Madison, 1180 Observatory Drive, Madison, Wisconsin 53706 and at <http://www.ssc.wisc.edu/WLSresearch/data/>

QIMR: Queensland Berghofer Medical Research Institute

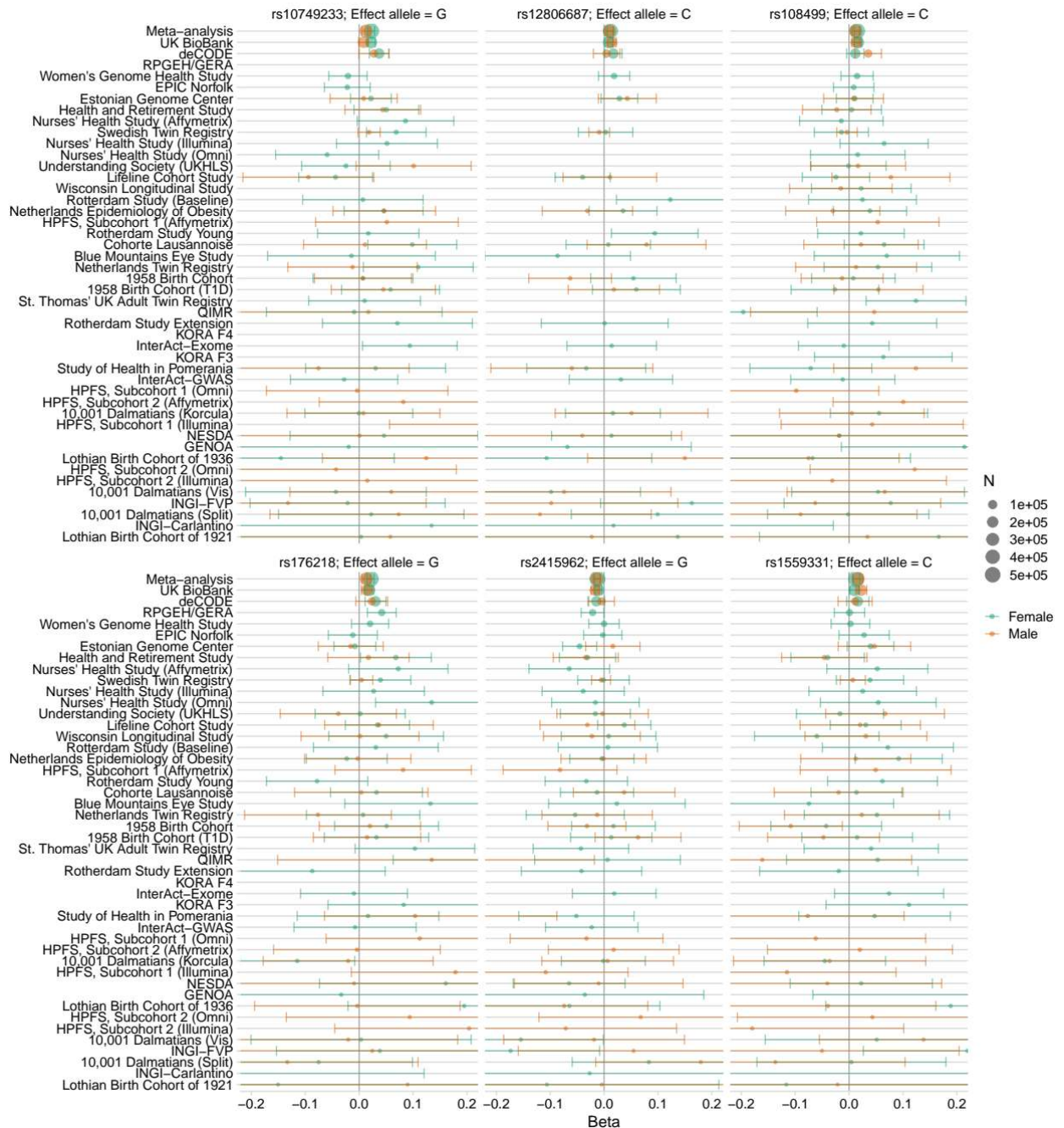
Funding was provided by the Australian National Health and Medical Research Council (241944, 339462, 389927, 389875, 389891, 389892, 389938, 442915, 442981, 496739, 552485, 552498), the Australian Research Council (A7960034, A79906588, A79801419, DP0770096, DP0212016,

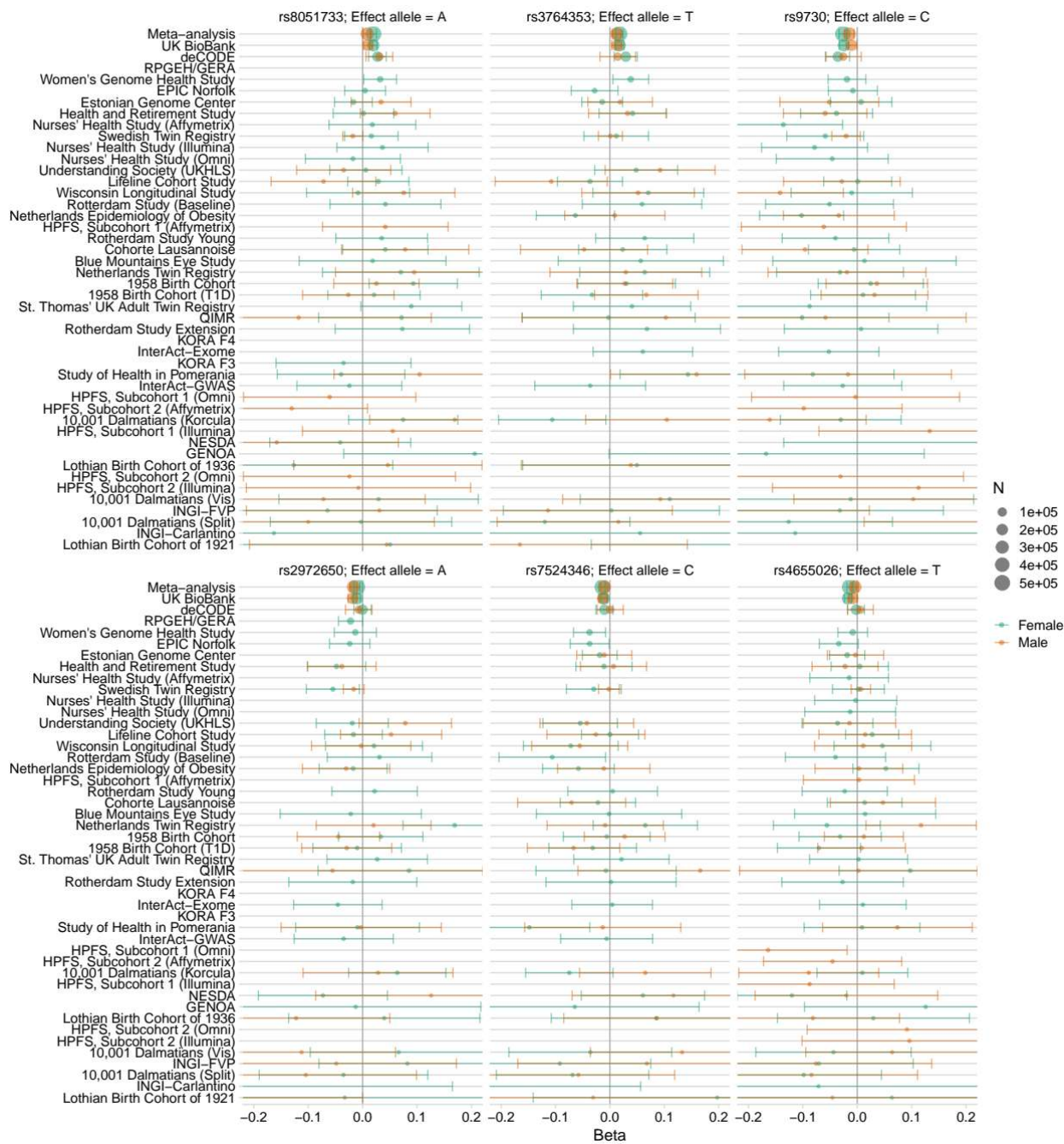
DP0343921), the FP-5 GenomeUtwinn Project (QLG2-CT-2002-01254), and the U.S. National Institutes of Health (NIH grants AA07535, AA10248, AA13320, AA13321, AA13326, AA14041, DA12854, MH66206). A portion of the genotyping on which the QIMR study was based (Illumina 370K scans) was carried out at the Center for Inherited Disease Research, Baltimore (CIDR), through an access award to the authors' late colleague Dr. Richard Todd (Psychiatry, Washington University School of Medicine, St Louis). S.E.M., is supported by an Australian National Health and Medical Research Council Fellowship APP1172917. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. Researchers interested in using QIMR data can contact Nick Martin (Nick.Martin@qimrberghofer.edu.au).

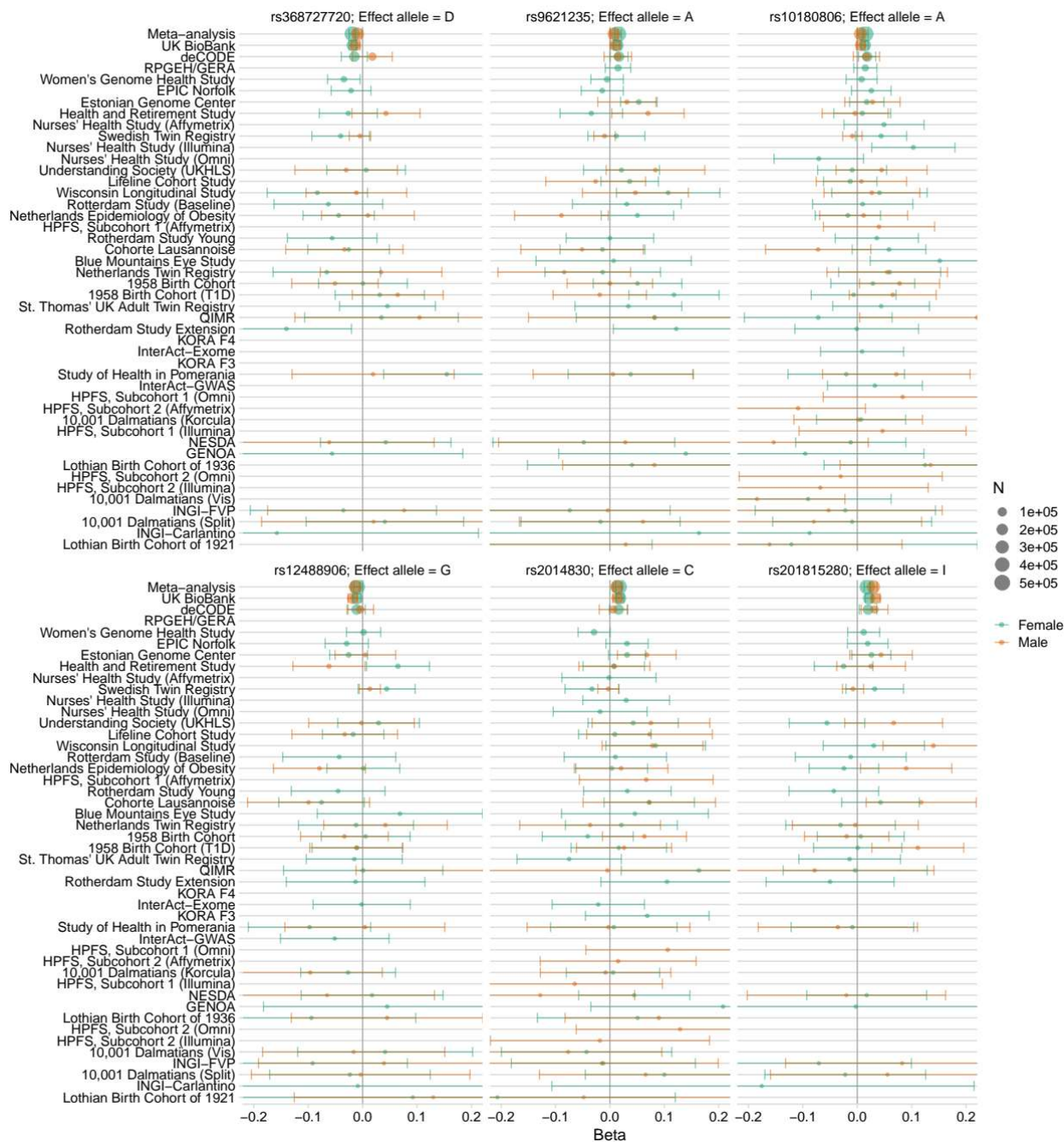
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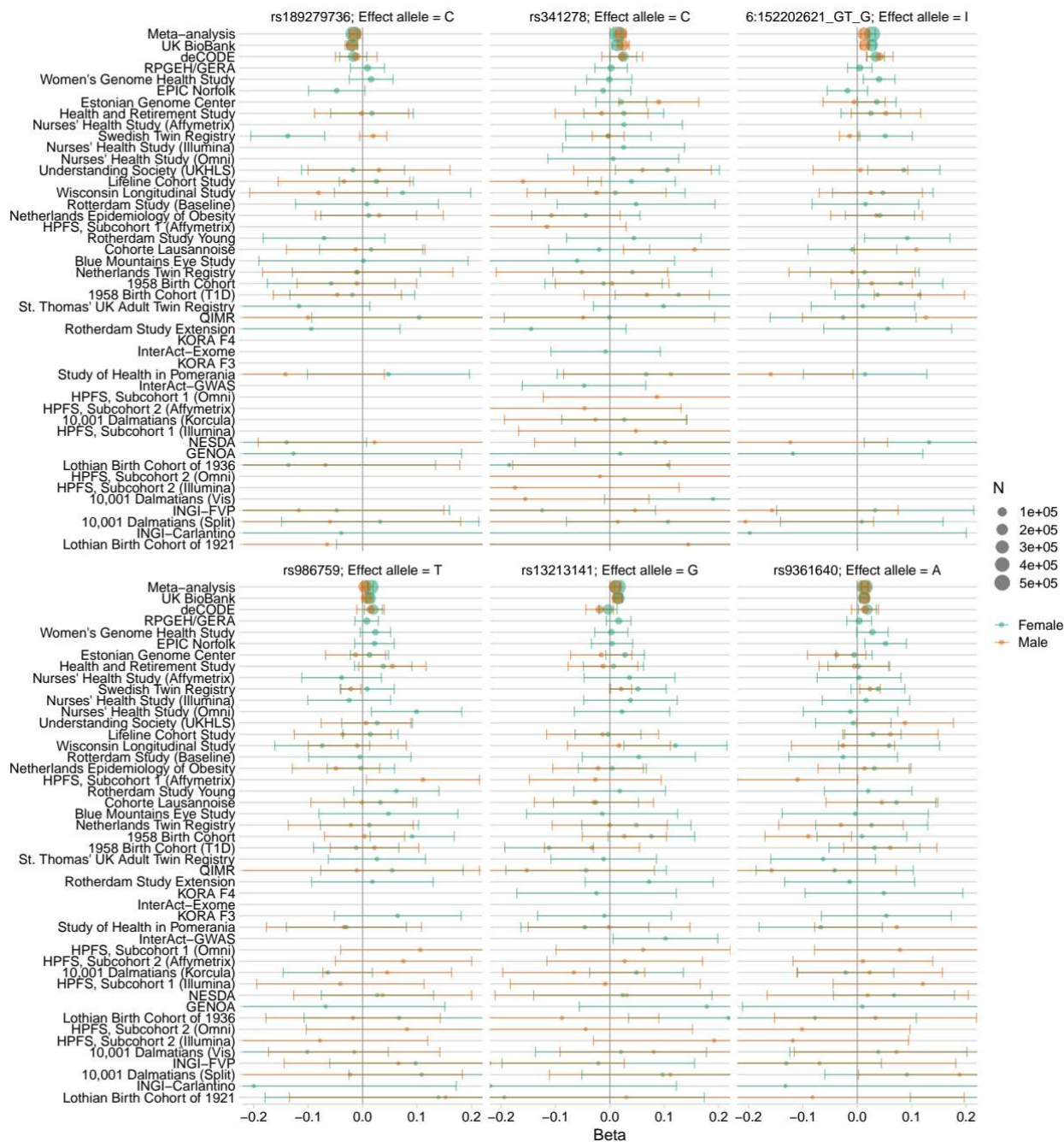
Eva R Hoffmann and Ajuna Azad were funded by an ERC Consolidator Grant (724718-ReCAP), a Novo Nordisk Foundation Young Investigator Award (NNF15OC0016662), and IRFD-FSS (0134-00299B) and the Danish National Research Foundation Center Grant (6110-00344B).

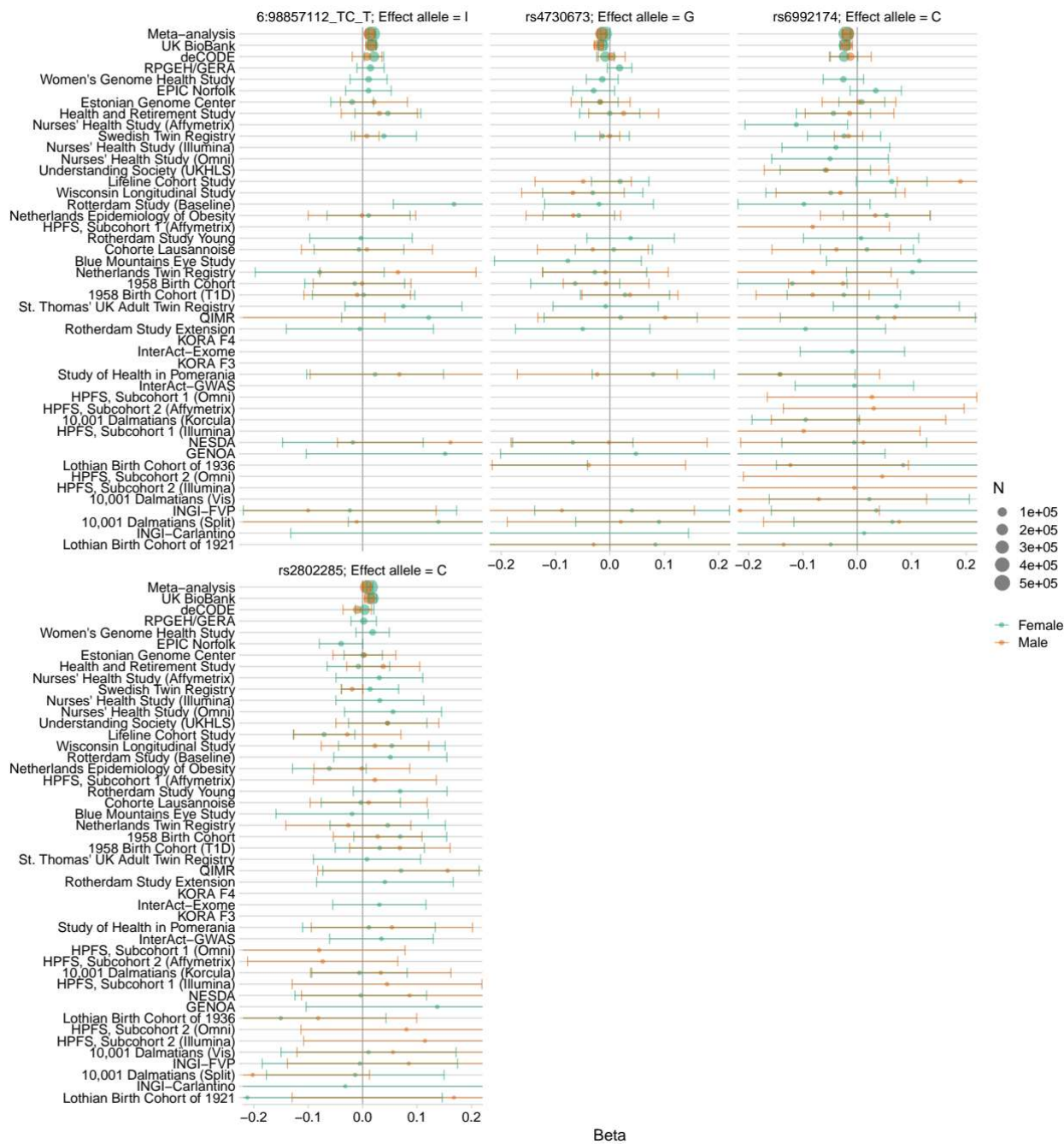
Supplementary Figure 1 | Forest plots showing individual study effect estimates for all genome-wide significant NEB loci. Error bars represent the study specific 95% confidence intervals.



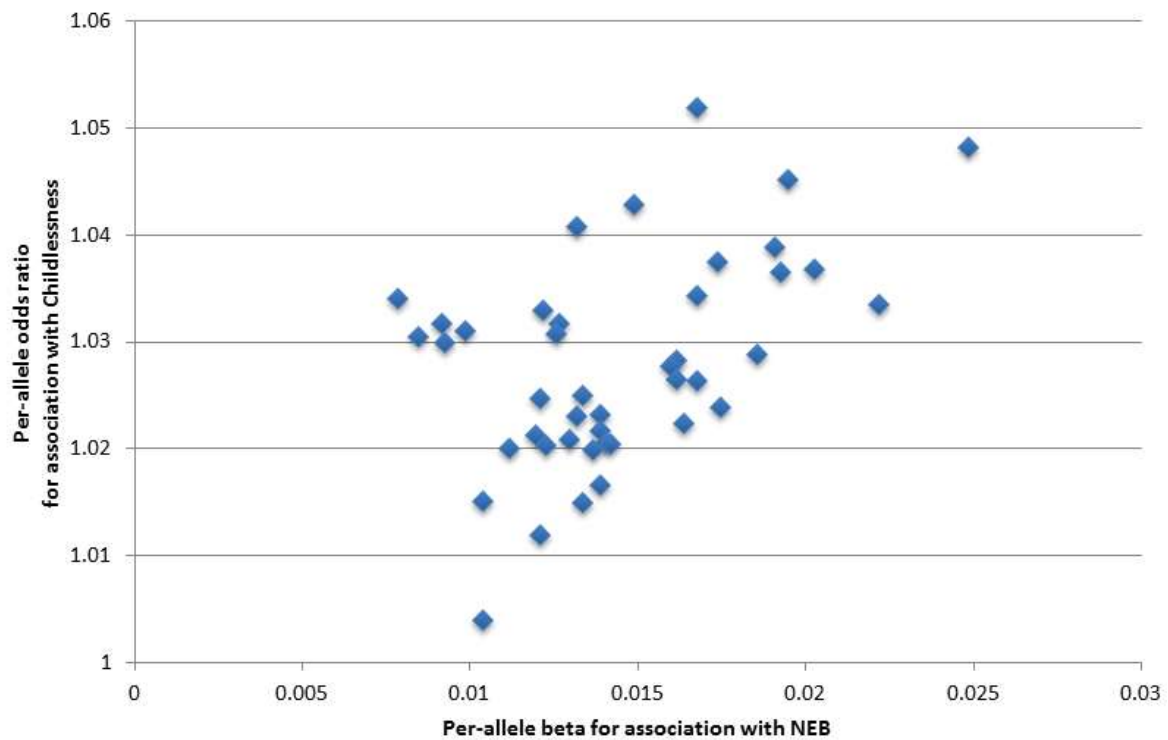








Supplementary Figure 2 | Association of the 43 identified loci on NEB and childlessness. The direction of effect has been reversed for childless to show a risk increasing odds-ratio for easier interpretation of effect magnitude. These analyses are based on 785,604 for NEB and 450,082 for CL.



Supplementary Figure 3 | Percentage of NEB trait variance explained by chromosome. The Y-axis shows size of chromosome proxied by number of directly genotyped SNPs included in the model. This analysis was based on 785,604 individuals.

