Genome-wide association study of kidney function decline: the CKDGen Consortium

Supplementary Information

Supplementary Table 1. Study-specific methods and full acknowledgments – stage 1 and stage 2 cohorts.

Study name (key references)	Study design	Total genotyped sample size	Study exclusions or disease enrichment	Exclusions	Creatinine measurements	Serial creatinine measurements	Acknowledgments and funding source
Stage 1 cohorts							
AGES [1]	Population-based	3,664	None	Sample exclusion criteria included sample failure, genotype mismatch with reference panel, and sex mismatch, resulting in clean genotype data on 3,219 individuals.	AGES: Serum creatinine was measured using the Roche-Hitachi 912 instrument with Roche Creatinine Jaffé compensated method; Roche Diagnostics, Mannheim, Germany. AGESII: Serum creatinine was measured using the Roche-Hitachi P-Module instrument with Roche Creatininase Plus assay.	Serum creatinine a was measured at baseline (AGES:2002-2006), and at a follow-up five years later (AGESII:2007-2011). Individuals were recruited in the same order.	AGES: This study has been funded by NIH contract N01-AG-1-2100, the NIA Intramural Research Program, Hjartavernd (the Icelandic Heart Association), and the Althingi (the Icelandic Parliament). The study is approved by the Icelandic National Bioethics Committee, VSN: 00-063. The researchers are indebted to the participants for their willingness to participate in the study
Amish studies [2,3]	Population-based founder cohort	1,264	None	Age<20, severe chronic disease, call rate<95%, pHWE<10E-6	Modified kinetic Jaffé reaction	All had baseline measures. Timing for repeat measures was variable	AMISH: The Amish studies are supported by grants and contracts from the NIH including R01 AG18728 (Amish Longevity Study), R01 HL088119 (Amish Calcification Study), U01 GM074518-04 (PAPI Study), U01 HL072515-06 (HAPI Study), U01 HL084756 and NIH K12RR023250 (University of Maryland MCRDP), NIH P30 DK072488 (Clinical Nutrition Research Unit), the University of Maryland General Clinical Research Center, grant M01 RR 16500 and the Baltimore Veterans Administration Medical Center Geriatrics Research and Education Clinical Center. We thank our Amish research volunteers for their long-standing partnership in research, and the research staff at the Amish Research Clinic for their hard work and dedication.

Atherosclerosis Risk in Communities (ARIC) Study [4]	Population-based	9,713 of European ancestry	None	Of the 9713 genotyped individuals of European ancestry, we excluded 658 individuals based on discrepancies with previous genotypes, disagreement between reported and genotypic sex, one randomly selected member of a pair of first-degree relatives, or outlier based on measures of average DST or more than 8 SD away on any of the first 10 principal components.	Modified kinetic Jaffe reaction (serum)	Serum creatinine from visits 1, 2, and 4 were used for phenotype definition	The Atherosclerosis Risk in Communities Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C), R01HL087641, R01HL59367 and R01HL086694; National Human Genome Research Institute contract U01HG004402; and National Institutes of Health contract HHSN268200625226C. The authors thank the staff and participants of the ARIC study for their important contributions. Infrastructure was partly supported by Grant Number UL1RR025005, a component of the National Institutes of Health and NIH Roadmap for Medical Research. A.K. was supported by the grant KO3598/2-1 (Emmy Noether Programme) of the German Research Foundation.
ASPS [5,6]	Prospective, single center study	922	History of neuropsychiatric disease, previous stroke and/or TIA, and dementia	Of the 922 participants who underwent genotyping, 74 with sample call rate < 98% were excluded resulting in a total of 848 genotyped individuals	Modified kinetic Jaffe reaction	Serum creatinine was measured at baseline and at the 3 year and 6 year follow-up.	ASPS: The research reported in this article was funded by the Austrian Science Fond (FWF) grant number P20545-P05 and P13180. The Medical University of Graz supports the databank of the ASPS. The authors thank the staff and the participants of the ASPS for their valuable contributions. We thank Birgit Reinhart for her long-term administrative commitment and Ing Johann Semmler for the technical assistance at creating the DNA-bank.
Cardiovascular Health Study (CHS) [7,8]	Prospective, population-based	3,397	In total, 1908 persons were excluded from the GWAS study sample due to the presence at study baseline of coronary heart disease, congestive heart failure, peripheral vascular disease, valvular heart disease, stroke or transient ischemic attack or lack of available DNA	This study is based upon genotyping results from 3,329 CHS Caucasian participants, who were free of clinical cardiovascular disease at baseline, consented to genetic testing, and had DNA available for genotyping. Genotypes were called using the Illumina BeadStudio software. Genotyping was successful in 3,291 persons.	Colorimetric method (Ektachem 700, Eastman Kodak) (serum)	The serum creatinine at baseline and at the 5 year follow-up were used to define the longitudinal renal phenotypes. If data from the 5 year follow-up were missing, the data from the 9 year follow-up were used.	The CHS research reported in this article was supported by contract numbers N01-HC-85079 through N01-HC-85086, N01-HC-35129, N01 HC-15103, N01 HC-55222, N01-HC-75150, N01-HC-45133, grant numbers U01 HL080295 and R01 HL087652 from the National Heart, Lung, and Blood Institute, with additional contribution from the National Institute of Neurological Disorders and Stroke. A full list of principal CHS investigators and institutions can be found at http://www.chs-nhlbi.org/pi.htm. DNA handling and genotyping was supported in part by National Center for Research Resources grant M01RR00425 to the Cedars-Sinai General Clinical Research Center Genotyping core and National Institute of Diabetes and Digestive and Kidney Diseases grant DK063491 to the Southern California Diabetes Endocrinology Research Center.

Cohorte Lausannoise (CoLauS) [9]	Prospective, population-based	5,636	Individuals <35 years were no included	Call rate <90%, related individuals, resulting in 5435 genotyped individuals in total	Modified kinetic Jaffe reaction (maximum inter and intra-batch CVs: 2.9% – 0.7%) (Roche Diagnostics, Switzerland) in the serum	Participants who took part at the baseline CoLaus examination were invited to a 5-year follow-up examination; which is still ongoing and covers the period 2009 to 2012. 1931 COLAUS participants had data available at the time of the stage 1 discovery; and 2238 additional COLAUS participants had data available to be included at the time of the replication	The CoLaus study received financial contributions from GlaxoSmithKline; the Faculty of Biology and Medicine of Lausanne; the Swiss National Science Foundation (33CSCO-122661; 3200BO-111361/2; 3100AO-116323/1;310000-112552). M.B is supported by the Swiss School of Public Health Plus.

Framingham Heart Study (FHS) [10-12]	Prospective, family-based	9,300	None	Of the 9,274 participants who underwent genotyping, we made the following exclusions: sample call rate <97% (n=666), genotype heterozygosity > 5 standard deviations, and ambiguous family data (n=127). This resulted in a total of 8,481 genotyped individuals.	Modified kinetic Jaffe reaction (serum)	Participants for the current study include individuals of European descent from the original cohort who attended cohort exam 15 (1977 to 1979) and exam 24 (1995 to 1998) [n=548], as well as participants from the offspring cohort who attended the sixth (1995 – 1998) and the eighth exams (2005-2008) [n=2234]. Incident CKD was defined as cases of CKD (eGFR <60 ml/min/1.73m2) present at exam cycle 24 (original cohort) and exam cycle 8 (offspring cohort) in individuals free of CKD at the earlier respective exam (i.e. exam 15 for the original cohort and exam 6 for the offspring cohort). In total 2523 participants had complete baseline and follow-up information, and were successfully genotyped for GWA analysis.	FHS: This research was conducted in part using data and resources from the Framingham Heart Study of the National Heart Lung and Blood Institute of the National Institutes of Health and Boston University School of Medicine. The analyses reflect intellectual input and resource development from the Framingham Heart Study investigators participating in the SNP Health Association Resource (SHARe) project. This work was partially supported by the National Heart, Lung and Blood Institute's Framingham Heart Study (Contract No. N01-HC-25195) and its contract with Affymetrix, Inc for genotyping services (Contract No. N02-HL-6-4278). A portion of this research utilized the Linux Cluster for Genetic Analysis (LinGA-II) funded by the Robert Dawson Evans Endowment of the Department of Medicine at Boston University School of Medicine and Boston Medical Center.

GENOA [13-15]	Family-based	1,553	5 Non-white, 1 Missing Exam	For the Affymetrix 6.0 data, we excluded: 25 subjects who failed pre-processing, 123 with Contrast QC < 0.4, 2 for inconsistent relatedness, 11 identical twins. We re-ran the samples that failed pre-processing or the Contrast QC filter on the Affymetrix 6.0 data along with 50 that had passed. Of these samples, 19 failed genotyping completely, 9 had call rate < 0.95, 2 had inconsistent relatedness, and 2 were identical twins. Of these 1509 remaining samples, 346 samples do not have serum creati-nine information. Our final data had 1163 samples with geno-type and phenotype data.	We performed a calibration study between serum creatinine levels in the 1st GENOA examination (1996-2000) assayed on a Monarch autoanalyzer (uncompensate d rate-Jaffe reaction) and in the 2nd and 3rd GENOA examinations assayed on a Hitachi 911 autoanalyzer (compensated rate-Jaffe reaction).	Serum creatinine was measured at baseline, at 5 year and 10 year follow-up.	GENOA: This research was partially supported by the National Heart Lung and Blood Institute of the National Institutes of Health R01 HL-87660.
Health ABC [16]	Prospective cohort study	888	None	Samples were excluded from the dataset for the reasons of sample failure, genotypic sex mismatch, and first-degree relative of an included individual based on genotype data.	Colorimetric technique on a Johnson & Johnson VITROS 950 Chemistry Ana-lyzer (Johnson & Johnson, New Brunswick, NJ, USA) using the enzymatic method.	Serum creatinine was measured at year1 and year 10 .	The Health Aging and Body Composition Study (Health ABC) was funded by the National Institutes of Aging. This research was supported by NIA contracts N01AG62101, N01AG62103, and N01AG62106. The genome-wide association study was funded by NIA grant 1R01AG032098-01A1 to Wake Forest University Health Sciences and genotyping services were provided by the Center for Inherited Disease Research (CIDR). CIDR is fully funded through a federal contract from the National Institutes of Health to The Johns Hopkins University, contract number HHSN268200782096C. This research was supported in part by the Intramural Research Program of the NIH, National Institute on Aging.

JUPITER [17]	Clinical trial	12,649	None	Successfully genotyped samples had >98.5% of SNPs genotyped. In JUPITER, the total number genotyped samples was 12,649 among which 8,782 had self-reported European ancestry that could be confirmed by the MDS procedure in PLINK.	Creatinine analyses were performed in JUPITER core central laboratories using the Roche Modular Analytics Chemistry System with Roche creatinine reagents (modified Jaffé reaction with rate blanking). Intra- and inter-assay coefficients of variation were 4.1% and 3.9%, respectively.	The phenotypes were calculated using two creatinines per patient, taken at the first and last exam of each patient in the Jupiter study.	The JUPITER trial and the genotyping were supported by AstraZeneca

KORA S3/F3 KORA S4/F4 [18,19]	Prospective population-based	F3: 1644 F4: 1814	None	None	S3 and S4: enzymatic assay. F3 and F4: Modified kinetic Jaffe reaction	Serum creatinine was measured at baseline and at the 10 year (F3) and 7 year (F4) follow-up.	KORA studies: The genetic epidemiological work was funded by the NIH subcontract from the Children's Hospital, Boston, US, (H.E.W., I.M.H, prime grant 1 R01 DK075787-01A1), the German National Genome Research Net NGFN2 and NGFNplus (H.E.W. 01GS0823; WK project A3, number 01GS0834), the Munich Center of Health Sciences (MC Health) as part of LMUinnovativ, and by the Else Kröner-Fresenius-Stiftung (P48/08//A11/08 to C.A.B. and B.K.K.; 2012_A147 to CAB and IMH). The kidney parameter measurements in F3 were funded by the Else Kröner-Fresenius-Stiftung (C.A.B., B.K.K.) and the Regensburg University Medical Center, Germany; in F4 by the University of Ulm, Germany (W.K.). Genome wide genotyping costs in F3 and F4 were in part funded by the Else Kröner-Fresenius-Stiftung (C.A.B., B.K.K.). De novo genotyping in F3 and F4 were funded by the Else Kröner-Fresenius-Stiftung (C.A.B., IMH). The KORA research platform and the MONICA Augsburg studies were initiated and financed by the Helmholtz Zentrum München, German Research Center for Environmental Health, by the German Federal Ministry of Education and Research and by the State of Bavaria. Geno-typing was performed in the Genome Analysis Center (GAC) of the Helmholtz Zentrum München. The LINUX platform for computation was funded by the University of Regensburg for the Department of Epidemiology and Preventive Medicine at the Regensburg University Medical Center.
MESA [20]	Prospective population-based	5955	Baseline cardiovascular disease excluded	Baseline cardiovascular disease	Serum creatinine measured at baseline and at EXAMS 3, 4 and 5 ; exams around 1.5 years apart	Vitros analyzer (Johnson and Johnson) with creatine aminohydrolase method	MESA and the MESA SHARe project are conducted and supported by the National Heart, Lung and Blod Institute (NHLBI) in collaboration with MESA Investigators. Support for MESA is provided by contracts N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168, N01-HC-95169 and CTSA UL1-RR-024156

The Rotterdam Study-I [21-23]	Prospective, population-based.	RS-I: 5,974	None	Any samples with a call rate<97.5%, excess autosomal heterozygosity >0.336 (~FDR <0.1%), mismatch between called and phenotypic gender, or if there were outliers identified by the IBS clustering analysis (see below) with >3 standard deviations from population mean or IBS probabilities >97% were excluded from the analysis.	Baseline and third periodical visit: modified kinetic Jaffe reaction	Creatinine levels were measured at baseline and at the third periodical visit.	Rotterdam Study 1: The GWA study was funded by the Netherlands Organisation of Scientific Research NWO Investments (nr. 175.010.2005.011, 911-03-012), the Research Institute for Diseases in the Elderly (014-93-015; RIDE2), the Netherlands Genomics Initiative (NGI)/Netherlands Consortium for Healthy Aging (NCHA) project nr. 050-060-810. We thank Pascal Arp, Mila Jhamai, Dr Michael Moorhouse, Marijn Verkerk, and Sander Bervoets for their help in creating the GWAS database. 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 very grateful to the participants and staff from the Rotterdam Study, the participating general practitioners and the pharmacists. We would like to thank Dr. Tobias A. Knoch, Luc V. de Zeeuw, Anis Abuseiris, and Rob de Graaf as well as their institutions the Erasmus Computing Grid, Rotterdam, The Netherlands, and especially the national German MediGRID and Services@MediGRID part of the German D-Grid, both funded by the German Bundes-ministerium für Forschung und Technology under grants #01 AK 803 A-H and #01 IG 07015 G, for access to their grid resources. Abbas Dehghan is supported by NWO grant (vici, 918-76-619).
The Study of Health in Pomerania (SHIP) [24,25]	Prospective population-based	4,105	None	The following samples were excluded: Affymetrix QC call rate <86%, sample call rate <92%, duplicate samples (by IBD estimation), individuals with reported/genotyped gender mismatch.	Jaffé method at both visits	Serum creatinine was measured at baseline and at the first follow-up visit.	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. Genome-wide data have been supported by the Federal Ministry of Education and Research (grant no. 03ZIK012) and a joint grant from Siemens Healthcare, Erlangen, Germany and the Federal State of Mecklenburg-West Pomerania. The University of Greifswald is a member of the 'Center of Knowledge Interchange' program of the Siemens AG.

Three Cities (3C) [26,27]	Prospective population-based	6748	None	DNA samples were transferred to the French Centre National de Génotypage (CNG) for genotyping. First stage samples that passed DNA quality control were genotyped with Illumina Human 610-Quad BeadChips. Genotype data were retained in the study for samples that had been successfully genotyped for >98% of the SNP markers. SNPs with call rate <98%, minor allele frequency<1% or exhi-biting departure from the Hardy-Weinberg equilibrium in the 3C population ($p<10^{-6}$) were excluded. We also removed 308 samples because they were found to be 1st or 2nd-degree relatives of other study partici-pants or were assessed non-European descent based on genetic analysis. This led us to retain 6440 individuals.	Jaffe assay was used to measure creatinine in all participants at baseline and at the 4-yr follow-up. In order to obtain isotope dilution mass spectrometry (IDMS) traceable creatinine, we used baseline and follow-up frozen serum samples from 20% of the participants to remeasure creatinine with an IDMS traceable enzymatic assay and developed equations relating the Jaffe and IDMS-traceable creatinine.	Serum creatinine was measured at baseline and at the 4-yr follow-up.	Three Cities: The work was made possible by the generous participation of the control subjects, the patients, and their families. We thank Dr. Anne Boland (CNG) for her technical help in preparing the DNA samples for analyses. This work was supported by the National Foundation for Alzheimer's disease and related disorders, the Institut Pasteur de Lille and the Centre National de Génotypage. The Three-City Study was performed as part of a collaboration between the Institut National de la Santé et de la Recherche Médicale (Inserm), the Victor Segalen Bordeaux II University and Sanofi-Synthélabo. The Fondation pour la Recherche Médicale funded the preparation and initiation of the study. The 3C Study was also funded by the Caisse Nationale Maladie des Travailleurs Salariés, Direction Générale de la Santé, MGEN, Institut de la Longévité, Agence Française de Sécurité Sanitaire des Produits de Santé, the Aquitaine and Bourgogne Regional Councils, Fondation de France and the joint French Ministry of Research/INSERM "Cohortes et collections de données biologiques" programme. Lille Génopôle received an unconditional grant from Eisai.
Stage 2 cohorts							

ADVANCE [28,29]	randomised controlled trial done by 215 collaborating centres in 20 countries	2301	All patients are T2D of Caucasian origin	None	Nationally approved standardized tests performed at each of the participating Centers in all countries	Serum creatinine was measured at baseline and at the end of the study which was 5 years later.	ADVANCE: The genetic epidemiological work was funded by Prognomix Inc. and by grants from Genome Quebec and Canadian Institutes for Health Research (CIHR). The clinical study was managed by the George Institute for International Health (Sydney, Australia) with grants received from Les Laboratoires Servier, France and from Medical Research Council of Australia. The genotyping was performed at the genomic platform of CRCHUM. The authors acknowledge the technical help of Carole Long and Mounsif Haloui and the bioinformatic analyses performed by Gilles Godefroid, François-Christophe Blanchet-Marois and François Harvey. The members of the genetic sub-study of ADVANCE, Stephen Harrap and Michel Marre are also acknowledged.
Blue Mountains Eye Study BMES [30-32]	Prospective cohort study	2,761 (2534 after QC)	None	Subjects with missing phenotype data or whose genotype data failed QC	Baseline Serum creatinine was measured using the Roche Jaffe assay; at the 10-year follow-up visit, it was assessed using Isotope Dilution Mass Spectrometry (IDMS). The CKDGene analysis protocol (Incident CKD and Rapid Decline Analysis Plan November 25, 2011) was followed to calibrate/convert creatinine measures at baseline to be in alignment with the measures in the 10-year visit (using IDMS).	Baseline and the 10-year follow-up visits	The Blue Mountains Eye Study (BMES) was supported by the Australian National Health & Medical Research Council (NHMRC), Canberra Australia (NHMRC project grant IDs 974159, 211069, 302068, and Centre for Clinical Research Excellence in Translational Clinical Research in Eye Diseases, CCRE in TCR-Eye, grant ID 529923). The BMES GWAS and genotyping costs was supported by Australian NHMRC, Canberra Australia (NHMRC project grant IDs 512423, 475604 and 529912), and the Wellcome Trust, UK as part of Wellcome Trust Case Control Consortium 2 (A Viswanathan, P McGuffin, P Mitchell, F Topouzis, P Foster, grant IDs 085475/B/08/Z and 085475/08/Z). EGH is supported by the NHMRC Fellowship scheme.

Cohorte Lausannoise (CoLauS)	See “stage 1 cohorts” above						
HYPERGENES [33]	case-control and prospective population based	651	none	none	Serum creatinine was measured using kinetic Jaffe reaction	The samples extracted from the HYPERGENES cohort with complete baseline and follow-up (mean 5.6 years) information were used for this analysis (651 subjects).	HYPERGENES (FP7 - HEALTH-F4-2007-201550); INTEROMICS (MIUR - CNR Italian Flagship Project); IC15-CT98-0329-EPOGH; LSHM-CT-2006-037093; HEALTH-2011-278249-EU-MASCARA; and ERC Advanced Grant-2011-294713-EPLORE and the Fonds voor Wetenschappelijk Onderzoek Vlaanderen; Ministry of the Flemish Community; Brussels; Belgium (grants G.0575.06 and G.0734.09)
KORA S3/F3 (non-GWAS) [18,19]	Prospective, population-based	1498	none	Individuals not genotyped genome-wide as described under “stage 1 cohorts”	S3: enzymatic assay. F3: Modified kinetic Jaffe reaction	Serum creatinine was measured at baseline and at the 10 year (F3) follow-up.	KORA studies: The genetic epidemiological work was funded by the NIH subcontract from the Children’s Hospital, Boston, US, (H.E.W., I.M.H, prime grant 1 R01 DK075787-01A1), the German National Genome Research Net NGFN2 and NGFNplus (H.E.W. 01GS0823; WK project A3,

KORA S4/F4 (non-GWAS) [18,19]	Prospective, population-based	1202	none	Individuals not genotyped genome-wide as described under “stage 1 cohorts”	S4: enzymatic assay. F5: Modified kinetic Jaffe reaction	Serum creatinine was measured at baseline and at the 7 year (F4) follow-up.	number 01GS0834), the Munich Center of Health Sciences (MC Health) as part of LMUinnovativ, and by the Else Kröner-Fresenius-Stiftung (P48/08//A11/08 to C.A.B. and B.K.K.; 2012_A147 to CAB and IMH). The kidney parameter measurements in F3 were funded by the Else Kröner-Fresenius-Stiftung (C.A.B., B.K.K.) and the Regensburg University Medical Center, Germany; in F4 by the University of Ulm, Germany (W.K.). Genome wide genotyping costs in F3 and F4 were in part funded by the Else Kröner-Fresenius-Stiftung (C.A.B., B.K.K.). De novo genotyping in F3 and F4 were funded by the Else Kröner-Fresenius-Stiftung (C.A.B., IMH). The KORA research platform and the MONICA Augsburg studies were initiated and financed by the Helmholtz Zentrum München, German Research Center for Environmental Health, by the German Federal Ministry of Education and Research and by the State of Bavaria. Geno-typing was performed in the Genome Analysis Center (GAC) of the Helmholtz Zentrum München. The LINUX platform for computation was funded by the University of Regensburg for the Department of Epidemiology and Preventive Medicine at the Regensburg University Medical Center.

NESDA [34]	Cohort of mostly patients with a major depressive or anxiety disorder	1925	Most individuals are patients with a major depressive or anxiety disorder	none	Enzymatic assay at both visits	Serum creatinine was measured at baseline and at follow-up 2 years later. Outliers (>4SD from mean) were excluded.	NESDA was supported by the Geestkracht program of ZonMW [grant 10-000-1002]; matching funds from universities and mental health care institutes involved in NESDA. Funding support was also provided by the Netherlands Scientific Organization (904-61-090, 904-61-193, 480-04-004, 400-05-717), Centre for Medical Systems Biology (NWO Genomics), the Neuroscience Campus Amsterdam and the EMGO institute; the European Union (EU/WLRT-2001-01254), NIMH (RO1 MH059160). Genotyping was funded by the Genetic Association Information Network (GAIN) of the Foundation for the US National Institutes of Health, and analysis were supported by grants from GAIN and the NIMH (MH081802) and the Center for Molecular and Systems Biology (CMSB). Genotype data were obtained from dbGaP (http://www.ncbi.nlm.nih.gov/dbgap, accession number phs000020.v1.p1. Statistical analyses were partly conducted at the Genetic Cluster Computer (http://www.geneticcluster.org), which is financially supported by the Netherlands Scientific Organization (NWO 480-05-003) along with a supplement from the Dutch Brain Foundation.
Popgen [35]	prospective population based	577	none	none	Serum creatinine was measured using an enzymatic assay for baseline and at the 5-year follow-up.	Serum creatinine was measured using an enzymatic assay for baseline and at the 5-year follow-up.	POPGEN: This study was funded by the German National Genome Research Network (NGFN; Federal Ministry of Education and Research, grant numbers 1GS0121, 01GS0171, 01GR0468) and by the DFG Excellence Cluster 'Inflammation at Interfaces' (EXC 306).
PREVEND (4 year follow-up) [36]	Prospective population-based	791	Enriched for higher levels of albuminuria	DM1 and pregnant women	Enzymatic assay	Serum creatinine was measured at baseline and follow-up screenings; in this subset, the follow-up took place for 4 years after recruitment.	The PREVEND Study was financially supported by several grants from the Dutch Kidney Foundation.

PREVEND (9 year follow-up) [36]	Prospective population-based	2169	Enriched for higher levels of albuminuria	DM1 and pregnant women	Enzymatic assay	Serum creatinine was measured at baseline and follow-up screenings, that took place approximatly every three years	The PREVEND Study was financially supported by several grants from the Dutch Kidney Foundation.
The Rotterdam Study-II [21-23]	Prospective, population-based.	1,895	None	Any samples with a call rate<97.5%, excess autosomal heterozygosity >0.336 (~FDR <0.1%), mismatch between called and phenotypic gender, or if there were outliers identified by the IBS clustering analysis (see below) with >3 standard deviations from population mean or IBS probabilities >97% were excluded from the analysis.	Baseline and the third periodical visit: enzymatic assay	Creatinine levels were measured at baseline and at the third periodical visit.	Rotterdam Study II: The GWA study was funded by the Netherlands Organisation of Scientific Research NWO Investments (nr. 175.010.2005.011, 911-03-012), the Research Institute for Diseases in the Elderly (014-93-015; RIDE2), the Netherlands Genomics Initiative (NGI)/Netherlands Consortium for Healthy Aging (NCHA) project nr. 050-060-810. We thank Pascal Arp, Mila Jhamai, Dr Michael Moorhouse, Marijn Verkerk, and Sander Bervoets for their help in creating the GWAS database. 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 very grateful to the participants and staff from the Rotterdam Study, the participating general practitioners and the pharmacists. We would like to thank Dr. Tobias A. Knoch, Luc V. de Zeeuw, Anis Abuseiris, and Rob de Graaf as well as their institutions the Erasmus Computing Grid, Rotterdam, The Netherlands, and especially the national German MediGRID and Services@MediGRID part of the German D-Grid, both funded by the German Bundes-ministerium für Forschung und Technology under grants #01 AK 803 A-H and #01 IG 07015 G, for access to their grid resources. Abbas Dehghan is supported by NWO grant (vici, 918-76-619).

SAPHIR [37,38]	healthy working population	1726	none	Of the 1726 subjects genotyped, 1374 had serum creatinine measurements at both examinations and were thus available for the current analyses.	Modified kinetic Jaffé reaction (CREA®, Roche Diagnostics GmbH, Mannheim, Ger-many) in the serum	In May 2003 the first follow-up examination was started. Follow-up of the study population was continued until 2008.	The SAPHIR-study was partially supported by a grant from the Kamillo Eisner Stiftung to B. Paulweber and by grants from the "Genomics of Lipid-associated Disorders – GOLD" of the "Austrian Genome Research Programme GEN-AU" to F. Kronenberg.
Cardiovascular risk in Young Finns Study (YFS) [39]	population-based follow up-study	1683	None	None	Serum creatinine was determined spectrophotom etrically by the Jaffé method (picric acid; Olympus Diagnostica GmbH) from frozen plasma samples.	Serum creatinine was measured at baseline and at the 6 year follow-up.	The Young Finns Study has been financially supported by the Academy of Finland: grants 134309 (Eye), 126925, 121584, 124282, 129378 (Salve), 117787 (Gendi), and 41071 (Skidi), the Social Insurance Institution of Finland, Kuopio, Tampere and Turku University Hospital Medical Funds (grant 9M048 and 9N035 for TeLeht), Juho Vainio Foundation, Paavo Nurmi Foundation, Finnish Foundation of Cardiovascular Research and Finnish Cultural Foundation, Tampere Tuberculosis Foundation and Emil Aaltonen Foundation (T.L). The expert technical assistance in the statistical analyses by Ville Aalto and Irina Lisinen is gratefully acknowledged.

Supplementary Table 2. Study-specific genotyping information for stage 1and stage 2 studies.

Study	Array type	Genotype calling	Quality control filters for genotyped SNPs used for imputation	No. of SNPs used for imputation	Imputation	Imputation backbone for phased CEU haplotypes (NCBI build)	Filtering of imputed genotypes[1]	Data management and statistical analysis	Population stratification or principal components (PCs)
Stage 1 cohorts									
AGES	Illumina Hu370CNV	Illumina	call rate<97%; MAF<1%; pHWE<1e-6 mishap p<1e-9, SNPs not in Hapmap or strandedness issues merging with Hapmap	329,804	MACH version 1.0.16	HapMap release 22 (build 36)	none	R, ProbABEL, Linear and Logistic Regression	We observed no association for the tested traits with the 10 PCs estimated using Eigenstrat.[1]
Amish Studies	Affymetrix 500K	BRLMM	call rate<95% MAF<1%, pHWE<10E-6 SNPs not in Hapmap	338,598	MACH version 1.0.15	phased CEU haplotypes, HapMap release 22 (build 36)	none	Measured genotype accounting for polygenic component	NA
ARIC	Affymetrix 6.0	Birdseed	call rate <95% MAF<1% pHWE <10E-5	669,450	MACH version 1.0.16	HapMap release 22 (build 36)	none	ProbABEL, PLINK, R	Significant association was observed between some of the top 10 PCs estimated using Eigenstrat. The appropriate PCs were therefore included in the respective stratum as covariates in the association analyses

ASPS	Illumina Human610-Quad BeadChip	Illumina	call rate<98% MAF<0.01 pHWE<1e-6 mishap p<1e-9 Mendelian errors>100, SNPs not in Hapmap or strandedness issues merging with Hapmap	550,635	MACH version 1.0.15	HapMap release 22 (build 36)	none	R, linear and logistic fixed effects model	NA
Cardio-vascular Health Study (CHS)	Illumina 370CNV	Illumina BeadStudio	call rate<97%, MAF<1% pHWE<10E-5 heterozygotes=0; SNPs not in HapMap	306,655	BimBam version 0.99	HapMap CEU release 22 (build 36)	dosage variance < 0.01	Linear and logistic regression using R, robust SE estimation	Study sites (clinic sites) were included as covariates in the regression to account for population stratification.
CoLaus	Affymetrix 500K	BRLMM	Call rate<70%, MAF<1% pHWE<1E-7	390,029	IMPUTE version 0.2.0	HapMap release 21 (build 35)	none	Matlab	First 4 ancestry PCs were significantly associated both with eGFR and CKD, thus were included in the analysis.
Framingham Heart Study (FHS)	Affymetrix 500K Affymetrix 50K supplemental	Affymetrix	call rate<97% pHWE<1e-6 MAF<1% mishap p<1e-9; Mendelian errors>100; SNPs not in Hapmap or strandedness issues merging with Hapmap	378,163	MACH version 1.0.15	HapMap release 22 (build 36)	none	R, linear mixed effect models and GEE models, robust variance option to account for relatedness	We observed no association with CKD with the 10 PCs estimated using Eigenstrat. Significant association between eGFR and the 10 PCs was observed therefore, PCs were included in the analysis for association between genotype and eGFR.

GENOA	Affymetrix 6.0 (primary), Illumina 610-Quad, Illumina 660-Quad, Illumina 1M-Duo	Birdseed (Affymetrix data), Genome Studio (Illumina data)	Call Rate<95%, MAF<1%; pHWE < 0.001	1,233,495 (because of the different platforms, some SNPs may have had many missings)	MACH version 1.0.16	HapMap release 22 (build 36), CEU founders	none	R, multic and GEE	Using the PLINK --cluster option, we did not observe any population stratification (all subjects placed within the same cluster). We did not adjust for PCs in the association analysis.
Health ABC	Illumina 1M	BeadStudio v3.3.7	MAF<1% call rate<97% pHWE<10^{-6}	914,263	MACH version 1.0.16	HapMap CEPH release 22 (build 36)	none	R, linear and logistic regression models	Adjust for the 1st PC
Hypergenes	Illumina 1M Duo	Illumina	call rate<99%, MAF<0.01	882935	MACH version 1.0	phased CEU haplotypes, HapMap release 22 (build 36)	none	No relatedness	correct for study center
JUPITER	Illumina Omni 1 Quad	Genome Studio	Call rate < 98.5%, MAF<1%, pHWE<1E-6	979,089	MACH version 1.0.15	1000 Genomes, release 6/2010	none	R	Ten PCs from EIGENSTRAT included
KORA S3/F3	Affymetrix 500K	BRLMM	per-chip call rate <93%; MAF<5%; discrepancy for one of the 50 SNPs common on both chips; gender checks	380,407	MACH	HapMap release 22 (build 35)	none	MACH2QTL, PROBABEL, R, VISUAL BASIC	NA
KORA S4/F4	Affymetrix 6.0	BRLMM	per-chip call rate <93%; per SNP call rate <93%; MAF<1%; gender checks	629,893	MACH	HapMap release 22 (build 36)	none	MACH2QTL, PROBABEL, R, VISUAL BASIC	NA

Rotterdam Study – I	Version 3 Illumina Infinium II HumanHap550	BeadStudio	call rate<90%; MAF<0.01; pHWE<1E-5; Mendelian errors>100; SNPs not in Hapmap or strandedness issues merging with Hapmap	491,875	MACH	HapMap release 22 (build 36)	none	ProbABEL	NA
SHIP	Affymetrix 6.0	Affymetrix Birdseed2	none	869,224	IMPUTE version 0.5.0	HapMap release 22 (build 36)	none	SNPTEST v1.1.5, QUICKTEST v0.94, R, InforSense, InterSystems Caché, SAS	We observed no population stratification using PCs estimated using Eigenstrat.[1]
3 City Study	Illumina 610K	Illumina	Call rate<98%, MAF<1%, pHWE<1E-6	537,029	MACH version 1.0.15	HapMap release 22 (build 36.3)	none	SAS, ProbABEL and R, linear or logistic regression	none
Stage 2 cohorts									
ADVANCE	Affymetrix 5.0 Affymetrix 6.0	Affymetrix	SNPs genotyped on affymetrix 5.0: call rate <96% (<99% if MAF <5%); SNPs genotyped on affymetrix 6.0: Call rate < 97% (<99% if MAF <5%)	876688	IMPUTE2 v2.1.2	Impute2 Website 1000G Pilot (CEU - Jun2010) + HapMap3 release 2 (all available haplotypes – Feb2009) (build 36)	YES (SNPs with imputation info < 0.5 were filtered out)	SNPTEST, frequentist additive model using a missing data likelihood score test	Eigenstrat. Two first principle components were included in the analysis for association between genotype and all phenotypes.

Blue Mountains Eye Study (BMES)	Custom Illumina Infinium 670k array	Illumina	Call rate<95%, MAF<1%, pHWE<1E-6, SNPs not in Hapmap or strandedness issues merging with Hapmap	501,910	MACH version 1.0.16	HapMap release 22 (build 36)	MAF<1% Rsq<0.3	SAS, linear and logistic models	No association was observed between either CKD or eGFR and the top 4 dimensions estimated using multi-dimensional scaling in PLINK. Therefore no ancestry dimensions were included in the analysis for association between genotype and either CKD or eGFR.
CoLaus	Affymetrix 500K	BRLMM	Call rate<70%, MAF<1% pHWE<1E-7	390,029	IMPUTE version 0.2.0	HapMap release 21 (build 35)	none	Matlab	First 4 ancestry PCs were significantly associated both with eGFR and CKD, thus were included in the analysis.
HYPERGENES	Illumina 1M Duo	Illumina	call rate<99%, MAF<0.01	882935	MACH version 1.0	phased CEU haplotypes, HapMap release 22 (build 36)	none	No relatedness	correct for study center

NESDA	Perlegen 600K, Affymetrix 600K	Perlegen, Birdseed v2	call rate<95%,MAF<1%, not mapped, HWE p <10^-6, strand ambiguities, high disconcordance between genotyping platforms or between positive controls, non-random genotypic failure, >5% Mendelian errors	435291, 560631	Beagle 3.04	HapMap release 23 (build 36)	none	SNPTEST, R	First 10 PCs were used as covariates
Popgen	Affymetrix 6.0	Birdseed v2	sample call rate <0.90; SNP call rate <0.95; MAF<1% pHWE<0.0001;	709,003	MACH version 1.0.16	phased CEU haplotypes, HapMap release 22 (build 36)	none	PLINK, R	NA
PREVEND	HumanCytoSNP-12v1	GenomeStudio	call rate <95%, pHWE<0.0001, MAF <0.01	232571	BEAGLE 3.2	phased CEU haplotypes, HapMap release 22 (build 36)	PLINK 1.07 filters INFO <0.1 and MAF <0.01	STATA 11MP, PLINK 1.07	-
Rotterdam Study – II	Version 3 Illumina Infinium II HumanHap550	BeadStudio	call rate<90% MAF<0.01; pHWE<1E-5 Mendelian errors>100; SNPs not in Hapmap or strandedness issues merging with Hapmap	495,478	MACH	HapMap release 22 (build 36)	none	ProbABEL	NA
Cardio-vascular risk in Young Finns Study (YFS)	Illumina Custom BeadChip Human670K	Illumina	Call rate < 95%, MAF<1%, pHWE<1E-6, pi-hat > 0.2 removed due to possible relatedness	546,677	MACH version 1.0	HapMap 2 release 22 (NCBI build 36 dbSNP 126)	Rsq<0.2	R, linear mixed effect models and GEE models, robust variance option to account for relatedness	We have used multidimensional scaling for genetic stratification and included the most affecting components in our model

De novo genotyping	**Genotyping Platform**	**Method**	**QC**						
SAPHIR	Applied Biosystems 7900HT	Taqman PCR	70 duplicates per SNP: 2 discordants for rs11803049, 0 discordants for the other SNPs HWE-testing: p>0.05 for all SNPs Call rate >98.5% for all SNPs						
KORA S3/F3 (non-GWAS)	Applied Biosystems 7900HT	Taqman PCR	18% duplicates per SNP: 0 discordants for all SNPs HWE-testing: p>0.05 for all SNPs Call rate >98.5% for all SNPs						
KORA S4/F4 (non-GWAS)	Applied Biosystems 7900HT	Taqman PCR	18% duplicates per SNP: 1 discordants for rs11803049, 0 discordants for the other SNPs HWE-testing: p>0.05 for all SNPs Call rate 97.2% for rs11803049, >99% for all other SNPs						

Supplementary Table 3: Details on kidney function measures over time in each study

	CKDi cases, n	CKDi25 cases, n	CKDi controls, n	eGFRchange* overall (ml/min/1.73m^2 per year)	eGFRchange* noCKD (ml/min/1.73m^2 per year)	eGFRchange* CKD (ml/min/1.73m^2 per year)	individuals with eGFR change <0, n	Rapid3 overall cases, n	Rapid3 noCKD cases, n	Rapid3 overall controls, n
stage 1 cohorts										
AGES	703	563	2408	0.8 (1.2)	0.8 (1.2)	0.1 (1.2)	597	105	105	3110
Amish	NA	NA	NA	1.2 (5.3)	1.4 (5.2)	NA	192	NA	NA	NA
ASPS	53	18	416	1.6 (3.8)	1.8 (3.89	-0.9 (3.0)	137	135	132	381
KORA3	153	104	1434	0.7 (1.8)	0.8 (1.8)	-1.0 (1.9)	511	144	144	1497
KORA4	94	52	1659	0.6 (3.3)	0.6 (2.3)	-0.1 (2.2)	662	222	217	1585
ARIC	732[A]	435[B]	7793	1.2 (2.6)[C]	1.2 (2.5)	-0.4 (2.5)	2059	1477	1465	7275
CoLaus	77	27	1778	1.2 (2.5)	1.3 (2.4)	-0.5 (2.6)	561	382	378	1549
FHS (Offspring and Cohort)	244	184	2069	0.8 (2.3)	0.9 (2.4)	-0.7 (1.4)	931	289	287	2234
GENOA	54	30	942	0.6 (5.1)	0.7 (5.1)	-0.6 (4.2)	451	265	256	776
HABC	135	81	563	-0.1 (1.9)	-0.1 (2.0)	-0.2 (1.6)	474	43	40	845
JUPITER	429	162	5739	1.7 (8.4)	2.2 (8.6)	-2.1 (5.2)	2808	2497	2434	4396
SHIP	165	88	2919	0.4 (3.4)	0.4 (3.4)	-0.2 (3.4)	1383	600	582	2603
The Rotterdam Study (RS-I)	283	129	1953	0.9 (2.2)	1.1 (2.2)	-0.3 (2.0)	783	371	367	2051
CHS	224	97	2129	0.4 (3.4)	0.6 (3.5)	-0.5 (2.7)	1356	430	397	2390
MESA	291	70	1723	0.7 (2.2)	0.8 (2.3)	0.1 (1.9)	499	283	270	2041
3C	282	80	1818	0.6 (3.2)	0.9 (3.2)	-0.5 (2.6)	1502	505	467	2084
stage 2 cohorts										
ADVANCE	230	138	1479	-0.2 (5.8)	-0.1 (6.0)	-0.6 (4.6)	990	457	413	1577
BMES	275	87	712	0.7 (1.7)	0.7 (1.9)	0.4 (0.8)	342	75	74	1229
COLAUS	51	15	2081	0.3 (2.5)	0.4 (2.4)	-1.3 (3.6)	991	250	246	1959
HYPERGENES	14	11	633	1.0 (7.5)	1.1 (7.6)	-1.4 (1.4)	208	199	199	452
KORA3	40	30	1191	0.5 (1.9)	0.5 (1.9)	-0.5 (1.6)	479	101	101	1169
KORA4	45	26	1101	0.6 (2.5)	0.7 (2.5)	-0.5 (1.7)	444	173	173	1016
NESDA	8	1	1262	-1.2 (7.7)	-1.2 (7.7)	4.1 (4.0)	695	304	296	966

popgen	46	14	496	0.9 (2.6)	1.0 (2.6)	-0.1 (1.7)	173	83	81	494
PREVEND 4yrs	17	10	725	-4.1 (6.4)	-4.1 (6.5)	-2.3 (4.0)	566	52	49	739
PREVEND 9yrs	101	49	2031	0.7 (1.4)	0.7 (1.4)	0.6 (1.1)	604	111	109	2058
RS-II	177	76	1030	0.9 (1.0)	0.9 (1.0)	0.4 (0.9)	205	56	56	1187
SAPHIR	33	10	1328	0.7 (2.9)	0.8 (2.9)	-2.2 (2.6)	521	244	244	1130
YFS	2	1	1678	0.8 (2.2)	0.8 (2.2)	0.4 (0.7)	534	160	160	1523

* A positive value for eGFRchange indicates a decline eGFR over time, a negative value in eGFRchange indicates a rise in eGFR over time.

[A] CKDi is defined as the first occurrence of eGFR < 60 at visit 2 or visit 4

[B] CKD25i is defined as the first occurrence of eGFR < 60 and greater than 25% drop at visit 2 or visit 4

[C] eGFRchange is calculated as (visit 1 eGFR - visit 4 eGFR)/(age at visit 4 - age at visit 1). If visit 4 eGFR is not available, then visit 2 eGFR and age are used. Twenty individuals with eGFRchange beyond 6SD were excluded from all analyses of eGFRchange and Rapid Decline.

Supplementary Table 4:

Association results of rs12917707 at UMOD in stage 1 meta-analysis for all traits analyzed. The effect allele is T, with an allele frequency of 0.18.

trait	beta	SE	pval2GC	I2
eGFRdecline overall	-0.15	0.02	2.60E-14	2.7
eGFRdecline noCKD	-0.15	0.02	8.21E-13	0
eGFRdecline CKD	-0.20	0.08	0.01	0
CKDi	-0.20	0.04	9.05E-08	5.5
CKDi25	-0.22	0.05	3.69E-06	18.8
Rapid3 overall	-0.10	0.03	0.0004	0
Rapid3 noCKD	-0.10	0.03	0.0007	0

Supplementary Table 5: Imputation scores of SNPs analyzed in stage 1 and stage 2 meta-analysis

Stage 1 cohorts

SNPID	variable	Ages	Amish	Aric	Chs	Colaus	Genoa	Habc	Jupiter	Kora3 GWA	Kora4 GWA	Mesa	Rotterdam	Ship	Three Cities	ASPS	FHS	median
rs1019173 (*GALNTL5/ GALNT11*)	oevar_imp	0.98	0.66	0.89	0.98	0.71	0.89	1.00	1.00	0.62	0.88	0.93	0.98	0.87	0.97	0.98	1.01	0.95
	imputed	1	1	1	1	1	1	1	1	1	1	NA	1	1	1	1	1	
	used_for_imp	0	0	0	0	0	0	1	0	0	0	NA	0	0	NA	0	1	
rs11764932 (*MEOX2*)	oevar_imp	0.99	0.94	0.99	0.86	0.95	0.99	0.99	0.99	0.98	NA	1.02	1.00	0.99	1.00	1.00	0.96	0.99
	imputed	1	1	1	1	1	1	1	1	1	0	NA	1	0	1	1	1	
	used_for_imp	0	0	0	0	0	1	0	0	0	1	NA	0	1	NA	0	0	
rs11803049 (*NPPA/NPPB*)	oevar_imp	0.86	0.78	0.99	0.22	0.70	0.89	1.00	0.99	0.63	NA	1.02	0.98	0.97	1.00	0.98	0.83	0.97
	imputed	1	1	0	1	1	1	1	0	1	0	NA	0	0	1	1	1	
	used_for_imp	0	0	1	0	0	1	1	1	0	1	NA	0	1	NA	0	0	
rs12917707 (*UMOD*)	oevar_imp	0.98	0.90	0.94	0.97	0.93	0.91	0.95	0.88	0.86	0.87	0.77	0.98	0.99	0.95	0.96	0.96	0.95
	imputed	1	1	1	1	1	1	1	1	1	1	NA	1	1	1	1	1	
	used_for_imp	0	0	0	0	0	1	0	0	0	0	NA	0	0	NA	0	0	
rs759341 (*C2orf48*)	oevar_imp	1.00	0.93	0.97	1.00	0.94	0.98	1.00	0.99	NA	NA	0.98	0.99	0.55	0.99	1.00	0.45	0.99
	imputed	1	1	0	0	0	1	1	0	0	0	NA	0	0	1	1	1	
	used_for_imp	1	1	1	1	1	0	1	1	1	1	NA	1	1	NA	1	0	
rs875860 (*CDH23*)	oevar_imp	0.73	0.44	0.75	0.22	0.55	0.78	1.00	0.99	0.55	0.72	0.66	0.80	0.73	0.88	0.80	0.63	0.73
	imputed	1	1	1	1	1	1	1	0	1	1	NA	1	1	1	1	1	
	used_for_imp	0	0	0	0	0	0	1	1	0	0	NA	0	0	NA	0	0	
rs9814367 (*IL1RAP*)	oevar_imp	0.99	0.99	1.00	0.96	1.00	1.00	1.00	0.88	NA	NA	0.97	0.98	0.97	0.43	1.00	1.01	0.99
	imputed	1	1	0	1	0	1	1	1	0	0	NA	1	0	1	1	1	
	used_for_imp	0	1	1	0	1	0	0	0	1	1	NA	0	1	NA	0	1	

stage 2 cohorts

SNPID	variable	Advance	BMES	Colaus	Hypergenes	KORAF3 NGWA	KORAF4 NGWA	Nesda	Popgen	Prevend4y	Prevend9y	Rotterdam Study II	Saphir	Young Finns	median
rs1019173 (*GALNTL5/ GALNT11*)	oevar_imp	0.96	0.98	0.71	NA	1.00	1.00	0.92	0.89	0.96	1.02	0.98	1.00	0.99	0.96
	imputed	NA	NA	NA	NA	0	0	NA	NA	1	1	NA	0	NA	
	used_for_imp	0	0	0	1	0	0	1	0	1	1	0	0	0	
rs11764932 (*MEOX2*)	oevar_imp	1.00	0.99	0.95	0.99	1.00	1.00	0.98	1.00	0.84	0.92	0.99	1.00	0.99	0.99
	imputed	NA	NA	NA	1	0	0	NA	NA	1	1	NA	0	NA	
	used_for_imp	1	0	0	0	0	0	1	0	0	0	0	0	0	
rs11803049 (*NPPA/NPPB*)	oevar_imp	1.00	1.00	0.72	1.00	1.00	1.00	0.98	0.99	0.66	0.63	0.98	1.00	NA	0.98
	imputed	NA	NA	NA	1	0	0	NA	NA	1	1	NA	0	NA	
	used_for_imp	1	1	0	0	0	0	1	0	0	0	0	0	NA	
rs12917707 (*UMOD*)	oevar_imp	0.83	0.96	0.93	1.00	1.00	1.00	0.88	0.92	0.45	0.46	0.98	1.00	0.88	0.90
	imputed	NA	NA	NA	1	0	0	NA	NA	1	1	NA	0	NA	
	used_for_imp	0	0	0	0	0	0	0	0	0	0	0	0	0	
rs759341 (*C2orf48*)	oevar_imp	1.00	0.99	0.96	NA	1.00	1.00	0.84	0.98	0.09	0.09	0.99	1.00	NA	0.99$
	imputed	NA	NA	NA	NA	0	0	NA	NA	1	1	NA	0	NA	
	used_for_imp	1	1	1	1	0	0	1	1	0	0	1	0	NA	
rs875860 (*CDH23*)	oevar_imp	0.83	0.80	0.53	NA	1.00	1.00	0.68	0.71	0.03	0.03	0.80	1.00	0.81	0.80*
	imputed	NA	NA	NA	NA	0	0	NA	NA	1	1	NA	0	NA	
	used_for_imp	0	0	0	1	0	0	0	0	0	0	0	0	0	
rs9814367 (*IL1RAP*)	oevar_imp	1.00	0.97	1.00	1.00	1.00	1.00	1.00	1.00	0.94	1.02	0.97	1.00	0.99	1.00
	imputed	NA	NA	NA	1	0	0	NA	NA	1	1	NA	0	NA	
	used_for_imp	1	0	1	0	0	0	1	0	0	0	0	0	0	

For each SNP, information on the imputation score ("oevar_imp"), on whether the SNP was imputed ("imputed") and on whether the SNP was used for imputation ("used_for_imp") is shown. “1” indicates “yes”, “0” indicates “no”. “NA”: information not provided by study.

* median of studies participating in eGFRdecline_CKD stage 2 meta-analysis (ADVANCE, BMES, COLAUS, RS-II)

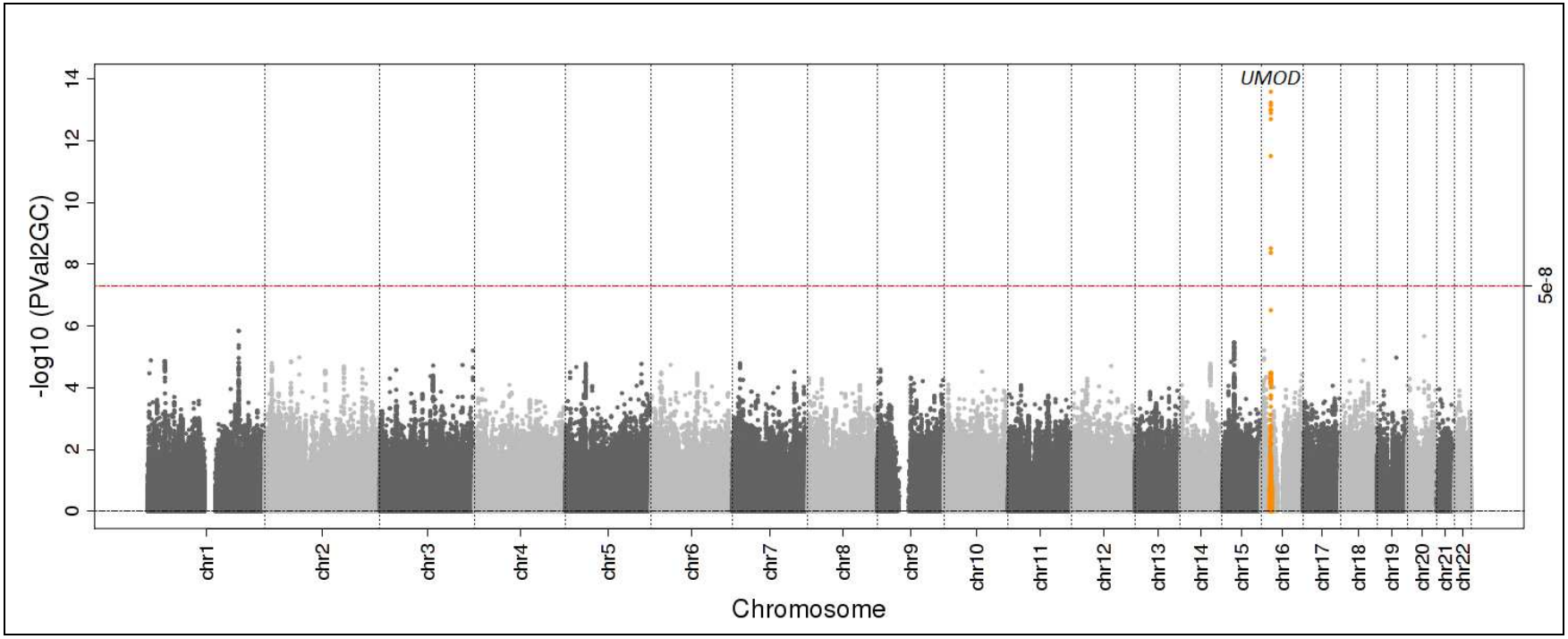
$ median of studies participating in CKDi25 stage 2 meta-analysis (ADVANCE, BMES, RS-II)

Supplementary Table 6: Morpholino sequences

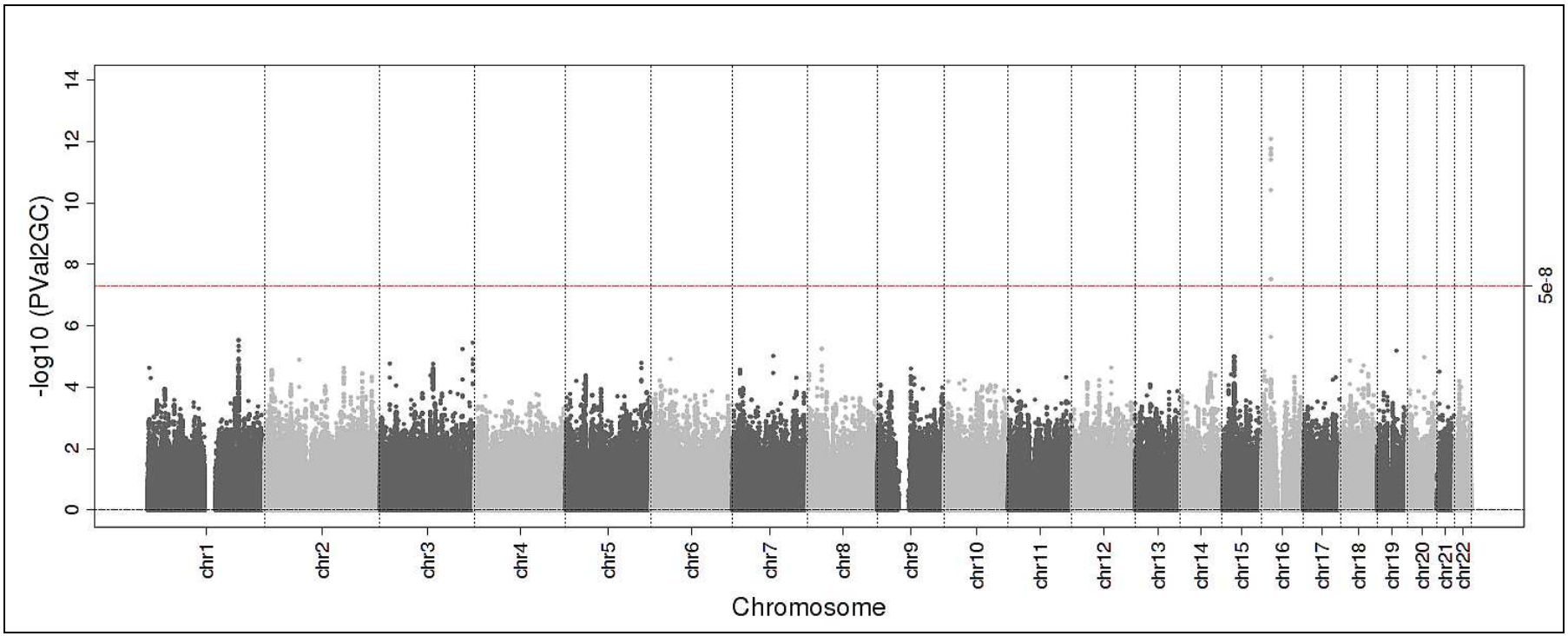
Target gene	ATG or splice	MO Sequence
cdh23	Splice	5’ CTCCCGAACCTTCACACCACGACAT 3’
galnt11	ATG	5’ AGTAGCGCAGAGTGACGCTGCCCAT 3’
prkag2	ATG	5’ AGTCCATCACTGTACTTCCCATTTT 3’
mll3a	Splice	5’ TGTGCAGTAAGATGTTTACCTGCTT 3’
mll3b	Splice	5’ ACATTTACTTCTGGTTTGACCTCTT 3’
umod	ATG	5' CATGTTGACTGATTTTGATGGCTGA 3'

Supplementary Figure 1: Genome-wide log_{10} P value and QQ plots of stage 1 meta-analysis for each trait.

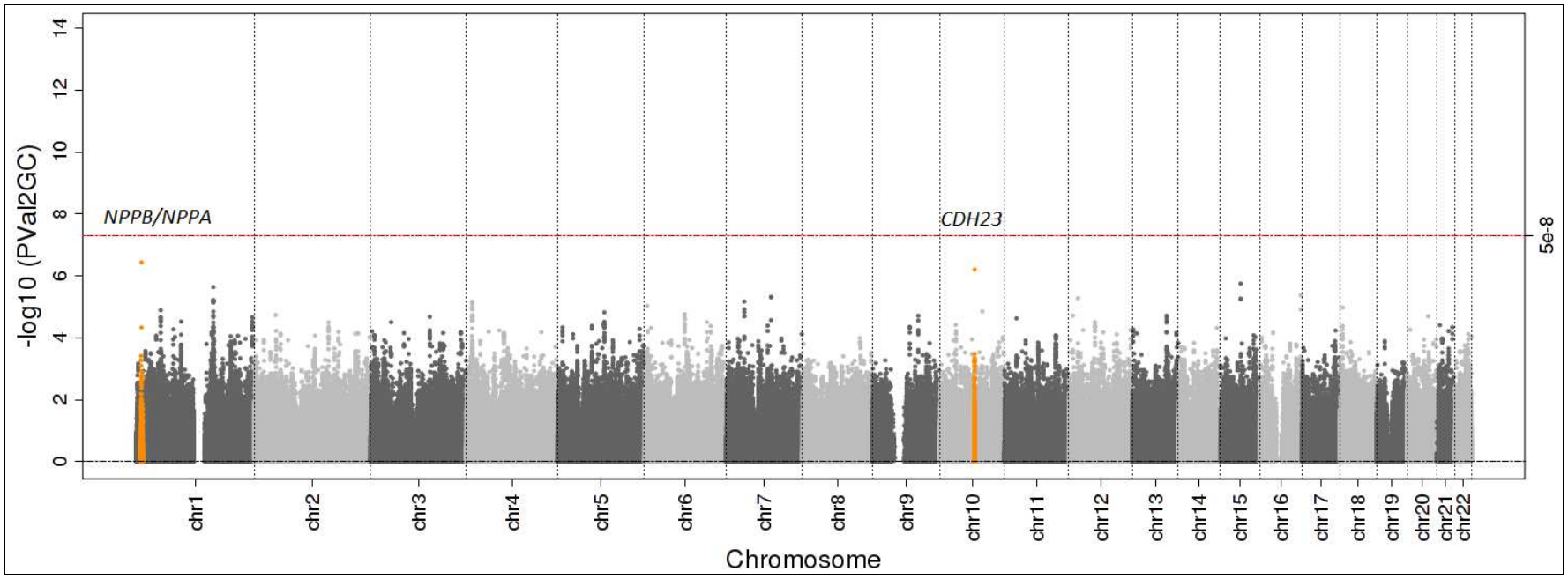
Genetic loci moved forward to stage 2 meta-analysis are highlighted in orange in the trait they were identified in.



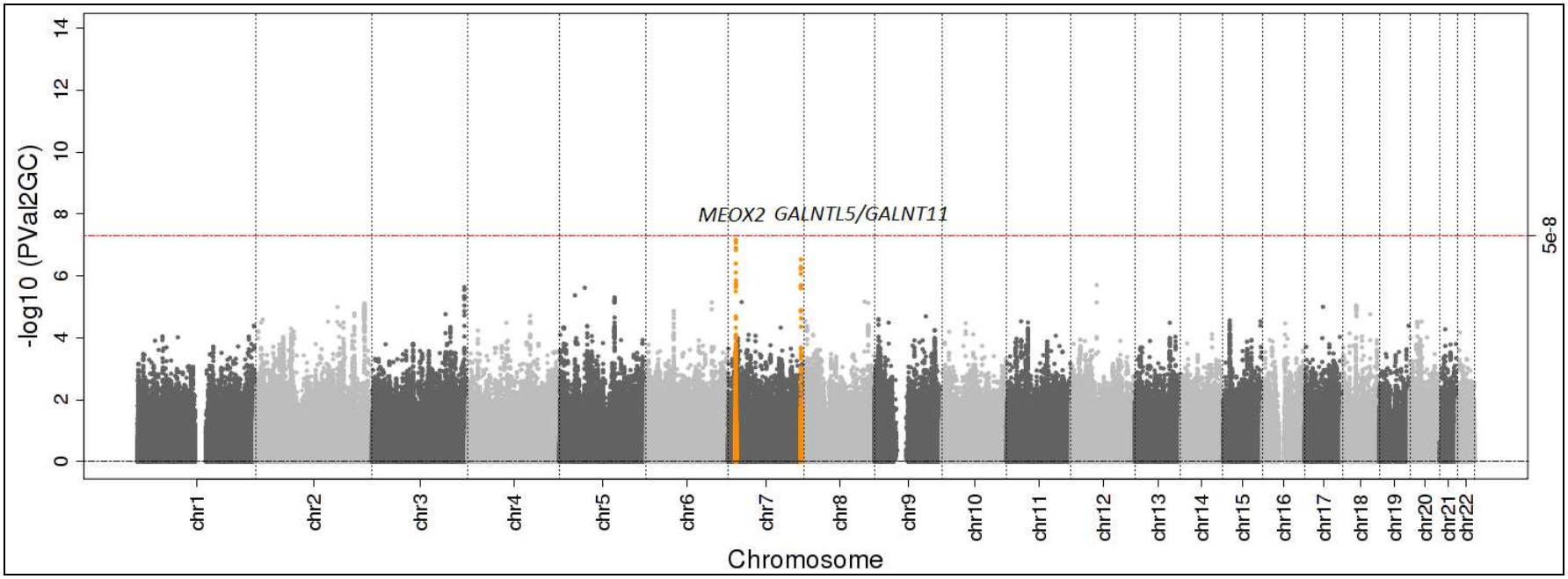
Supplementary Figure 1a: Genome-wide log_{10} P value plot of stage 1 meta-analysis of eGFRchange in the overall sample.



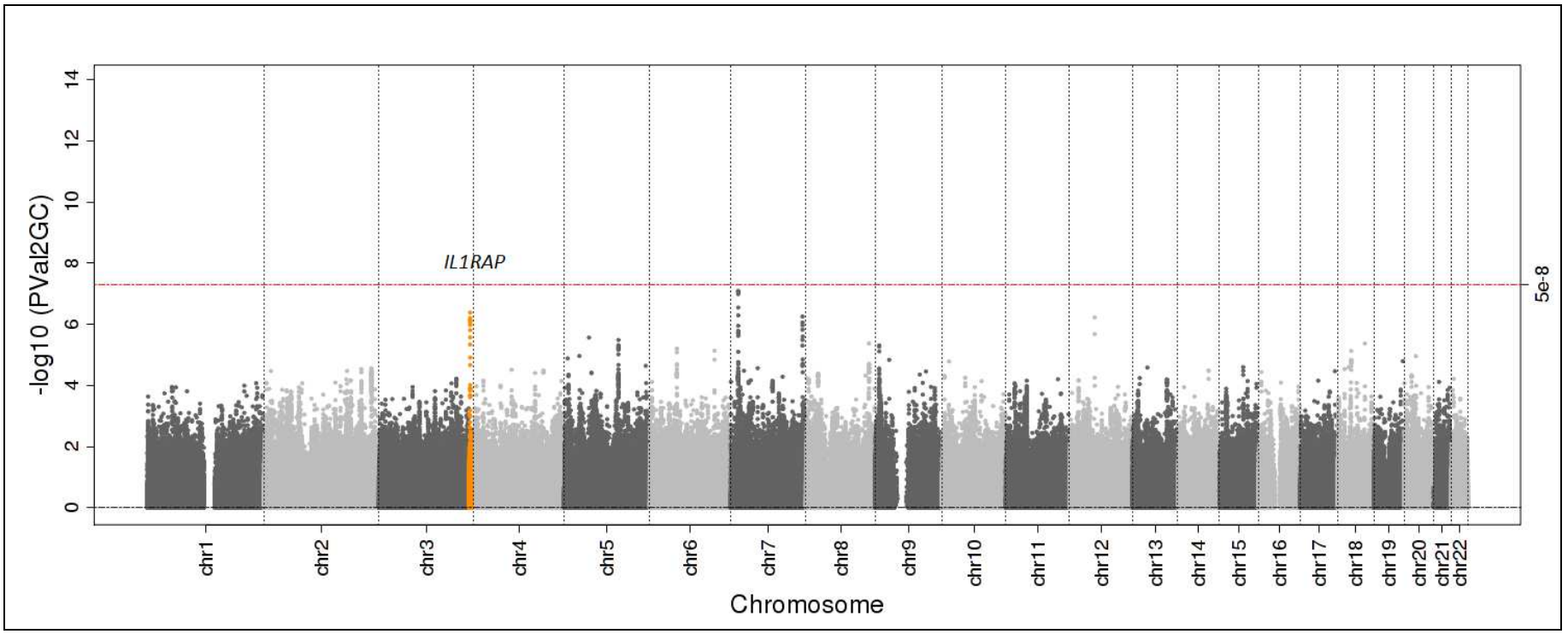
Supplementary Figure 1b: Genome-wide $\log_{10}$ P value plot of stage 1 meta-analysis of eGFRchange in those without CKD at baseline.



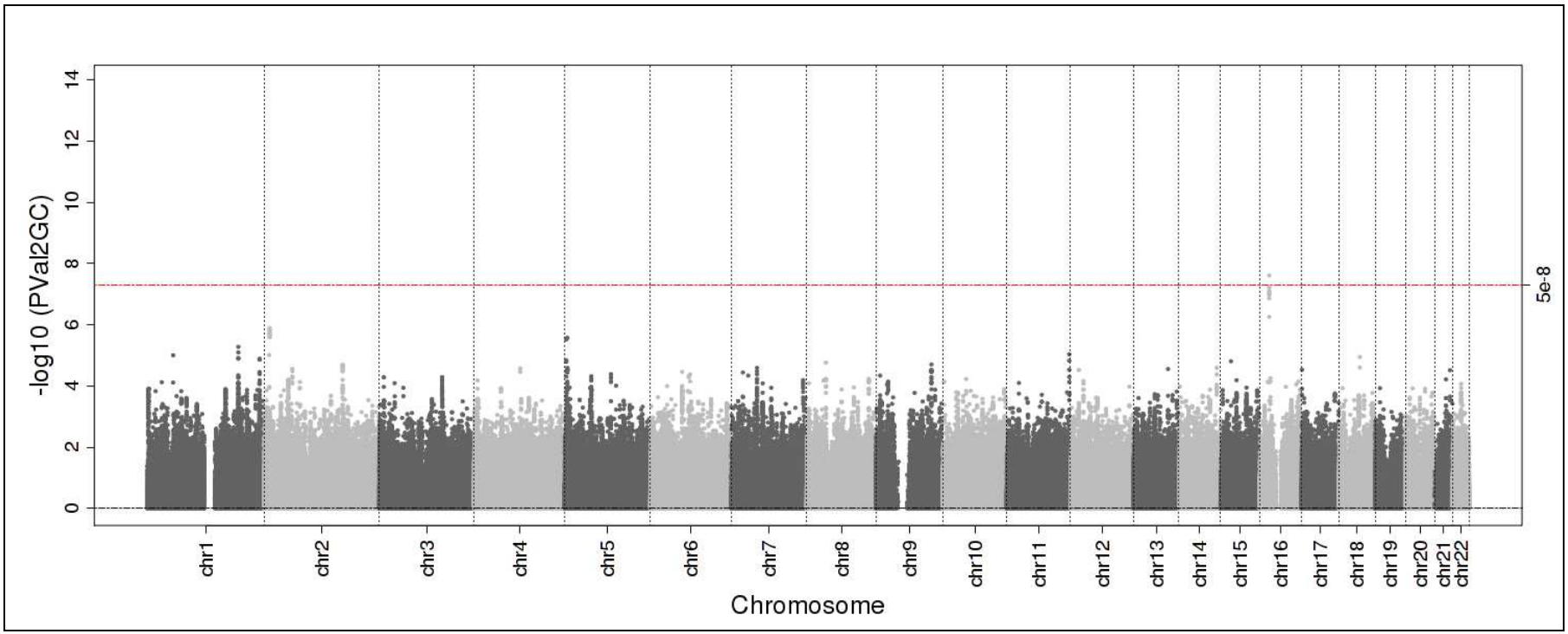
Supplementary Figure 1c: Genome-wide $\log_{10}$ P value plot of stage 1 meta-analysis of eGFRchange in those with CKD at baseline.



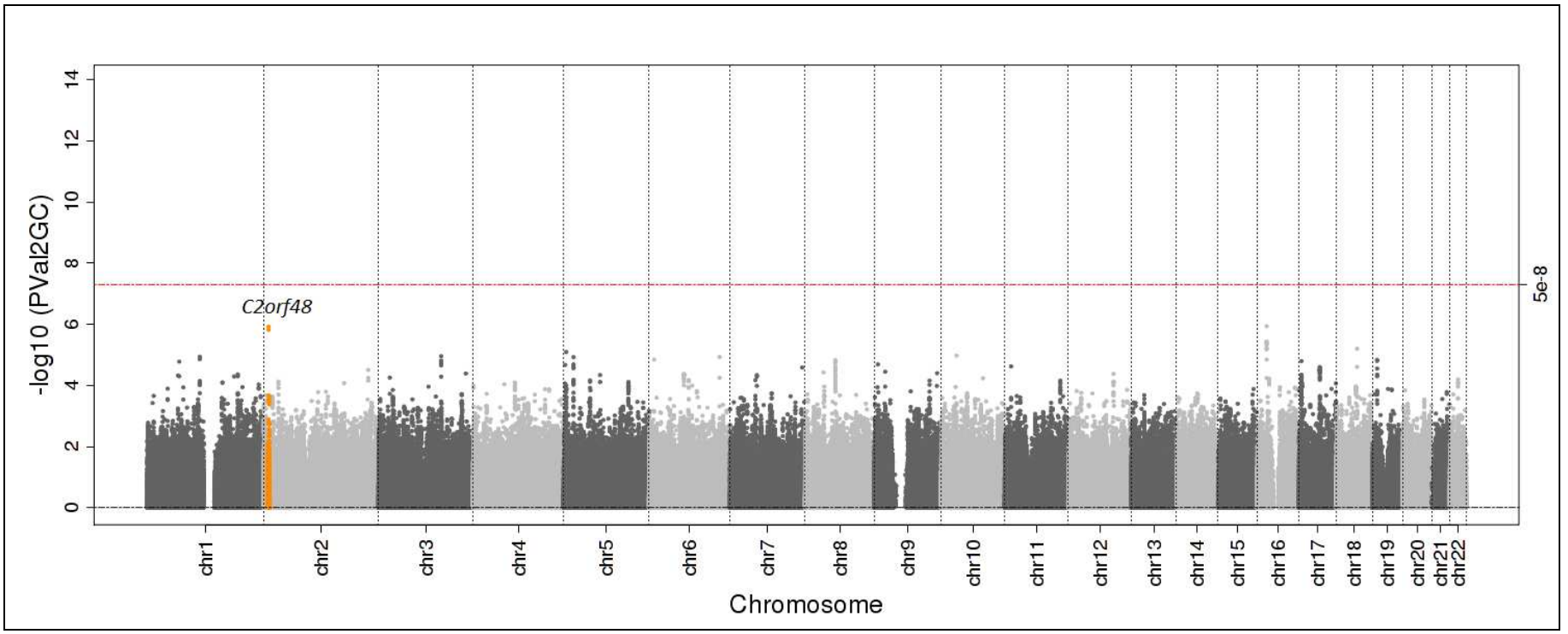
Supplementary Figure 1d: Genome-wide $\log_{10}$ P value plot of stage 1 meta-analysis of Rapid Decline in the overall sample.



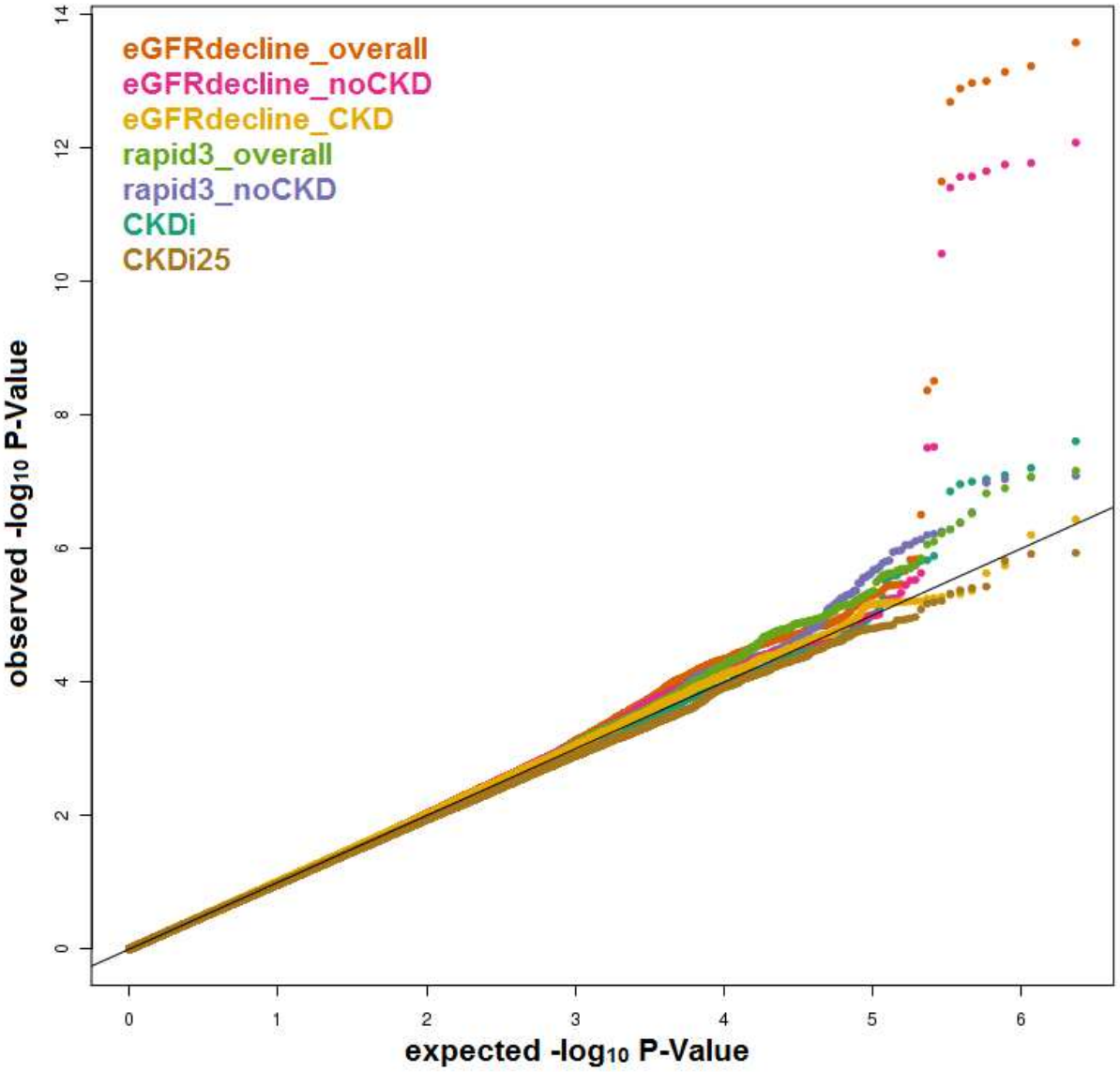
Supplementary Figure 1e: Genome-wide $\log_{10}$ P value plot of stage 1 meta-analysis of Rapid Decline in those without CKD at baseline.



Supplementary Figure 1f: Genome-wide $\log_{10}$ P value plot of stage 1 meta-analysis of incident CKD.



Supplementary Figure 1g: Genome-wide $\log_{10}$ P value plot of stage 1 meta-analysis of CKDi25.



Supplementary Figure 1h: Quantile-Quantile plots of stage 1 meta-analyses.

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