SUPPLEMENTAL INFORMATION

Contents

SUPPLEMENTAL METHODS.

Cohorts in GWAS. The GWAS meta-analysis included up to 19,406 patients with type 1 diabetes and of European origin from 17 cohorts: The Austrian Diabetic Nephropathy Study (AusDiane); The Coronary Artery Calcification in Type 1 Diabetes (CACTI)[1]; the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC)[2, 3]; Pittsburgh Epidemiology of Diabetes Complications Study (EDC)[4]; The Finnish Diabetic Nephropathy (FinnDiane) Study[5, 6]; French and Belgian subjects from the Genetics of Diabetic Nephropathy (GENEDIAB)[7] and Genesis[8] studies; Genetics of Kidneys in Diabetes US Study (GoKinD) from George Washington University (GWU-GoKinD)[9]; patients from the Joslin Kidney Study[9, 10]; individuals with T1D from Italy[5]; The Latvian Diabetic Nephropathy Study (LatDiane)[11]; The Lithuanian Diabetic Nephropathy Study (LitDiane) [Reference pending, submitted]; The Romanian Diabetic Nephropathy Study (RomDiane)[12]; The Scottish Diabetes Research Network Type 1 Bioresource (SDRNT1BIO)[13, 14]; individuals with T1D from Steno Diabetes Center[15]; individuals with T1D from Uppsala, Sweden[16, 17]; UK GoKinD, Warren 3 and All Ireland (UK-ROI) study[18]; and The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR)[19]. All participants gave informed consent and all studies were approved by ethics committees from all participating institutions.

GWAS Genotyping. Samples were genotyped on the HumanCore BeadChip (Illumina, San Diego, CA, USA), which contains 250,000 genome-wide tag SNPs (and other variants) and over 200,000 exome-focused variants. All samples were passed through a stringent quality control protocol. Following initial genotype calling with Illumina software, all samples were re-called with zCall, a calling algorithm specifically designed for rare SNPs from arrays. Once calling was completed for all cohorts, our pipeline updated variant orientation and position aligned to hg19

(Genome Reference Consortium Human Build 37, GRCh37). Variant names were updated using 1000 Genomes as a reference. The data were then filtered for low quality variants (e.g. call rates <95% or excessive deviation from Hardy-Weinberg equilibrium) or samples (e.g. call rates <98%, gender mismatch, extreme heterozygosity). Principal Component Analysis (PCA) was performed separately for each cohort in order to empirically detect and exclude outliers with evidence of non-European ancestry. Genotypes were expanded to a total of approximately 49 million by imputation, using 1,000 Genomes Project (phase 3 version 5) as a reference.

GWAS Phenotype definitions. Participant renal status was evaluated on the basis of both albuminuria and eGFR. We defined a total of 10 different case-control outcomes to cover the different aspects of renal complications (**Figure 1**). Five comparisons ("All vs. ctrl", "Micro", "DN", "Macro", and "ESRD vs. macro") were based on albuminuria, measured by albumin excretion rate (AER) from overnight or 24-h urine collection, or by albumin creatinine ratio (ACR). Two out of three consecutive collections were required (when available) to classify the renal status of subjects as either normoalbuminuria, microalbuminuria, macroalbuminuria, or ESRD; for detailed thresholds, see **Table S9**. Controls with normal AER were required to have a minimum diabetes duration of 15 years; subjects with microalbuminuria/ macroalbuminuria/ ESRD were required to have minimum diabetes duration of 5/ 10/ 10 years, respectively, in order to exclude renal complications of non-diabetic origins. Two comparisons ("ESRD vs. ctrl" and "ESRD vs. non-ESRD") were based on presence of end-stage renal disease as defined by eGFR< 15 mL/min or dialysis or renal transplant. Two phenotypes ("CKD" and "CKD extreme") were defined based on estimated glomerular filtration rate (eGFR; evaluated with the CKD-EPI formula): Controls had eGFR ≥ 60ml/min/1.73m^2 for both phenotypes, and minimum of 15 years of diabetes duration; cases had eGFR <60ml/min/1.73m^2 for the "CKD" phenotype, and eGFR <15 ml/min/1.73m^2 or dialysis or renal transplant for the "CKD extreme" phenotype, and

minimum of 10 years of diabetes duration. For the "CKD-DN" phenotype that combined both albuminuria and eGFR data, controls were required to have both eGFR ≥60ml/min/1.73m^2 and normoalbuminuria; cases had both eGFR <45ml/min/1.73m^2 and micro- or macroalbuminuria, or ESRD.

GWAS Statistical Analysis. A genome-wide association analysis of each of the case-control definitions was performed using logistic regression under an additive genetic model, adjusting for age, sex, diabetes duration, study site (where applicable) and principal components. As disease onset and progression is also closely related to BMI and HbA1c levels,[20] we conducted a second set of analyses adjusting for BMI and HbA1c which we refer to as our fully adjusted covariate model. Allele dosages were used to account for imputation uncertainty. Inverse-variance fixed effects meta-analysis was performed using METAL and the following filters: INFO score >0.3, minor allele count >10, and presence of variant in at least two cohorts. The X chromosome was similarly analyzed for males and females both separately and in a combined analysis, with the exception of using hard call genotypes in place of allele dosages. The study-wide significance threshold ($P<6.76\times10^{-9}$) was calculated by applying a Bonferroni correction to the traditional GWAS threshold ($P<5.00\times10^{-8}$), based on the number of effectively independent tests, using methods previously described on the eigenvalues of the GWAS summary statistics correlation matrix[21].

Glomerular basement membrane measurement in Renin-Angiotensin System Study (RASS). RASS was a double-blind placebo-controlled randomized trial of the angiotensin converting enzyme inhibitor (ACEi) enalapril and the angiotensin II receptor blocker (ARB) losartan on renal pathology among 285 normoalbuminuric, normotensive subjects with T1D and had normal or increased measured glomerular filtration rate (>90 ml/min/1.73m^2)[22]. Beginning in

2005, participants were recruited from three centers: University of Minnesota (Minneapolis, Minnesota), McGill University (Montreal, Canada) and University of Toronto (Toronto, Canada) and included those with 2 to 20 years of diabetes and excluded those on any antihypertensive medications. Written informed consent was obtained from each participant and the study was approved by the relevant institutional review boards. RASS study participants were followed for 5 years with percutaneous kidney biopsy completed prior to randomization and at 5 years. Structural parameters measured by electron microscopy on biopsy included GBM width, measured by the electron microscopic orthogonal intercept method[22].

RASS study participants were followed for 5 years with percutaneous kidney biopsy completed prior to randomization and at 5 years. Structural parameters measured by electron microscopy on biopsy included GBM width, measured by the electron microscopic orthogonal intercept method22.

RASS genotyping: All RASS participants contributed DNA for genotyping on the Illumina HumanOmni1-Quad and HumanCoreExome beadchip arrays. Genotypes were called using BeadStudio/Genomestudio software (Illumina®). Quality control (QC) measures included removing duplicate samples, samples with evidence of contamination (heterozygosity range 0.25-0.32) and those with cryptic relatedness identity-by-state (IBS) (n=24). Principal component analyses were completed and 7 non-European outliers were removed. Of those genotyped, 1 participant was missing kidney biopsy data.

RASS GBM width analysis: We completed linear regression of the COL4A3 variant (rs55703767) and within person mean GBM width (nm) from both baseline and 5 year measures, in additive and genotypic genetic models. Both univariate and multivariate analyses were run including sex, baseline age and diabetes duration, within person mean HbA1c over 5 years, indicators for treatment group assignment and treatment center. A two-sided significance threshold of alpha <0.05 was applied.

In silico replication in SUMMIT consortium. The SUMMIT consortium included up to 5193 subjects with type 2 diabetes, with and without kidney disease, of European ancestry. All studies were approved by ethics committees from relevant institutions and all participants gave informed consent[23]. Complete list of SUMMIT Consortium members provided in Table S13.

SUMMIT genotyping and statistical analysis: SUMMIT Cohorts were genotyped on the Affymetrix SNP 6.0, the Illumina Omni express and the Illumina 610Quad arrays. QC measures included filtering out low frequency (<1% MAF) variants, filtering out low quality variants or samples, removal of duplicate samples, and removal of non-European samples based on principal component analysis.[23] Genome-wide association analyses were performed for DKD trait definitions harmonized with seven of our primary T1D analyses: “DN”, “Micro”, “Macro”, “ESRD”, “ESRD vs. non-ESRD”, “CKD”, and “CKD-DN” under an additive model, adjusting for age, gender and duration of diabetes.

RNA-sequencing and cis-eQTL analysis in human kidney samples from University of Pennsylvania cohort. Human kidney tissue collection was approved by the University of Pennsylvania Institutional Review Board. Kidney samples were obtained from surgical nephrectomies. Nephrectomies were de-identified, and the corresponding clinical information was collected through an honest broker; therefore, no consent was obtained from the subjects. Tubular and glomerular eQTL data sets were generated by 121 samples of tubules and 119 samples of glomeruli, respectively. The cis window was defined as 1 megabase up- and down-stream of the transcriptional start site (±1Mb). Whole kidney cis-eQTL (further just referred to as eQTL) data set was generated from 96 human samples were obtained from The Cancer Genome Atlas (TCGA) through the TCGA Data portal[24].

RNA-sequencing of human kidney samples in the University of Pennsylvania cohort: Human kidney tissue was manually microdissected under a microscope in RNAlater for glomerular and tubular compartments. The local renal pathologist performed an unbiased review of the tissue section by scoring multiple parameters, and RNA were prepared using RNAeasy mini columns (Qiagen, Valencia, CA) according to manufacturer's instructions. RNA quality was assessed with the Agilent Bioanalyzer 2100 and RNA integrity number scores above 7 were used for cDNA production. The library was prepared in the DNA Sequencing Core at University of Texas Southwestern Medical Center. One microgram total RNA was used to isolate poly(A) purified mRNA using the Illumina TruSeq RNA Preparation Kit. We sequenced samples for single-end 100bp, and the annotated RNA counts (fastq) were calculated by Illumina's CASAVA 1.8.2. Illumina sequence quality was surveyed with FastQC. Adaptor and lower-quality bases were trimmed with Trim-galore. Trimmed reads were aligned to the Gencode human genome(GRCh37) with STAR-2.4.1d. The readcount of each sample was obtained using HTSeq-0.6.1 (htseq-count) and then normalized fragments per kilobase million values were used to perform association analysis with fibrosis and sclerosis using linear regression.

Human kidney cis-eQTL analysis. Nominal p-values were calculated for each SNP-gene pair with FastQTL using linear regression with an additive effects model, and adjusted by six genotype PCs.

RNA-sequencing of human kidney samples. Normalized fragment per kilobase million values were used to perform association analysis with fibrosis and sclerosis using linear regression.

RNAseq and microarray profiling of human kidney samples from the Pima cohort. Kidney biopsy samples from the Pima Indian cohort were manually micro-dissected into 119 glomerular and 100 tubule-interstitial tissues to generate gene expression profiles[25]. Expression profiling in the Pima Indian cohort kidney biopsies was carried out using Affymetrix GeneChip Human

Genome U133 Array and U133Plus2 Array, as reported previously, and Affymetrix Human Gene ST Genechip 2.1[26, 27], and on RNA-seq (Illumina). The libraries were prepared using the ClonTech SMARTSeq v4 Ultra Low Input polyA selection kit. Samples were sequenced on a HiSeq 4000, single end, 75bp. Mapping to human reference genome GRCh38.7 was performed with STAR 2.5.2b (https://github.com/alexdobin/STAR). For annotation and quantification of mapping results we used cufflinks, cuffquant and cuffnorm in version 2.2.1 (https://cole-trapnell-lab.github.io/cufflinks/). After mapping and quantification, PCA and Hierarchical Clustering was used to identify outliers and reiterated until no more outliers could be identified.

eQTL analysis. Analysis was performed with Robust Multi-array Average quantile normalization[28] after removing probes overlapping with variants identified by WGS. Batch effects between platforms were corrected using ComBat[*29*] and unknown batch effects were also adjusted using singular value decomposition with first four eigenvectors. eQTL mapping was performed using EPACTS (https://genome.sph.umich.edu/wiki/EPACTS) software tool using linear mixed model accounting for hidden familial relatedness, after inverse Gaussian transformation of expression levels, adjusting for age and sex.

Mouse kidney single cell RNA-sequencing. Animal studies were approved by the Institutional Animal Care and Use Committee of the University of Pennsylvania. We mated Cdh16^{Cre} mice (Jackson Lab, 012237), Nphs2^{Cre} mice (Jackson Lab, 008205) and SclCre mice (MGI number is 3579158) with Tomato-GFP (mT/mG) mice (Jackson Lab, 007576) to generate Cdh16^{Cre}mT/mG, Scl^{Cre}mT/mG and Nphs2cremT/mG mice[30].

Mouse kidney single cell RNA-sequencing: Kidneys were harvested from 4 to 8-week-old male mice with C57BL/6 background and dissociated into single cell suspension as described in our previous study31. The single cell sequencing libraries were sequenced on an Illumina HiSeq with 2x150 paired-end kit. The sequencing reads were demultiplexed, aligned to the mouse

genome (mm10) and processed to generate gene-cell data matrix using Cell Ranger 1.3 (http://10xgenomics.com)[31].

To calculate the average expression level for each cluster, a z-score of normalized expression value was first obtained for every single cell. Then, we calculated the mean z-scores for individual cells in the same cluster, resulting in 16 values for each gene.

Genomic features of human kidney. Human kidney-specific chromatin immunoprecipitation followed by sequencing (ChIP-seq) data can be found at GEO: GSM621634, GSM670025, GSM621648, GSM772811, GSM621651, GSM1112806, GSM621638. Different histone markers were combined into chromatin states using ChromHMM[32].

Gene and gene set analysis. PASCAL gene and pathway scores were conducted on all 20 sets of GWAS summary statistics (10 outcomes and 2 covariate models). Gene scores were derived using the sum option, averaging association signal across each gene using the default 50kb window size. Pathway scores were then computed from pathway member gene scores where membership was defined using default pathway libraries from BioCarta, REACTOME, and KEGG. Using a similar approach, MAGMA (v1.06) gene and pathway scores were conducted on all GWAS summary statistics using both the default gene region defined by the transcription start and stop sites and a 5kb window definition. MAGMA pathway analysis included all 1077 of the PASCAL reported libraries plus an additional 252 pathways included in MSigDB canonical pathway set. MAGENTA (vs2, July 2011) pathway analysis included 4725 pathways with a minimum of five genes within the gene set. Gene sets were obtained with the MAGENTA distribution and included Gene ontology terms, PANTHER sets (biological processes, molecular functions, metabolic and signaling pathways), KEGG pathways, and

Ingenuity pathways. DEPICT gene set enrichment uses a more comprehensive collection of gene sets that allows genes to have a continuous probability for gene set membership. We conducted DEPICT individually on all 20 sets of GWAS summary statistics with $P < 1.0 \times 10^{-5}$. We conducted two additional pooled analyses using genome-wide minimum P-values from: 1) All 20 analyses (10 phenotypes and 2 covariate models) and 2) Sixteen analyses of the 8 most related phenotypes (8 phenotypes and 2 covariate models) which excluded ESRD vs Macro and Micro.

Data and Software Availability

All cohorts can share genome-wide meta-analysis summary statistics. Individual level genotype data: due to restrictions set by study consents and by EU and national regulations, individual genotype data cannot be shared for all cohorts

Table S1. Cohorts contributing to analyses.

This table can be found in a separate excel sheet, Supplemental_table_S1.xlsx

Table S2. Characteristics of RASS participants. Categorical variables display counts and percentage. Continuous values are mean ± standard deviation.

Variables (Total N = 253)	**Freq(%)/Mean±SD**
Sex - Female	134 (53%)
Age (years)	30 ± 10
T1D duration (years)	11 ± 5
Within-person mean HbA1c (%) (mmol/mol)	8.6 ± 1.4 70 ± 15
Mean GBMW (nm)	480 ± 88
rs55703767 – GG GT TT	163 (64%) 80 (32%) 10 (4%)

Table S3. Multivariate analysis of association between rs55703767 and GBM width

Variables		Adjusted model			Fully adjusted model*	
		Effect (SE)	P		Effect (SE)	P
rs55703767 (T allele)[¶]		-22.8 (8.2)	0.006		-19.7 (8.2)[¶]	0.0172
Females (vs males)		-48.4 (9.3)	<.0001		-50.4 (9.3)	<.0001
Age at baseline (yrs)		-2.4 (0.5)	<.0001		-2.4 (0.5)	<.0001
Diabetes duration (yrs)		3.8 (1.0)	0.0002		3.8 (1.0)	0.0002
Mean HbA1c (%)		27.2 (3.3)	<.0001		27.4 (3.3)	<.0001
Treatments	Placebo	-	-		Reference	
	Enalapril	-	-		-6.9 (11.2)	0.538
	Losartan	-	-		1.4 (10.9)	0.896
Centres	Montreal	-	-		Reference	
	Toronto	-	-		0.8 (12.8)	0.952
	Minnesota	-	-		18.9 (13.7)	0.169

* Fully adjusted model also included 3 principal components for population structure within Europeans.
[¶] SNP genotypes modelled as additive genetic effects.

Table S4: Look-up of the lead loci in GWAS on eGFR in the general population (Gorski et al., 2017).[33]

		Meta-analysis results							GWAS on eGFR (Gorski 2017)				
Nearest Gene	**SNP**	**EA**	**NEA**	**EAF**	**SE**	**OR**	**P_{min}**	**P_{Full}**	**EAF**	**β**	**SE**	**P**	**N**
COL4A3	rs55703767	T	G	0.206	0.03	0.79	**5.34×10^{-12}**	**8.19×10^{-11}**	0.142	0.002	0.0013	0.132	110517
COL4A3	rs55703767	T	G	0.209	0.04	0.79	**9.28×10^{-9}**	**9.38×10^{-9}**	0.142	0.002	0.0013	0.132	110517
COL4A3	rs55703767	T	G	0.205	0.03	0.84	**3.88×10^{-10}**	**9.68×10^{-9}**	0.142	0.002	0.0013	0.132	110517
COL4A3	rs55703767	T	G	0.208	0.04	0.77	**5.30×10^{-9}**	**3.77×10^{-8}**	0.142	0.002	0.0013	0.132	110517
PRNCR1	rs551191707	CA	C	0.122	0.1	1.7	**4.39×10^{-8}**	3.15×10^{-6}					
STXBP6	rs61983410	T	C	0.787	0.04	1.26	9.84×10^{-8}	**3.06×10^{-8}**	0.841	-0.001	0.0012	0.336	110516
COLEC11	rs12615970	A	G	0.867	0.05	1.31	**9.43×10^{-9}**	1.60×10^{-7}					
LINC01266	rs115061173	A	T	0.014	0.41	9.39	**4.07×10^{-8}**	4.08×10^{-5}					
SNCAIP	rs149641852	T	G	0.012	0.39	9.03	**1.37×10^{-8}**	---	0.009	0.002	0.0042	0.643	109257
PAPLN	rs113554206	A	G	0.012	0.3	4.62	5.39×10^{-7}	**8.46×10^{-9}**	0.007	-0.005	0.0064	0.408	95870
STAC	rs116216059	A	C	0.016	0.38	8.76	**1.37×10^{-8}**	1.41×10^{-4}	0.006	3.00×10^{-4}	0.0043	0.953	108165
HAND2-AS1	rs145681168	A	G	0.986	0.33	0.18	2.06×10^{-7}	**5.40×10^{-9}**	0.993	0.003	0.0067	0.612	64752
TAMM41	rs142823282	A	G	0.983	0.31	0.15	**8.32×10^{-10}**	**1.13×10^{-11}**					
VARS2	rs118124843	T	C	0.011	0.24	3.78	**4.42×10^{-8}**	**3.37×10^{-8}**	0.031	0.011	0.0055	*0.040*	58794
MUC7	rs191449639	A	T	0.005	0.61	32.46	**1.32×10^{-8}**	**2.09×10^{-8}**					
MBLAC1	rs77273076	T	C	0.008	0.39	9.12	**1.04×10^{-8}**	2.28×10^{-7}	0.007	0.006	0.0051	0.236	108694
BMP7	rs144434404	T	C	0.011	0.32	6.75	**2.67×10^{-9}**	**4.65×10^{-9}**	0.004	1.00×10^{-4}	0.0072	0.993	91428
PLEKHA7	rs183937294	T	G	0.993	0.5	0.06	**1.65×10^{-8}**	2.10×10^{-6}					
	rs185299109	T	C	0.007	0.53	20.7	**1.28×10^{-8}**	4.99×10^{-7}					

EA: Effect allele. Positive odds ratio indicates that EA is associated with higher risk; positive beta indicates that EA is associated with higher eGFR, i.e. lower renal risk.

Table S5: Look-up of the lead loci in GWAS in the SUMMIT consortium (van Zuydam et al., 2018).[23]

SNP	Chr:pos	EA	NEA	EAF	Notable gene(s)	Phenotype	N	OR	P-value
rs55703767	2:228121101	T	G	0.211	*COL4A3*	**DN**	**5190**	**0.911**	**0.08**
				0.213		**CKD+DN**	**2243**	**0.867**	**0.09**
rs145681168	4:174500806	G	A	0.017	*HAND2-AS1*	**Micro**	**3477**	**1.034**	**0.97**
rs149641852	5:121774582	T	G	0.018	*SNCAIP*	**CKD**	**4676**	**1.032**	**0.30**
rs118124843	6:30887465	T	C	0.018	*DDR1, VARS2*	**Micro**	**2439**	**1.137**	**0.63**
rs77273076	7:99728546	T	C	0.014	*MBLAC1*	Micro	3252	0.866	0.48
rs61983410	14:26004712	T	C	0.184	*STXBP6*	**Micro**	**3760**	**0.990**	**0.58**
rs144434404	20:55837263	T	C	0.011	*BMP7*	**Micro**	**2439**	**1.100**	**0.78**

Chr, chromosome; pos, position; EA: Effect allele; EAF, effect allele frequency; OR, odds ratio.

Table S6: Association at lead loci stratified by HbA1c <7.5%.

					ALL				HbA1c < 7.5%			HbA1c >= 7.5%			
Locus	SNP	Pheno	EA	NEA	N	MAF	P	INFO	N (case/ctrl)	P	OR (95% CI)	N (case/ctrl)	P	OR (95% CI)	P_HET
COL4A3	rs55703767	MACROESRD	G	T	3611	0.19	**2.16E-03**	1.00	1165 (499/666)	0.659	0.95 (0.76;1.19)	2495 (884/1611)	**9.55E-04**	0.77 (0.66;0.9)	0.132
COL4A3	rs55703767	MACRO	G	T	2803	0.19	0.06	1.00	837 (164/673)	0.663	1.08 (0.78;1.49)	2006 (373/1633)	**6.63E-03**	0.75 (0.61;0.92)	0.068
COL4A3	rs55703767	ALLvCTRL	G	T	4271	0.19	**7.04E-03**	1.00	1344 (692/652)	0.870	0.98 (0.8;1.2)	2977 (1391/1586)	**1.76E-03**	0.81 (0.71;0.92)	0.114
COL4A3	rs55703767	CKDDN	G	T	3059	0.19	**1.17E-02**	1.00	984 (379/605)	0.973	1 (0.78;1.28)	2102 (624/1478)	**7.90E-03**	0.79 (0.67;0.94)	0.136
PRNCR1	rs551191707	ESRDvMACRO	C	CA	1371	0.14	**2.50E-03**	0.81	498 (340/158)	**1.92E-02**	1.71 (1.09;2.67)	885 (524/361)	**4.79E-02**	1.38 (1;1.91)	0.453
STXBP6	rs61983410	MICRO	T	C	2976	0.23	**3.75E-03**	0.93	863 (195/668)	**1.34E-02**	0.69 (0.52;0.93)	2155 (526/1629)	0.067	0.85 (0.71;1.01)	0.248
COLEC11	rs12615970	CKD	A	G	4264	0.14	**3.13E-03**	0.82	1432 (531/901)	0.086	0.81 (0.63;1.03)	3014 (833/2181)	**1.62E-02**	0.8 (0.66;0.96)	0.949
LINC01266	rs115061173	ESRD	T	A	3119	0.00	**1.89E-02**	0.36	1012 (340/672)	0.284	2.63 (0.45;15.36)	2156 (524/1632)	0.085	5.98 (0.78;45.9)	0.550
SNCAIP	rs149641852	CKDEXTREMES	G	T	3907	0.01	**3.04E-03**	0.33	1323 (415/908)	0.559	1.53 (0.37;6.35)	2765 (559/2206)	**6.27E-04**	10.78 (2.76;42.09)	0.052
PAPLN	rs113554206	MACRO	G	A	2803	0.00	0.32	0.34	837 (164/673)	0.793	0.39 (0;417.59)	2006 (373/1633)	0.114	21.87 (0.48;999.19)	0.322
STAC	rs116216059	ESRDvALL	C	A	4272	0.01	0.48	0.67	1340 (340/1000)	0.867	0.88 (0.2;3.89)	2984 (524/2460)	0.453	0.67 (0.23;1.93)	0.764
HAND2-AS1	rs145681168	MICRO	A	G	2976	0.01	0.50	0.48	863 (195/668)	0.509	3.48 (0.09;141.38)	2155 (526/1629)	0.395	0.61 (0.19;1.91)	0.378
TAMM41	rs142823282	MICRO	A	G	2976	0.00	0.93	0.15				2155 (526/1629)	0.886	1.19 (0.11;13.33)	NA
VARS2	rs118124843	MICRO	C	T	2976	0.01	0.93	1.00	863 (195/668)	0.533	0.59 (0.11;3.16)	2155 (526/1629)	0.769	1.15 (0.46;2.85)	0.492
MUC7	rs191449639	MACROESRD	T	A	3611	0.00	0.09	0.28	1165 (499/666)	0.487	2.17 (0.24;19.36)	2495 (884/1611)	0.246	3.58 (0.42;30.94)	0.749
MBLAC1	rs77273076	MICRO	C	T	2976	0.01	**1.36E-04**	0.37	863 (195/668)	**3.98E-03**	168.26 (5.14;5507.78)	2155 (526/1629)	**1.68E-03**	11.25 (2.48;50.97)	0.163
BMP7	rs144434404	MICRO	C	T	2976	0.01	0.57	0.67	863 (195/668)	0.407	0.49 (0.09;2.61)	2155 (526/1629)	0.911	0.94 (0.3;2.91)	0.534
PLEKHA7	rs183937294	MICRO	T	G	2976	0.00	0.22	0.26				2155 (526/1629)	0.288	3.79 (0.32;44.52)	NA
18p11.32	rs185299109	CKD	C	T	4264	0.00	0.68	0.32	1432 (531/901)	0.147	0.12 (0.01;2.09)	3014 (833/2181)	0.956	0.96 (0.21;4.45)	0.212

Association stratified by HbA1c in the FinnDiane study. *P*-values <0.05 are given with scientific notation and bold. Lines with gray text had minor allele count (MAC)<10 in cases and/or controls and did not contribute to the meta-analysis.

Table S7. Association of rs55703767 with DN in DCCT/EDIC subgroups.

Cohort	Treatment Group	DN %	MAF	Last measure		Time to Event	
				OR (95%CI)	P value	HR (95%CI)	P value
Primary Prevention (diabetes dur 1-5 yrs)	Intensive	3%	0.22	2.86 (0.4-22)	0.32	0.91 (0.2-4.0)	0.90
	Conventional	10%	0.21	0.67 (0.3-1.4)	0.31	0.66 (0.32-1.33)	0.24
Secondary Intervention (diabetes dur 1-15 yrs)	Intensive	5%	0.20	0.86 (0.3-2.6)	0.79	0.65 (0.22-1.9)	0.43
	Conventional	13%	0.22	0.18 (0.1-0.5)	0.003	0.30 (0.13-0.68)	0.004

OR=Odds Ratio for last measure, HR=Hazard Ratio for time to event phenotype

Table S8. Significant (*P*<0.05/18,222 genes tested = 2.74×10^{-6}) gene level associations with diabetic kidney disease in MAGMA.

Gene	Phenotype	Model	Window	Number of SNPs	Total Sample Size	MAGMA P-value	PASCAL P-value
SLC46A2	All vs. ctrl	Min	nowindow	66	17817	6.74×10^{-7}	1.57×10^{-5}
			5kbwindow	93	17832	7.38×10^{-7}	
		Full	nowindow	64	16821	8.13×10^{-7}	6.93×10^{-5}
			5kbwindow	90	16855	1.03×10^{-6}	
SFXN4	Macro	Full	nowindow	69	11953	3.98×10^{-7}	1.45×10^{-4}
			5kbwindow	86	11857	1.65×10^{-7}	
COL20A1	Ckdextreme	Min	nowindow	111	11165	2.47×10^{-6}	7.88×10^{-5}
			5kbwindow	137	11603	2.01×10^{-6}	
		Full	nowindow	110	8533	6.65×10^{-7}	4.47×10^{-5}
			5kbwindow	136	9044	5.77×10^{-7}	
	ESRD vs. All	Min	nowindow	111	12063	1.34×10^{-6}	3.76×10^{-5}
			5kbwindow	137	12362	1.04×10^{-6}	
		Full	nowindow	110	8638	1.12×10^{-6}	5.81×10^{-5}
			5kbwindow	136	9045	9.53×10^{-7}	
GLT6D1	ESRD vs. Macro	min	5kbwindow	96	4248	1.49×10^{-6}	2.15×10^{-5}
SNX30	All vs. ctrl	min	5kbwindow	434	18249	2.49×10^{-6}	1.05×10^{-5}

Table S9. Top nominally significant gene level associations (P < 1.0×10^{-5}) with diabetic kidney disease in PASCAL.

Gene	Phenotype	Model	Number of SNPs	PASCAL P-value
INIP	All vs. ctrl	Min	248	1.99×10^{-6}
		Full	248	5.54×10^{-6}
LCN9	ESRD vs. macro	Min	301	5.25×10^{-6}
CBX8	DN	Min	119	8.47×10^{-6}

Table S10: Significant gene set and pathway analysis results. Significantly enriched gene sets identified from at least one of the following methods: MAGENTA (FDR < 0.05, MAGMA (P<0.05 empirical permutation multiple testing correction), PASCAL (P<0.05/1,078 gene sets tested = 4.64 × 10-5), and DEPICT (FDR < 0.01).

Gene set	Gene set database	Phenotype	Model	Method
negative regulators of RIG I MDA5 signaling	REACTOME	ESRD vs. Macro	Full	MAGMA
Platelet aggregation plug formation	REACTOME	Micro	Min	MAGMA
negative regulators of RIG I MDA5 signaling	REACTOME	ESRD vs. Macro	Full	PASCAL
RIG I MDA5 mediated induction of IFN alpha beta pathways	REACTOME	ESRD vs. Macro	Full	PASCAL
TRAF3 dependent IRF activation pathway	REACTOME	ESRD vs. Macro	Full	PASCAL
TRAF6 mediated IRF activation	REACTOME	ESRD vs. Macro	Full	PASCAL
Nitric Oxide Signaling in the Cardiovascular System	Ingenuity	ESRD vs. ctrl	Min	MAGENTA
Nicotinic acetylcholine receptor signaling pathway	Panther	ESRD vs. non-ESRD	Min	MAGENTA
ACTIVATED TLR4 SIGNALLING	REACTOME	All vs. ctrl	Min	MAGENTA
Other lipid, fatty acid and steroid metabolism	PANTHER BIOLOGICAL PROCESS	CKD	Min	MAGENTA
DNA degradation	PANTHER BIOLOGICAL PROCESS	CKD	Min	MAGENTA
Tumor necrosis factor family member	PANTHER MOLECULAR FUNCTION	CKD-extreme	Min	MAGENTA
TUFM (Tu Translation Elongation Factor, Mitochondrial) PPI subnetwork	InWeb protein-protein interaction database	DN	Min	DEPICT

Table S11. eQTL associations and chromatin conformation interactions for the lead SNPs.

SNP	Chr:pos	EA	NEA	EAF	Notable gene(s)	eQTL				PC-HiC	
						GENE	P	HIGH A	Tissue	*Gene*	*Score (Tissue)*
rs12615970	2:3745215	G	A	0.133	*COLEC11* (B); *ALLC (G)*					***ALLC***	10.42 (GM12878);
										COLEC11, *AC010907.2*	9.67 (GM12878);
										ADI1, *AC142528.1*	8.75 (GM12878);
										RP13-512J5.1	8.58 (GM12878);
										RPS7	8.13 (GM12878);
rs55703767	2:228121101	T	G	0.206	*COL4A3* (M, B, N)	***MFF***	5.63×10^{-38}	T	blood	***COL4A3, COL4A4***	8.89 (GM12878);
						MFF	9.0×10^{-8}	T	Cells - Transformed fibroblasts	***IRS****, RP11-395N3.2*	9.36 (GM12878);
						TM4SF20	2.2×10^{-7}	T	Cells - Transformed fibroblasts		
rs115061173	3:926345	A	T	0.014	*LINC01266* (N)						
rs142823282	3:11910635	G	A	0.011	*TAMM41* (N, B)	***PPARG***	4.6×10^{-7}	G	Colon - Sigmoid	***TAMM41***	10.65 (GM12878);
rs116216059	3:36566312	A	C	0.016	*STAC* (G)					***DCLK3***	8.8 (GM12878);
										STAC	10.87 (GM12878);
rs191449639	4:71358776	A	T	0.005	*MUC7* (N)						
rs145681168	4:174500806	G	A	0.014	*HAND2-AS1*(G, B)					***HAND2****, HAND2-AS1*	10.49 (GM12878);
rs149641852	**5:121774582**	**T**	**G**	**0.012**	***SNCAIP* (G)**					***SNX24***	9.2 (GM12878);
										snoU13	8.93 (GM12878);
										SNCAIP, *CTD-2544H17.2*	9.69 (GM12878);
										CTD-2280E9.1	10.81 (GM12878);
rs118124843	6:30887465	T	C	0.011	*DDR1* (B); *VARS2* (G)	***HLA-C***	1.00×10^{-18}	C	eQTLgen blood	***PSORS1C1***	12.3 (Endothelial Precursors); 12.3 (Endothelial Precursors); 7.84 (Megacaryocytes); 5.63 (Pancreatic islets);
										DPCR1, HCG21	11.49 (GM12878);
						HLA-U	3.56×10^{-10}	T	eQTLgen blood	*DDR1-AS1,* ***DDR1***	10.97 (GM12878);
						PSORS1C3	4.13×10^{-9}	T	eQTLgen blood	*RNU6-1133P*	7.27 (Macrophages M2);

SNP	Chr:pos	EA	NEA	EAF	Notable gene(s)	eQTL				PC-HiC	
						GENE	P	HIGH A	Tissue	*Gene*	*Score (Tissue)*
						NCR3	9.35×10^{-6}	C	eQTLgen blood	*RN7SL175P,* ***DDR1, GTF2H4, VARS2***	7.07 (Endothelial Precursors); 7.07 (Endothelial Precursors); 6.95 (Cardiomyocytes); 6.89 (Pancreatic islets); 5.43 (Megacaryocytes); 5.09 (Macrophages M1);
						HCG22	1.5×10^{-5}	T	eQTLgen blood	*C6orf15*	6.95 (Macrophages M1); 6.95 (Macrophages M1); 6.18 (Macrophages M0);
						VARS2	1.71×10^{-5}	C	eQTLgen blood		
						GTF2H4	9.70×10^{-7}	T	Esophagus - Gastroesophageal Junction		
						POU5F1	3.3×10^{-5}	T	Esophagus - Gastroesophageal Junction		
						PSORS1C3	5.6×10^{-5}	T	Esophagus - Gastroesophageal Junction		
						C6orf48	1×10^{-4}	C	Nerve - Tibial		
rs77273076	7:99728546	T	C	0.008	*MBLAC1* (N, B)	***CNPY4***	1.17×10^{-7}	C	eQTLgen blood	***MBLAC1,*** *AC073842.19, RP11-506M12.1*	***NA (withn the same fragment);***
						AP4M1	1.04×10^{-5}	C	eQTLgen blood	***LAMTOR4, GAL3ST4, GPC2,*** *C7orf43, MIR4658*	14.82 (CD34); 14.82 (CD34); 14.56 (GM12878);
						ZSCAN21	1.29×10^{-5}	C	eQTLgen blood	***LAMTOR4***	14.14 (CD34); 14.14 (CD34); 13.1 (GM12878);
										GATS, STAG3, PVRIG, *AC005071.1*	14.11 (CD34); 14.11 (CD34); 13.68 (GM12878);
										MCM7, AP4M1	14.11 (CD34); 14.11 (CD34); 13.68 (GM12878);
										STAG3, GPC2	13.75 (CD34); 13.75 (CD34); 13.36 (GM12878);
										MCM7, COPS6*, MIR93, MIR106B, MIR25*	13.69 (CD34); 13.69 (CD34); 13.67 (GM12878);
										CNPY4, TAF6	13.37 (GM12878); 13.37 (GM12878); 13.14 (CD34);
										ZKSCAN1	13.23 (GM12878); 13.23 (GM12878); 11.87 (CD34);
										ZSCAN21	13.14 (GM12878);

SNP	Chr:pos	EA	NEA	EAF	Notable gene(s)	eQTL				PC-HiC	
						GENE	P	HIGH A	Tissue	*Gene*	*Score (Tissue)*
										ZCWPW1, MEPCE	12.72 (GM12878); 12.72 (GM12878); 11.48 (CD34);
										PILRA	12.65 (GM12878);
										TRIM4	12.64 (GM12878);
										ZCWPW1	12.61 (GM12878);
										SAP25, FBXO24, LRCH4, *RP11-44M6.3*	12.59 (GM12878);
										PILRB, PVRIG2P, *STAG3L5P-PVRIG2P-PILRB,*	12.38 (GM12878); 12.38 (GM12878); 5.94 (Naive B); 5.02 (Total B);
										TSC22D4, NYAP1*, AC092849.1, RN7SL161P, C7orf61*	12.21 (GM12878);
										RP11-758P17.2, PPP1R35, RP11-758P17.3	12.02 (GM12878); 12.02 (GM12878); 11.55 (CD34);
										AZGP1, AZGP1P1	11.3 (Neutrophils); 11.3 (Neutrophils); 6.07 (Macrophages M2); 5.65 (Total CD4 MF); 5.65 (Total CD4 MF); 5.1 (Total CD4 Activated);
										BUD31, *snoU13*	11.03 (GM12878);
										ZNF3	10.83 (GM12878);
										ZCWPW1	8.39 (Naive B); 8.39 (Naive B); 5.52 (Total CD4 Activated);
										PMS2P1	5.16 (Foetal Thymus);
rs551191707	8:128100029	CA	C	0.122	*PRNCR1* (N)	*-NONE-*					
rs183937294	11:16937846	G	T	0.007	*PLEKHA7* (G)	*-NONE-*				*RNU6-585P, PRP11-466H18.1*	10.77 (cd34); 10.77 (cd34); 9.2 (GM12878);
										AC116533.1, SNORD14B, SNORD14A, rps13	10.19 (GM12878);
										PLEKHA7, OR7E14P	9.49 (GM12878);

SNP	Chr:pos	EA	NEA	EAF	Notable gene(s)	eQTL				PC-HiC	
						GENE	P	HIGH A	Tissue	*Gene*	*Score (Tissue)*
										SOX6, *C11orf58*	9.15 (GM12878);
										SERGEF, *RP1-59M18.2*	7.56 (GM12878);
										OTOG	5.89 (Total CD8);
										USH1C	5.07 (Naive CD8);
rs61983410	14:26004712	T	C	0.213	*STXBP6* (N)	*-NONE-*				*SNORD37*	10.97 (GM12878);
rs113554206	14:73740250	A	G	0.012	*PAPLN* (G)	*-NONE-*				*RP4-647C14.3*	***NA (within the same fragment);***
										NUMB	21.42 (Endotheial precursors); 21.42 (Endotheial precursors); 17.38 (Pancreatic islets); 12.32 (Megacaryocytes); 11.56 (CD34); 9.65 (Neutrophils); 9.61 (Naive B); 9.06 (Total B); 7.55 (cardiomyocytes); 5.33 (Naive CD4); 5.11 (Naive CD8);
										PAPLN, *RNU6-419P, RP4-647C14.2*	13.67 (CD34); 13.67 (CD34); 13.24 (GM12878);
										PAPLN	13.24 (CD34); 13.24 (CD34); 12.47 (GM12878);
										PSEN1	12.08 (GM12878); 12.08 (GM12878); 5.4 (cardiomyocytes);
										HEATR4	12.05 (Endotheial precursors); 12.05 (Endotheial precursors); 10.98 (Megacaryocytes); 10.45 (GM12878); 10.37 (CD34); 9.92 (Neutrophils); 8.84 (Pancreatic islets); 7.98 (Monocytes); 7.3 (Total B); 7.02 (Naive B); 6.6 (cardiomyocytes); 5.81 (Erythroblasts); 5.53 (Total CD4 Activated);
										RP1-240K6.3	11.84 (GM12878); 11.84 (GM12878); 11.15 (CD34); 7.49 (Endotheial precursors); 5.62 (Pancreatic islets); 5.34

SNP	Chr:pos	EA	NEA	EAF	Notable gene(s)	eQTL				PC-HiC	
						GENE	P	HIGH A	Tissue	*Gene*	*Score (Tissue)*
											(Total B); 5.02 (Megacaryocytes);
										DNAL1, *RNU6-240P*	11.07 (GM12878);
										PSEN1	10.96 (Endotheial precursors); 10.96 (Endotheial precursors); 10.56 (CD34);
										PNMA1	10.9 (GM12878);
										RP3-414A15.2	10.64 (GM12878); 10.64 (GM12878); 7.24 (Monocytes); 5.99 (Neutrophils);
										ZFYVE1	10.53 (GM12878);
										PTGR2, *Y_RNA, RP5-1021I20.4*	10.42 (CD34); 10.42 (CD34); 10.16 (GM12878);
										RP4-693M11.3	10.33 (GM12878);
										RP4-687K1.2	9.96 (GM12878);
										HEATR4, *C14orf169, AC005280.1*	9.52 (GM12878); 9.52 (GM12878); 5.35 (Pancreatic islets);
										RBM25	9.34 (GM12878);
										RP3-414A15.10	9.32 (GM12878);
										ELMSAN1	9.12 (GM12878);
										CCDC176	8.85 (GM12878);
										RBM25, *RP11-109N23.5*	8.74 (GM12878);
										ACOT6	8.74 (GM12878);
										DNAL1	8.7 (GM12878);
										FAM161B*, RP5-1021I20.5*	5.58 (Total CD8);
rs185299109	18:1811108	T	C	0.007		*-NONE-*				*-NONE-*	
rs144434404	**20:55837263**	**T**	**C**	**0.011**	***BMP7*** **(G, B)**	*-NONE-*				*-NONE-*	

SNP	Chr:pos	EA	NEA	EAF	Notable gene(s)	eQTL				PC-HiC	
						GENE	P	HIGH A	Tissue	*Gene*	*Score (Tissue)*

Notable Genes: based on genetic findings (G), (B), (N), (M); eQTL associations were searched from GTEX and eQTLgen (cis-eQTL) data sets. HIGH A: allele associated with higher gene expression levels. Promoter Capture Hi-C (PCHi-C) data: searched from www.chicp.org (date accessed: 1.12.2018; Schofield EC, Carver T, Achuthan P, Freire-Pritchett P, Spivakov M, Todd JA, Burren OS. CHiCP: a web-based tool for the integrative and interactive visualization of promoter capture Hi-C datasets. Bioinformatics. (2016) 15:32(16):2511-3), including 16 primary blood cell types and foetal thymocytes (Javierre et al.), CD34 and GM12878 cell line (Mifsud et al.), pancreatic isles (Miguel-Escalada et al,), and hESC derived cardiomyocytes (Choy et al.). Score: CHiCAGO score, values >5 were considered significant and listed. Protein coding genes are highleghted with bold typing.

Table S12: Transcriptome-wide association analysis (TWAS) results with p<1×10^{-4}

							Prediction performance			N SNPs		
tissue	**GWAS phenotype**	**GENE**	**Z Score**	**Effect**	**P-value**	**Var_G**	**r2**	**P-value**	**Q-value**	**used**	**in cov**	**in model**
tub	ESRD vs macro_min	*ACOT8*	4.02	0.76	5.80E-05	0.06	0.04	2.46E-02	2.02E-02	30	30	31
tub	DN_min	*AKIRIN2*	4.17	0.32	3.03E-05	0.09	0.05	1.30E-02	1.19E-02	36	39	42
tub	Macro_min	*AKIRIN2*	4.36	0.42	1.32E-05	0.09	0.05	1.30E-02	1.19E-02	36	39	42
glom	Macro_min	*ARL17B*	-4.02	-0.21	5.91E-05	0.32	0.51	1.28E-19	1.77E-18	53	54	65
tub	All vs ctrl_min	*CALCOCO2*	3.93	0.29	8.55E-05	0.06	0.10	3.23E-04	4.93E-04	37	37	40
glom	All vs ctrl_max	*EXOC2*	4.10	0.20	4.06E-05	0.15	0.21	1.74E-07	3.79E-07	60	60	62
glom	ESRD vs non-ESRD_max	*FAM132B*	-3.95	-0.52	7.73E-05	0.06	0.07	4.84E-03	3.91E-03	33	33	35
tub	CKD extreme_min	*FES*	-3.89	-0.40	9.97E-05	0.08	0.09	7.57E-04	1.05E-03	34	34	34
tub	ESRD_min	*FES*	-3.97	-0.42	7.07E-05	0.08	0.09	7.57E-04	1.05E-03	34	34	34
tub	ESRD vs non-ESRD_min	*FES*	-4.24	-0.42	2.27E-05	0.08	0.09	7.57E-04	1.05E-03	34	34	34
glom	ESRD vs macro_min	*GSDMB*	-3.96	-0.46	7.37E-05	0.11	0.07	4.54E-03	3.71E-03	35	35	35
glom	Macro_max	*HOXD1*	4.02	0.88	5.71E-05	0.01	0.03	5.51E-02	3.10E-02	12	12	13
glom	Macro_min	*HOXD1*	4.13	0.83	3.70E-05	0.01	0.03	5.51E-02	3.10E-02	12	12	13
glom	DN_max	*ITPR3*	4.30	0.21	1.74E-05	0.19	0.38	1.09E-13	6.21E-13	33	33	35
glom	DN_min	*ITPR3*	4.00	0.17	6.26E-05	0.19	0.38	1.09E-13	6.21E-13	33	33	35
glom	Macro_max	*ITPR3*	4.31	0.25	1.62E-05	0.19	0.38	1.09E-13	6.21E-13	33	33	35
glom	Macro_min	*ITPR3*	4.03	0.21	5.69E-05	0.19	0.38	1.09E-13	6.21E-13	33	33	35
glom	ESRD_min	*MORC1*	3.94	0.44	8.03E-05	0.06	0.08	1.58E-03	1.47E-03	83	87	88
glom	Macro_max	*NLN*	4.07	0.26	4.61E-05	0.21	0.15	1.09E-05	1.71E-05	85	86	110
glom	Macro_min	*NLN*	4.53	0.27	5.99E-06	0.21	0.15	1.09E-05	1.71E-05	85	86	110
glom	All vs ctrl_max	*NPNT*	3.90	0.37	9.51E-05	0.08	0.16	5.26E-06	8.75E-06	2	2	4
glom	ESRD_min	*PRC1*	4.03	0.41	5.54E-05	0.09	0.11	3.23E-04	3.59E-04	33	33	34
tub	CKD-DN_min	*PRRC2C*	3.92	0.81	8.74E-05	0.02	0.03	4.40E-02	3.27E-02	10	10	10
tub	ESRD_min	*PRRC2C*	3.92	0.91	8.76E-05	0.02	0.03	4.40E-02	3.27E-02	10	10	10
tub	Macro_min	*TENM2*	3.98	0.83	6.92E-05	0.02	0.11	1.59E-04	2.64E-04	23	59	60
glom	DN_min	*VPS33B*	4.09	0.24	4.40E-05	0.15	0.37	2.23E-13	1.19E-12	24	24	26
glom	ESRD_min	*VPS33B*	4.20	0.35	2.69E-05	0.15	0.37	2.23E-13	1.19E-12	24	24	26
tub	CKD extreme_max	*VPS9D1*	-4.17	-0.54	3.01E-05	0.06	0.11	2.78E-04	4.30E-04	20	20	21

Tissue: glomeruli (glom) or tubuli (tub); Z-core, Effect and P-value: MetaXcan's association results for the gene. Var_g: variance of the gene expression, calculated as W' * G * W (where W is the vector of SNP weights in a gene's model, W' is its transpose, and G is the covariance matrix). Prediction performance r2, P-value and Q-value: r2, p-value and q-value of tissue model's correlation to gene's measured transcriptome (prediction performance). N SNPs ... used: number of snps from GWAS that got used in MetaXcan analysis; ... in cov: number of snps in the covariance matrix; ... in model: number of snps in the model

Table S13: Pseudo-R2 of all SNPs across all GWAS as calculated by the McKelvey and Zavoina method.[34] Total variance explained is the sum of pseudo-R2 across all SNPs with minor allele frequency (MAF) greater than 5% or 1%, noting that effect size and therefore variance explained tend to be overestimated with rare variants. Missing values indicate SNPs that did not pass our GWAS filters for those disease definitions as described in the methods section.

Minimally Adjusted Model

SNP	Minor allele frequency	DN	All vs. ctrl	CKD	CKD-DN	CKD extreme	ESRD vs. ctrl	ESRD vs. non-ESRD	ESRD vs. macro	Macro	Micro
rs61983410	0.213	**0.00%**	**0.09%**	**0.01%**	**0.00%**	**0.04%**	**0.01%**	**0.04%**	**0.05%**	**0.01%**	**0.54%**
rs55703767	0.206	**0.57%**	0.33%	0.23%	0.65%	0.34%	0.55%	0.27%	0.03%	0.60%	0.11%
rs12615970	0.133	**0.16%**	0.06%	0.52%	0.48%	0.41%	0.26%	0.21%	0.08%	0.05%	0.00%
rs551191707	0.122	**0.02%**	0.00%	0.14%	0.33%	0.70%	0.69%	0.75%	1.76%	0.06%	0.01%
rs142823282	0.017	**0.04%**	0.58%	0.01%	NA	NA	NA	NA	NA	0.11%	3.50%
rs116216059	0.016	**0.00%**	0.00%	0.13%	0.23%	2.96%	1.95%	4.40%	NA	0.01%	0.00%
rs145681168	0.014	**0.01%**	0.15%	0.00%	0.08%	0.17%	NA	NA	NA	0.03%	2.41%
rs115061173	0.014	**0.47%**	0.24%	0.34%	1.44%	2.24%	3.96%	2.57%	NA	0.12%	0.01%
rs113554206	0.012	**0.97%**	0.27%	0.42%	NA	NA	NA	NA	NA	1.64%	NA
rs149641852	0.012	**0.12%**	0.02%	0.21%	2.14%	3.39%	1.94%	1.30%	NA	0.07%	0.03%
rs144434404	0.011	**0.05%**	0.38%	0.12%	NA	NA	NA	NA	NA	NA	2.43%
rs118124843	0.011	**0.06%**	0.22%	0.05%	0.09%	NA	NA	NA	NA	NA	1.17%
rs77273076	0.008	**0.08%**	0.30%	0.09%	0.12%	NA	NA	NA	NA	NA	2.28%
rs183937294	0.007	**0.09%**	0.47%	NA	NA	NA	NA	NA	NA	NA	3.49%
rs185299109	0.007	**0.08%**	0.05%	3.84%	NA	NA	NA	NA	NA	NA	NA
rs191449639	0.005	**3.46%**	0.17%	NA	NA	NA	NA	NA	NA	NA	NA
variance explained (MAF>5%)		**0.75%**	0.48%	0.89%	1.47%	1.49%	1.50%	1.26%	1.92%	0.73%	0.65%
variance explained (MAF>1%)		**2.46%**	2.34%	2.17%	5.44%	10.26%	9.36%	9.53%	1.92%	2.68%	10.21%

Fully Adjusted Model

SNP	Minor allele frequency	DN	All vs. ctrl	CKD	CKD-DN	CKD extreme	ESRD vs. ctrl	ESRD vs. non-ESRD	ESRD vs. macro	Macro	Micro
rs61983410	0.213	**0.01%**	**0.14%**	**0.02%**	**0.01%**	**0.04%**	**0.00%**	**0.02%**	**0.01%**	**0.02%**	**0.63%**
rs55703767	0.206	**0.60%**	0.31%	0.25%	0.72%	0.33%	0.51%	0.27%	0.02%	0.70%	0.11%
rs12615970	0.133	**0.17%**	0.07%	0.50%	0.46%	0.34%	0.22%	0.22%	0.29%	0.04%	0.00%
rs551191707	0.122	**0.01%**	0.00%	0.08%	0.23%	0.41%	0.49%	0.49%	1.88%	0.07%	0.00%
rs142823282	0.017	**0.04%**	0.86%	0.01%	NA	NA	NA	NA	NA	0.12%	4.65%
rs116216059	0.016	**0.00%**	0.00%	0.03%	NA	NA	NA	NA	NA	0.00%	0.00%
rs145681168	0.014	**0.01%**	0.18%	0.00%	NA	NA	NA	NA	NA	NA	3.33%
rs115061173	0.014	**0.61%**	0.26%	0.40%	2.53%	2.11%	3.01%	1.63%	NA	NA	0.00%
rs113554206	0.012	**1.12%**	0.26%	NA	NA	NA	NA	NA	NA	3.99%	NA
rs149641852	0.012	**0.27%**	0.04%	0.74%	2.69%	NA	NA	NA	NA	0.01%	0.05%
rs144434404	0.011	**0.03%**	0.40%	0.11%	NA	NA	NA	NA	NA	NA	2.38%
rs118124843	0.011	**0.12%**	0.34%	0.17%	NA	NA	NA	NA	NA	NA	1.23%
rs77273076	0.008	**NA**	0.37%	0.04%	NA	NA	NA	NA	NA	NA	1.80%
rs183937294	0.007	**NA**	0.90%	NA	NA	NA	NA	NA	NA	NA	NA
rs185299109	0.007	**NA**	0.00%	NA	NA	NA	NA	NA	NA	NA	NA
rs191449639	0.005	**3.60%**	0.26%	NA	NA	NA	NA	NA	NA	NA	NA
variance explained (MAF>5%)		**0.78%**	0.52%	0.84%	1.41%	1.12%	1.22%	1.00%	2.20%	0.83%	0.74%
variance explained (MAF>1%)		**2.98%**	2.86%	2.30%	6.62%	3.23%	4.23%	2.63%	2.20%	4.95%	12.38%

Table S14. Physicians and nurses at health care centers participating in the collection of FinnDiane patients.

FinnDiane Study Centers	Physicians and nurses
Anjalankoski Health Centre	S. Koivula, T. Uggeldahl
Central Finland Central Hospital, Jyväskylä	T. Forslund, A. Halonen, A. Koistinen, P. Koskiaho, M. Laukkanen, J. Saltevo, M. Tiihonen

FinnDiane Study Centers	Physicians and nurses
Central Hospital of Åland Islands, Mariehamn	M. Forsen, H. Granlund, A-C. Jonsson, B. Nyroos
Central Hospital of Kanta-Häme, Hämeenlinna	P. Kinnunen, A. Orvola, T. Salonen, A. Vähänen
Central Hospital of Länsi-Pohja, Kemi	H. Laukkanen, P. Nyländen, A. Sademies
Central Ostrabothnian Hospital District, Kokkola	S. Anderson, B. Asplund, U. Byskata, P. Liedes, M. Kuusela, T. Virkkala
City of Espoo Health Centre	
Espoonlahti	A. Nikkola, E. Ritola
Tapiola	M. Niska, H. Saarinen
Samaria	E. Oukko-Ruponen, T. Virtanen
Viherlaakso	A. Lyytinen
City of Helsinki Health Centre	
Puistola	H. Kari, T. Simonen
Suutarila	A. Kaprio, J. Kärkkäinen, B. Rantaeskola
Töölö	P. Kääriäinen, J. Haaga, A-L. Pietiläinen
City of Hyvinkää Health Centre	S. Klemetti, T. Nyandoto, E. Rontu, S. Satuli-Autere
City of Vantaa Health Centre	
Korso	R. Toivonen, H. Virtanen
Länsimäki	R. Ahonen, M. Ivaska-Suomela, A. Jauhiainen
Martinlaakso	M. Laine, T. Pellonpää, R. Puranen
Myyrmäki	A. Airas, J. Laakso, K. Rautavaara
Rekola	M. Erola, E. Jatkola
Tikkurila	R. Lönnblad, A. Malm, J. Mäkelä, E. Rautamo
Heinola Health Centre	P. Hentunen, J. Lagerstam
Helsinki University Central Hospital, Department of Medicine, Division of Nephrology	A. Ahola, J. Fagerudd, M. Feodoroff, D. Gordin, O. Heikkilä, K Hietala, L. Kyllönen, J. Kytö, S. Lindh, K. Pettersson-Fernholm, M. Rosengård-Bärlund, M. Rönnback, A. Sandelin, A-R Salonen, L. Salovaara, L. Thorn, J. Tuomikangas, T. Vesisenaho, J. Wadén
Herttoniemi Hospital, Helsinki	V. Sipilä
Hospital of Lounais-Häme, Forssa	T. Kalliomäki, J. Koskelainen, R. Nikkanen, N. Savolainen, H. Sulonen, E. Valtonen
Iisalmi Hospital	E. Toivanen
Jokilaakso Hospital, Jämsä	A. Parta, I. Pirttiniemi

FinnDiane Study Centers	Physicians and nurses
Jorvi Hospital, Helsinki University Central Hospital	S. Aranko, S. Ervasti, R. Kauppinen-Mäkelin, A. Kuusisto, T. Leppälä, K. Nikkilä, L. Pekkonen
Jyväskylä Health Centre, Kyllö	K. Nuorva, M. Tiihonen
Kainuu Central Hospital, Kajaani	S. Jokelainen, P. Kemppainen, A-M. Mankinen, M. Sankari
Kerava Health Centre	H. Stuckey, P. Suominen
Kirkkonummi Health Centre	A. Lappalainen, M. Liimatainen, J. Santaholma
Kivelä Hospital, Helsinki	A. Aimolahti, E. Huovinen
Koskela Hospital, Helsinki	V. Ilkka, M. Lehtimäki
Kotka Heath Centre	E. Pälikkö-Kontinen, A. Vanhanen
Kouvola Health Centre	E. Koskinen, T. Siitonen
Kuopio University Hospital	E. Huttunen, R. Ikäheimo, P. Karhapää, P. Kekäläinen, M. Laakso, T. Lakka, E. Lampainen, L. Moilanen, L. Niskanen, U. Tuovinen, I. Vauhkonen, E. Voutilainen
Kuusamo Health Centre	T. Kääriäinen, E. Isopoussu
Kuusankoski Hospital	E. Kilkki, I. Koskinen, L. Riihelä
Laakso Hospital, Helsinki	T. Meriläinen, P. Poukka, R. Savolainen, N. Uhlenius
Lahti City Hospital	A. Mäkelä, M. Tanner
Lapland Central Hospital, Rovaniemi	L. Hyvärinen, S. Severinkangas, T. Tulokas
Lappeenranta Health Centre	P. Linkola, I. Pulli
Lohja Hospital	T. Granlund, M. Saari, T. Salonen
Loimaa Health Centre	A. Mäkelä, P. Eloranta
Länsi-Uusimaa Hospital, Tammisaari	I-M. Jousmaa, J. Rinne
Malmi Hospital, Helsinki	H. Lanki, S. Moilanen, M. Tilly-Kiesi
Mikkeli Central Hospital	A. Gynther, R. Manninen, P. Nironen, M. Salminen, T. Vänttinen
Mänttä Regional Hospital	I. Pirttiniemi, A-M. Hänninen
North Karelian Hospital, Joensuu	U-M. Henttula, P. Kekäläinen, M. Pietarinen, A. Rissanen, M. Voutilainen
Nurmijärvi Health Centre	A. Burgos, K. Urtamo
Oulankangas Hospital, Oulainen	E. Jokelainen, P-L. Jylkkä, E. Kaarlela, J. Vuolaspuro
Oulu Health Centre	L. Hiltunen, R. Häkkinen, S. Keinänen-Kiukaanniemi
Oulu University Hospital	R. Ikäheimo
Päijät-Häme Central Hospital	H. Haapamäki, A. Helanterä, S. Hämäläinen, V. Ilvesmäki, H. Miettinen
Palokka Health Centre	P. Sopanen, L. Welling
Pieksämäki Hospital	V. Javtsenko, M. Tamminen
Pietarsaari Hospital	M-L. Holmbäck, B. Isomaa, L. Sarelin

FinnDiane Study Centers	Physicians and nurses
Pori City Hospital	P. Ahonen, P. Merensalo, K. Sävelä
Porvoo Hospital	M. Kallio, B. Rask, S. Rämö
Raahe Hospital	A. Holma, M. Honkala, A. Tuomivaara, R. Vainionpää
Rauma Hospital	K. Laine, K. Saarinen, T. Salminen
Riihimäki Hospital	P. Aalto, E. Immonen, L. Juurinen
Salo Hospital	A. Alanko, J. Lapinleimu, P. Rautio, M. Virtanen
Satakunta Central Hospital, Pori	M. Asola, M. Juhola, P. Kunelius, M-L. Lahdenmäki, P. Pääkkönen, M. Rautavirta
Savonlinna Central Hospital	E. Korpi-Hyövälti, T. Latvala, E. Leijala
South Karelia Central Hospital, Lappeenranta	T. Ensala, E. Hussi, R. Härkönen, U. Nyholm, J. Toivanen
Tampere Health Centre	A. Vaden, P. Alarotu, E. Kujansuu, H. Kirkkopelto-Jokinen, M. Helin, S. Gummerus, L. Calonius, T. Niskanen, T. Kaitala, T. Vatanen
Tampere University Hospital	I. Ala-Houhala, T. Kuningas, P. Lampinen, M. Määttä, H. Oksala, T. Oksanen, K. Salonen, H. Tauriainen, S. Tulokas
Tiirismaa Health Centre, Hollola	T. Kivelä, L, Petlin, L. Savolainen
Turku Health Centre	I. Hämäläinen, H. Virtamo, M. Vähätalo
Turku University Central Hospital	K. Breitholz, R. Eskola, K. Metsärinne, U. Pietilä, P. Saarinen, R. Tuominen, S. Äyräpää
Vaajakoski Health Centre	K. Mäkinen, P. Sopanen
Valkeakoski Regional Hospital	S. Ojanen, E. Valtonen, H. Ylönen, M. Rautiainen, T. Immonen
Vammala Regional Hospital	I. Isomäki, R. Kroneld, M. Tapiolinna-Mäkelä
Vaasa Central Hospital	S. Bergkulla, U. Hautamäki, V-A. Myllyniemi, I. Rusk

Table S14: Members of the SUMMIT consortium.

Partner	**Name**	**Position**
1	**Michael Mark**	**Coordinator, WP6 leader**
Boehringer-Ingelheim	Markus Albertini	Project manager
Ingelheim, Germany	Carine Boustany	Chronic Kidney Disease, Head of Lab
	Alexander Ehlgen	Transmed
	Martin Gerl	Biomarker & Bioanlysis, Groupleader
	Jochen Huber	In vivo Scientist CMDR, Head of Lab
	Corinna Schölch	Biomarker & Bioanlysis, Head of Lab
	Heike Zimdahl-Gelling	Pharmacogenomics, Head of Lab
2	**Leif Groop**	Prof. Endocrinology; Coordinator Managing entity IMI-JU; PI; **WP1 and WP6 leader**
Lund University	Elisabet Agardh	Prof. Ophthalmology
Clinical Research Centre	Emma Ahlqvist	Postdoc
Malmö, Sweden	Tord Ajanki	Communication strategist
	Nibal Al Maghrabi	Research nurse
	Peter Almgren	Biostatistician
	Jan Apelqvist	Diabetologist
	Eva Bengtsson	Assis. Prof. Cardiovascular research
	Lisa Berglund	Postdoc
	Harry Björckbacka	Assis. Prof. Cardiovascular research
	Ulrika Blom-Nilsson	LUDC administrator
	Mattias Borell	Website, server management
	Agneta Burström	Research nurse
	Corrado Cilio	Assoc. Prof. Cellular autoimmunity
	Magnus Cinthio	Assist. Prof. Electrical Measurements, Lund Technical University
	Karl Dreja	Nephrologist
	Pontus Dunér	Postdoc Exp. Cardiovasc. Research
	Daniel Engelbertsen	PhD student Exp. Cardiovasc. Research
	Joao Fadista	Postdoc
	Maria Gomez	Assoc. Prof. Cardiovascular disease, **WP4 co-leader**
	Isabel Goncalves	Assis. Prof. Cardiovascular research

	Bo Hedblad	Prof. Cardiovascular epidemiology
	Anna Hultgårdh	Prof. Vessel Wall Biology
	Martin E. Johansson	Pathologist
	Cecilia Kennbäck	Laboratory Engineer
	Jasmina Kravic	Database manager
	Claes Ladenvall	Genetic statistician
	Åke Lernmark	Prof. Type 1 diabetes and celiac disease
	Eero Lindholm	Physician, Researcher Diabetic Complications
	Charlotte Ling	Assist. Prof. Epigenetics
	Holger Luthman	Prof. Medical genetics
	Olle Melander	Assoc. Prof. Hypertension and cardiovascular disease
	Malin Neptin	Biomedical analyst
	Jan Nilsson	Prof. Experimental Cardiovascular research, **WP3 leader**
	Peter Nilsson	Prof. Internal medicine
	Tobias Nilsson	PhD student Electrical Measurements, Lund Technical University
	Gunilla Nordin Fredriksson	Prof. Cardiovascular research
	Marju Orho-Melander	Prof. Genetic epidemiology
	Emilia Ottoson-Laakso	PhD student
	Annie Persson	Research nurse
	Margaretha Persson	Laboratory Engineer
	Mats-Åke Persson	Database manager
	Jacqueline Postma	Project manager
	Elisabeth Pranter	Research nurse
	Sara Rattik	PhD student Exp. Cardiovasc. Research
	Gunnar Sterner	Chief physician Internal Medicine Research Unit
	Lilian Tindberg	Research nurse
	Maria Wigren	Postdoc Exp. Cardiovasc. Research
	Anna Zetterqvist	PhD student
	Mikael Åkerlund	Postdoc
	Gerd Östling	Laboratory Engineer
3	**Timo Kanninen**	Technical director; PI
Biocomputing Platforms	Anni Ahonen-Bishopp	Software development manager

(BC Platforms)	Anita Eliasson	Financial and administrative director
Espoo, Finland	Timo Herrala	System (server) specialist
	Päivi Tikka-Kleemola	Service manager
4	**Anders Hamsten**	Prof. Cardiovascular disease; Atherosclerosis Research Unit; PI
Karolinska Institute	Christer Betsholtz	Prof. Vascular biology
Stockholm, Sweden	Ami Björkholm	Administrator
	Ulf de Faire	Professor emeritus Cardiovascular epidemiology
	Fariba Foroogh	Research engineer
	Guillem Genové	Scientist
	Karl Gertow	Research Assist. Prof. Cardiovascular genetics
	Bruna Gigante	Assoc. Professor Cardiovascular epidemiology
	Bing He	Postdoc
	Karin Leander	Assoc. Professor Cardiovascular epidemiology
	Olga McLeod	Postdoc
	Maria Nastase-Mannila	Postdoc
	Jaako Patrakka	Postdoc
	Angela Silveira	Assoc. Prof. Cardiovascular genetics
	Rona Strawbridge	Postdoc
	Karl Tryggvason	Prof. Medical Chemistry
	Max Vikström	Statistician
	John Öhrvik	Professor
	Anne-May Österholm	Postdoc
5	**Barbara Thorand**	Nutritional scientist, epidemiologist
Helmholtz Centre	Christian Gieger	Statistician
Munich, Germany	Harald Grallert	Biologist
	Tonia Ludwig	Statistician
	Barbara Nitz	Scientist
	Andrea Schneider	Data manager
	Rui Wang-Sattler	Scientist
	Astrid Zierer	Statistician

6	**Giuseppe Remuzzi**	Institute director; PI
Mario Negri Institute for	Ariela Benigni	Head of department Molecular Medicine
Pharmacological Research	Roberta Donadelli	Scientist
	Maria Domenica Lesti	Researcher
Bergamo, Italy	Marina Noris	Head Laboratory Immunology and genetics of transplantation and rare diseases
	Norberto Perico	Senior scientist
	Annalisa Perna	Biostatistician
	Rossella Piras	Postdoc
	Piero Ruggenenti	Head of department Renal medicine, Assist. Prof. Nephrology and dialysis
	Erica Rurali	Postdoc
7	**David Dunger (att: Jane Horsford)**	Prof. Paediatrics; PI
University of Cambridge	Ludo Chassin	Senior Data Manager
UK	Neil Dalton, London	Clinical biochemistry
	John Deanfield, London	Paediatric cardiology
	Jane Horsford	PA to Prof. Dunger
	Clare Rice	Operations manager/financial contact
	James Rudd	Cardiovascular imaging
	Neil Walker	Head Data services
	Karen Whitehead	Technician
	Max Wong	Postdoc
8	**Helen Colhoun**	Prof. Public health and epidemiology; PI; Vice coordinator Managing entity; **WP2 leader**
	Fiona Adams	
University of Dundee	Tahira Akbar	PA to Helen Colhoun
Scotland	Jill Belch	Prof. Vasucular disease
	Harshal Deshmukh	PhD student
	Fiona Dove	
	Angela Ellingford	NHS Tayside Diabetic Retinopathy Screening Programme manager
	Bassam Farran	Statistician
	Mike Ferguson	Dean of research Biological chemistry and drug discovery
	Gary Henderson	

	Graeme Houston	Consultant radiologist/senior lecturer
	Faisel Khan	Reader, Vascular & Inflammatory Diseases Research Unit
	Graham Leese	Consultant diabetologist/reader
	Yiyuan Liu	PhD student
	Shona Livingstone	Senior statistician
	Helen Looker	Epidemiologist
	Margaret McCann	Project assistant
	Stuart McGurnaghan	Lead data programmer
	Andrew Morris	Prof. Diabetic medicine
	David Newton	
	Colin Palmer	Prof. Pharmacogenomics
	Ewan Pearson	Consultant diabetologist/senior lecturer
	Gillian Reekie	Research Nurse
	Natalie Smith	Research Nurse
9	**Angela Shore**	Prof. Cardiovascular Science, PI
Peninsula Medical School	Kuni Aizawa	Postdoc
Exeter, UK	Claire Ball	Research nurse
	Nick Bellenger	Cardiologist
	Francesco Casanova	Associate Research Fellow Vascular medicine
	Tim Frayling	Prof. Genetics
	Phil Gates	Senior lecturer Cardiovascular science
	Kim Gooding	Postdoc Vascular medicine
	Andrew Hatttersley	Prof. Molecular medicine
	Roland Ling	Consultant opthalmologist
	David Mawson	Research technician
	Robin Shandas	Prof. Bioengineering (Colorado)
	David Strain	Stroke physician, clinical lecturer
	Clare Thorn	Postdoc Vascular medicine
10	**Ulf Smith**	Prof. ; PI
University of Gothenburg	Ann Hammarstedt	Researcher Molecular and clinical medicine
Sweden	Hans Häring	Prof. University of Tübingen

	Oluf Pedersen	Prof. Steno Centre, Copenhagen
	Georgio Sesti	Prof. Universtiy of Catanzaro
11	**Per-Henrik Groop**	Prof. Diabetes genetics; PI
	Emma Fagerholm	MSc; PhD student, genetics
Folkhälsan	Carol Forsblom	Clinical coordinator
Helsinki, Finland	Valma Harjutsalo	PhD; FinnDiane Co-PI
	Maikki Parkkonen	Laboratory manager
	Niina Sandholm	DSc(PhD); GWAS and bioinformatics, FinnDiane Co-PI
	Nina Tolonen	MD PhD
	Iiro Toppila	BSc, MSc; bioinformatician
	Erkka Valo	MSc; PhD student, bioinformatician
12	**Veikko Salomaa**	Prof. Epidemiology; PI; **deputy leader WP2**
The National Institute for Health and Welfare	Aki Havulinna	DSc. (tech), statistician
Helsinki, Finland	Kati Kristiansson	PhD
	Pia Okamo	THL press officer
	Tomi Peltola	PhD
	Markus Perola	Professor
	Arto Pietilä	Statistician
	Samuli Ripatti	Professor, Statistics
	Marketta Taimi	Research assistant
13	**Seppo Ylä-Herttuala**	Prof.; PI; **WP4 leader**
University of Eastern Finland	Mohan Babu	PhD student
Kuopio, Finland	Marike Dijkstra	PhD student
	Erika Gurzeler	PhD student
	Jenni Huusko	PhD student
	Ivana Kholová	Postdoc
	Markku Laakso	Prof.
	Mari Merentie	PhD student

	Marja Poikolainen	PA Prof Ylä-Herttuala
14	**Mark McCarthy**	Prof. Human type 2 diabetes; Oxford Centre for Diabetes, Endocrinology and Metabolism; Wellcome Trust Centre for Human Genetics; PI; **deputy leader WP1**
University of Oxford	Will Rayner	Database manager
UK	Neil Robertson	Informatics
	Natalie van Zuydam	Postdoc
15	**Claudio Cobelli**	Prof. ; PI; **WP5 leader**
University of Padova	Barbara Di Camillo	Assist. Prof.
Italy	Francesca Finotello	PhD student
	Francesco Sambo	Postdoctoral fellow
	Gianna Toffolo	Prof.
	Emanuele Trifoglio	PhD student
16	**Riccardo Bellazzi**	Prof. Bioengineering; PI; **deputy leader WP5**
	Nicola Barbarini	Postdoctoral fellow
University of Pavia	Mauro Bucalo	Software engineer
Italy	Christiana Larizza	Assist. Prof.
	Paolo Magni	Assoc. Prof.
	Alberto Malovini	Postdoctoral fellow
	Simone Marini	Postdoctoral fellow
	Francesca Mulas	Postdoctoral fellow
	Silvana Quaglini	Prof.
	Lucia Sacchi	Assist. Prof.
	Francesca Vitali	
17	**Ele Ferrannini**	Prof. Medicine; PI
	Beatrice Boldrini	Postdoctoral fellow
University of Pisa	Michaela Kozakova	Senior investigator Medical Pathophysiology
Italy	Andrea Mari	Senior researcher Biomedical engineering (ISIB-CNR, Padova)
	Carmela Morizzo	Biologist, Sonographer Cardiovascular ultrasound
	Lucrecia Mota	EGIR administrative office

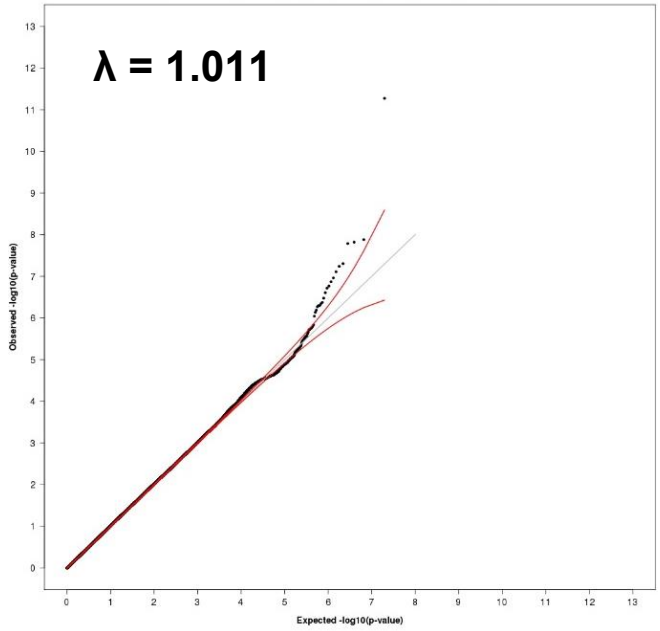
	Andrea Natali	Assoc. Prof. Medicine
	Carlo Palombo	Assoc. Prof. Medicine; **deputy leader WP3**
	Elena Venturi	Researcher
	Mark Walker	Prof. Molecular diabetic medicine (Univ Newcastle-upon-Tyne)
18	**Carlo Patrono**	Prof.Pharmacology; PI
Catholic University of Rome	Francesca Pagliaccia	PhD student
Italy	Bianca Rocca	Assist. Prof. Pharmacology
19	**Pirjo Nuutila**	Prof. ; PI
University of Turku	Johanna Haukkala	PhD student
Finland	Juhani Knuuti	Prof. ; Director Turku PET Centre
	Anne Roivainen	Prof.
	Antti Saraste	Adj. Prof.
20	**Paul McKeague**	Prof. Genetic Epidemiology; PI
University of Edinburgh	Norma Brown	Research administrator, Public Health Services
Scotland	Marco Colombo	Bioinformaticist
21	**Birgit Steckel-Hamann**	Deputy coordinator; PI, Manager IMI, LRL
Eli Lilly	Krister Bokvist	Biostatistician
	Sudha Shankar	Diabetologist
	Melissa Thomas	Translational Science
22	**Li-ming Gan**	Prof.; Translational Science Director Cardiovascular Disease; PI, **WP3 leader**
AstraZeneca	Suvi Heinonen	PhD, Internal AZ postdoc, Bioscience
	Ann-Cathrine Jönsson-Rylander	PhD, Assoc. Prof., Team Leader Bioscience, **WP4 leader**
	Remi Momo	Postdoctoral fellow
	Volker Schnecke	Informatician Translational Science, **WP5 leader**
	Robert Unwin	Translational Science Director Diabetic Nephropathy
	Anna Walentinsson	Geneticist Translational Science
	Carl Whatling	Bioscientist

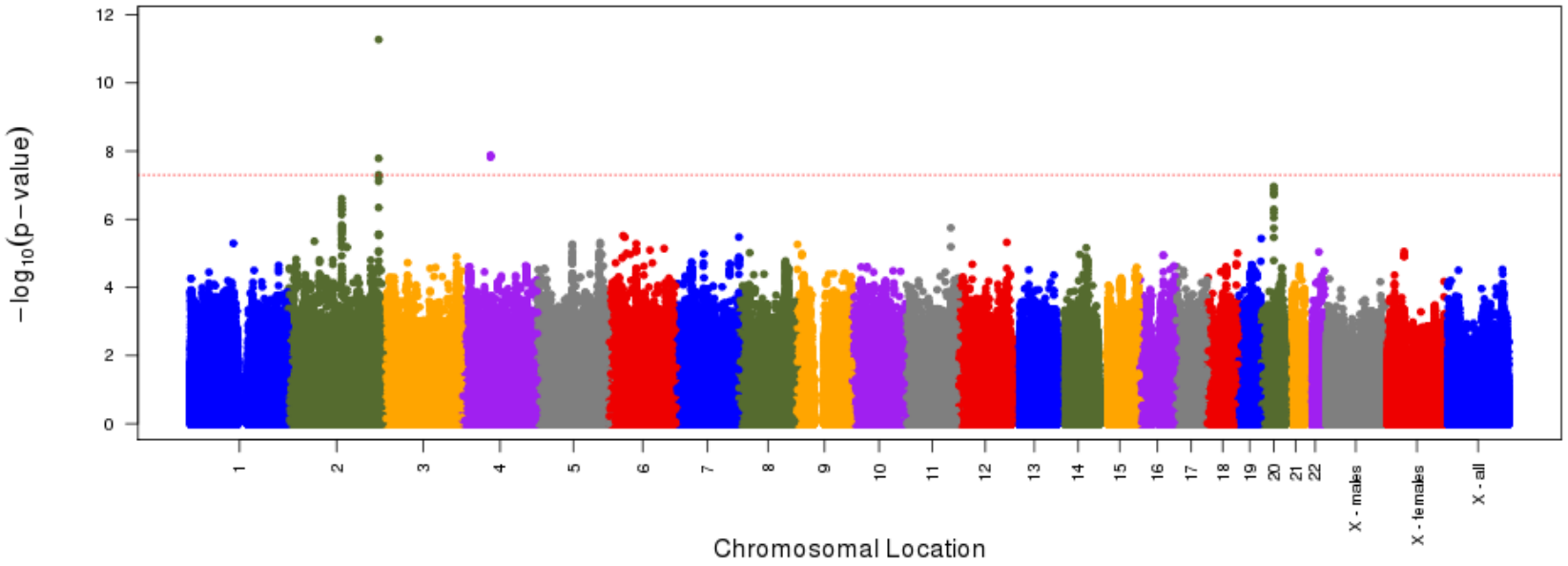
23	**Everson Nogoceke**	Pre-clinical and clinical aspects of metabolic and vascular disease; PI; **WP2 leader**
Roche	Gonzalo Durán Pacheco	Senior Research Statistician
	Ivan Formentini	Biomarker & Experimental Medicine Leader
	Thomas Schindler	Pre-clinical and clinical and clinical biomarkers
24	**Piero Tortoli**	Professor of Electronics
University of Florence	Luca Bassi	Postdoctoral fellow
	Enrico Boni	Postdoctoral fellow
	Alessandro Dallai	Postdoctoral fellow
	Francesco Guidi	Technician
	Matteo Lenge	PhD student
	Riccardo Matera	PhD student
	Alessandro Ramalli	PhD student
	Stefano Ricci	Assist. Prof.
	Jacopo Viti	PhD student
25	**Bernd Jablonka**	SAD internal IMI coordinator
Sanofi-aventis	Dan Crowther	Biomarker researcher
	Johan Gassenhuber	Biostatistician
	Sibylle Hess	Biomarker researcher
	Thomas Hübschle	Pharmacologist Diabetes
	Hans-Paul Juretschke	Imaging
	Hartmut Rütten	Head Translational Medicine
	Thorsten Sadowski	Pharmacologist Diabetes
	Paulus Wohlfart	Pharmacologist Diabetes
26	**Julia Brosnan**	Biochemist, (pre)clinical research CVD, Pfizer US; **WP2 leader**
Pfizer	Valerie Clerin	Cardio-renal biologist, WP2
	Eric Fauman	Computational biologist
	Craig Hyde	Statistician
	Anders Malarstig	Human genetics, Pfizer Europé; **WP1 leader**
	Nick Pullen	Renal Disease Research Director

	Mera Tilley	
	Theresa Tuthill	Imaging specialist
	Ciara Vangjeli	Cardiovascular genetic epidemiologist, Pfizer Europe
	Daniel Ziemek	Computational biologist

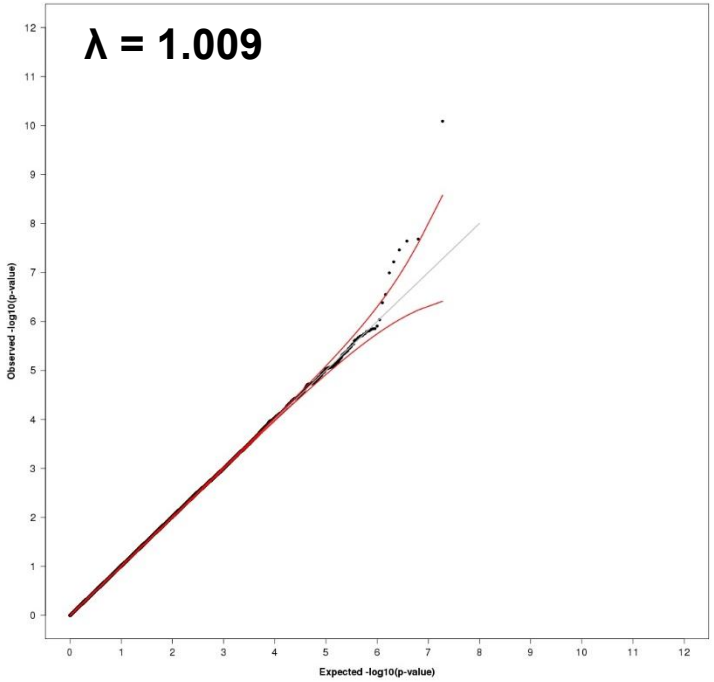
Figure S1. Manhattan and QQ Plots for each case-control definition and covariate model (minimal and full)

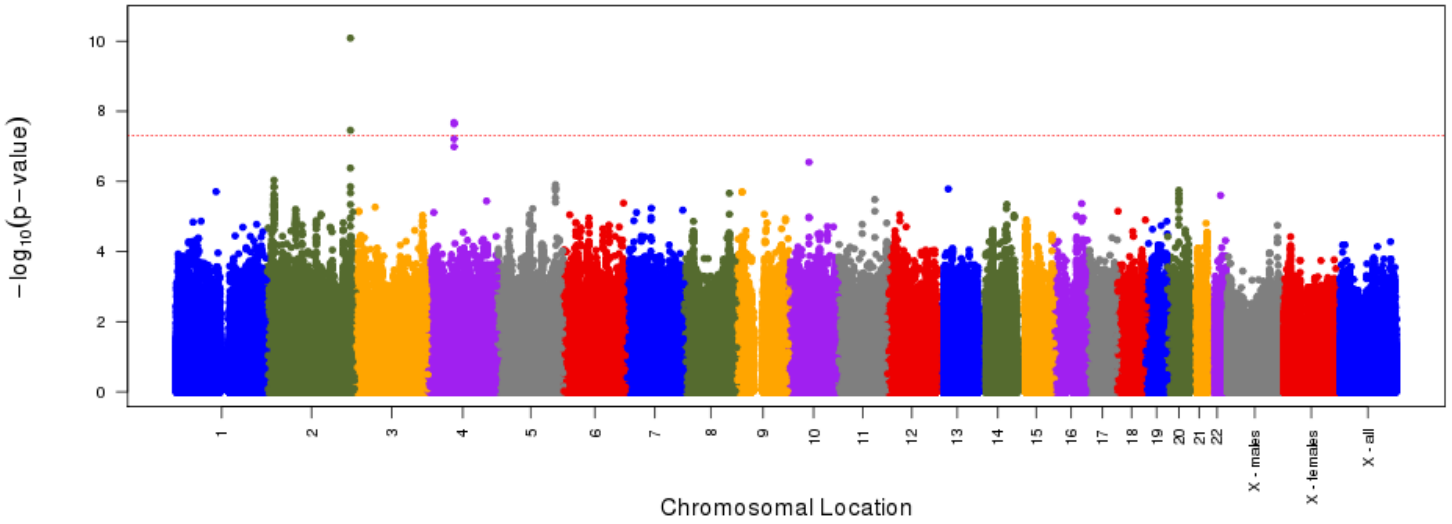
DN - minimal



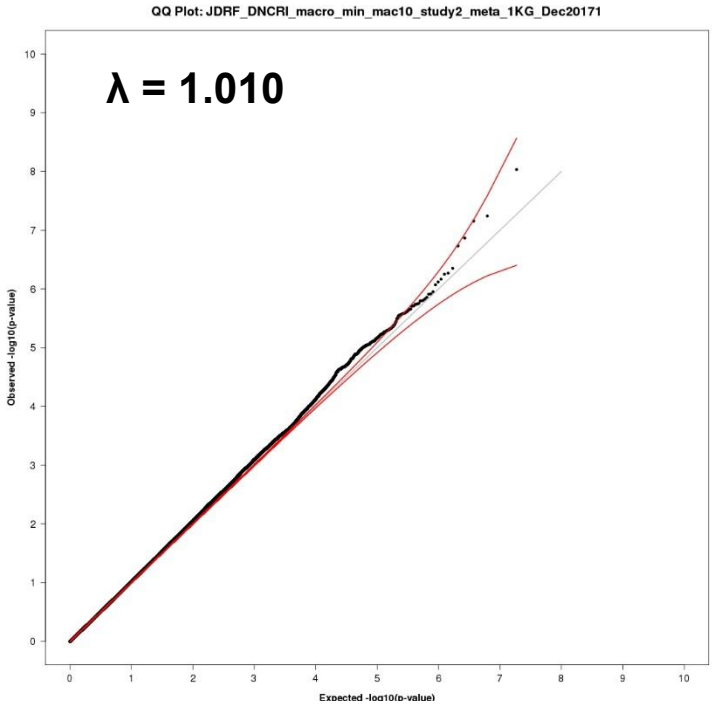


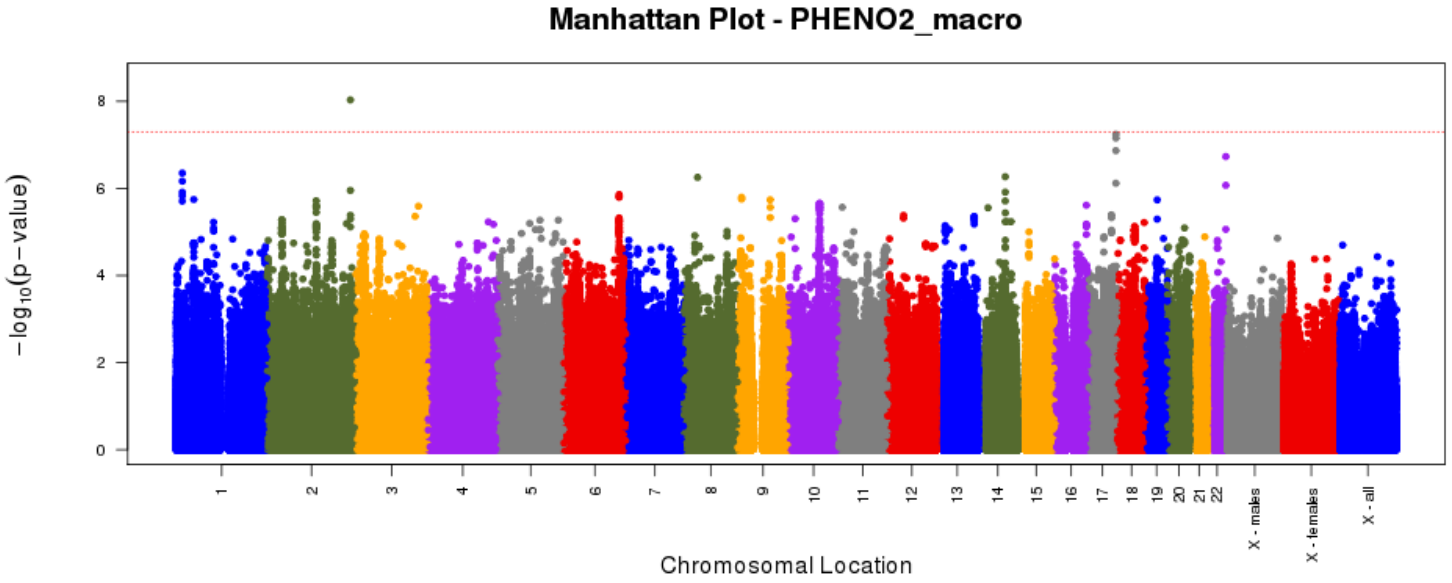
DN - full


λ = 1.009
Observed -log10(p-value)
Expected -log10(p-value)

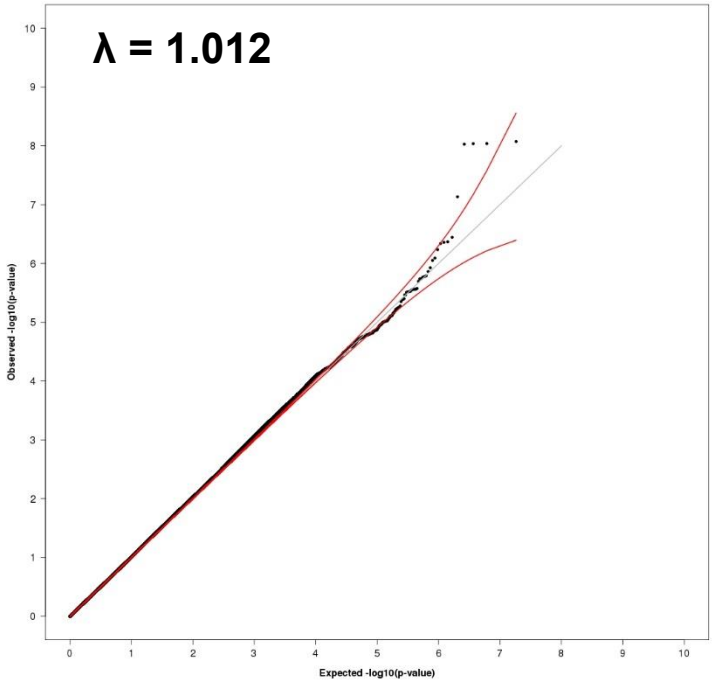

−log10(p−value)
Chromosomal Location
X - males
X - females
X - all

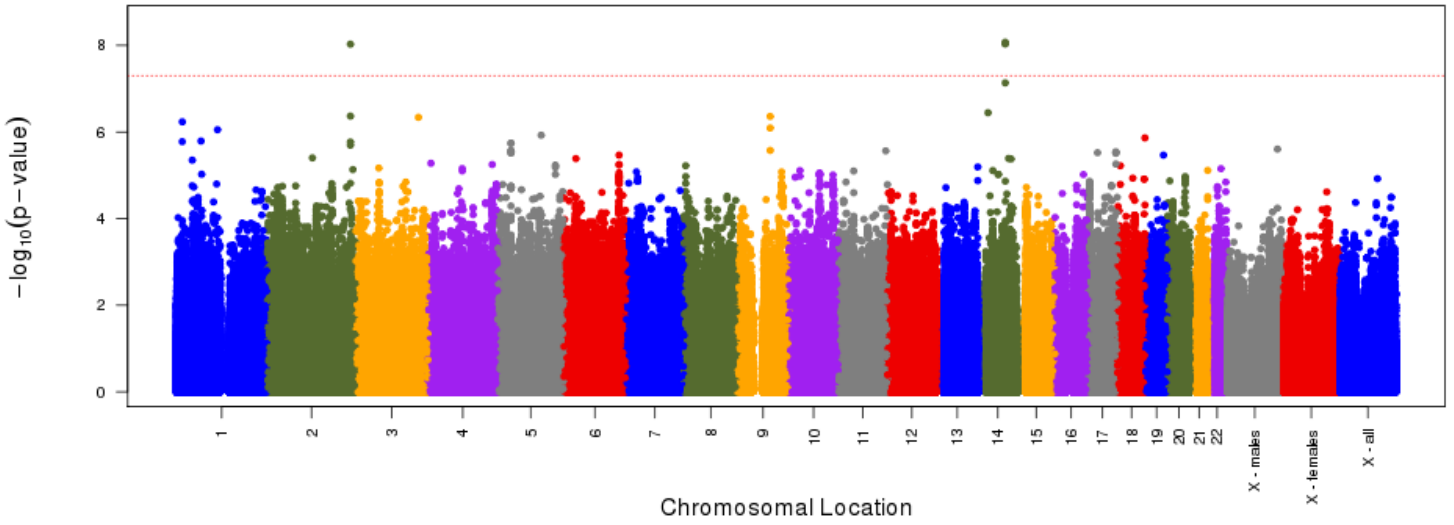
macro - min


QQ Plot: JDRF_DNCRI_macro_min_mac10_study2_meta_1KG_Dec20171
λ = 1.010
Observed -log10(p-value)
Expected -log10(p-value)

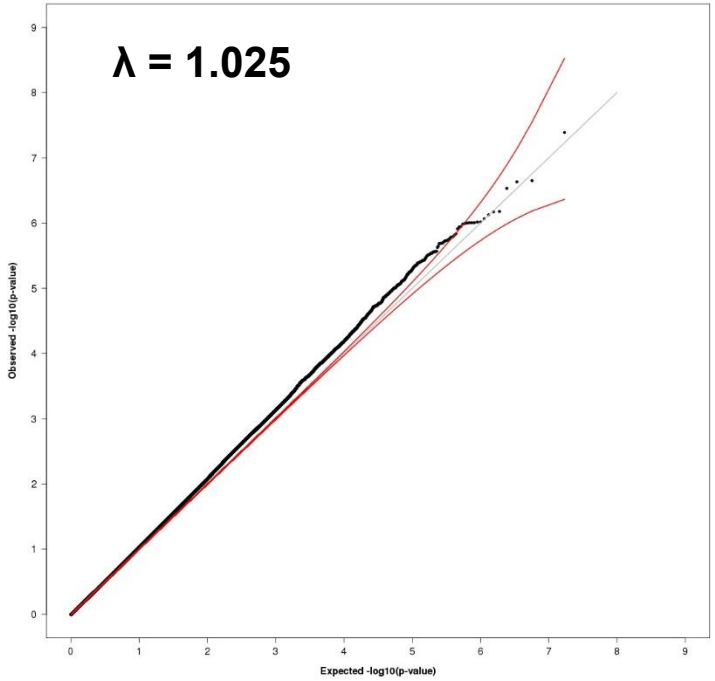

Manhattan Plot - PHENO2_macro
−log10(p−value)
Chromosomal Location
X - males
X - females
X - all

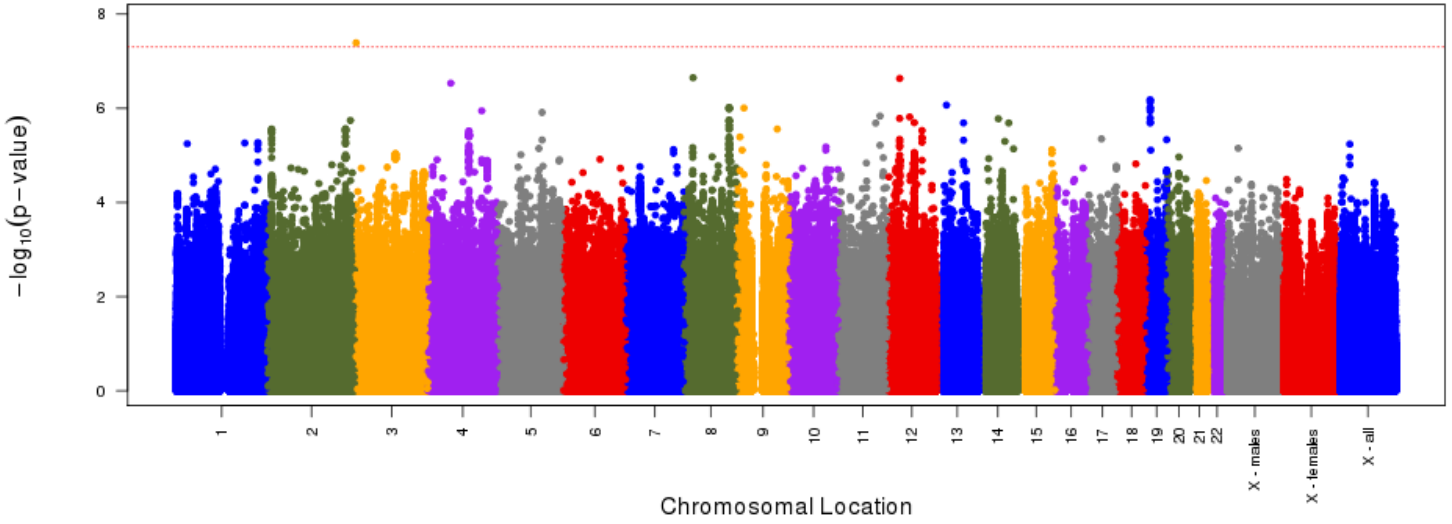
macro - full


λ = 1.012
Observed -log10(p-value)
Expected -log10(p-value)

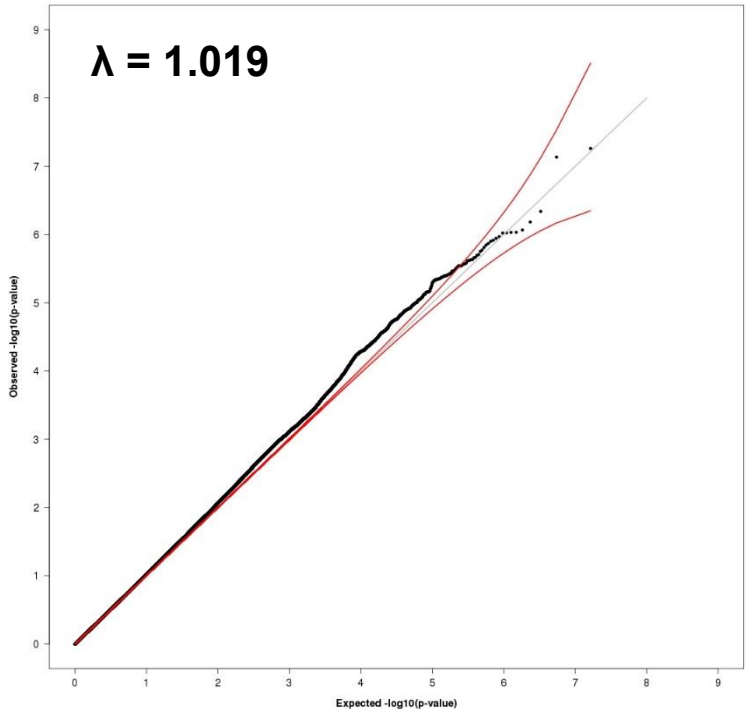

−log10(p−value)
Chromosomal Location
X - males
X - females
X - all

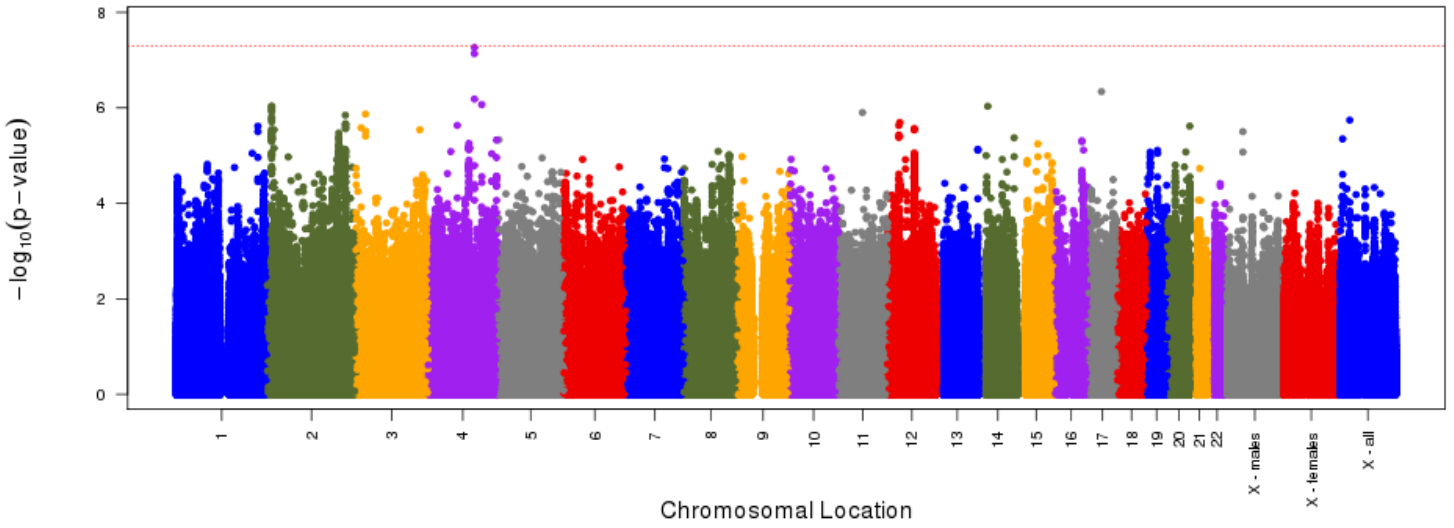
ESRD vs. ctrl- min



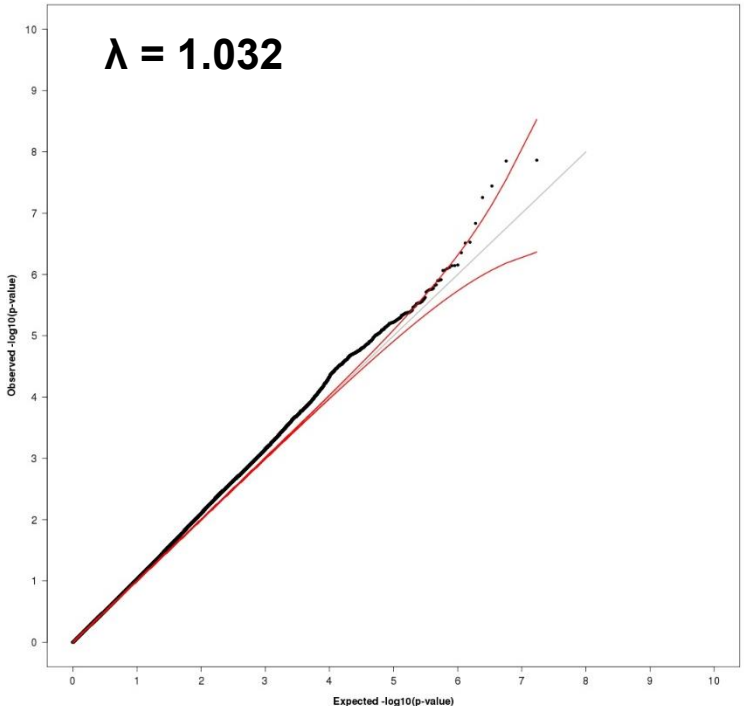


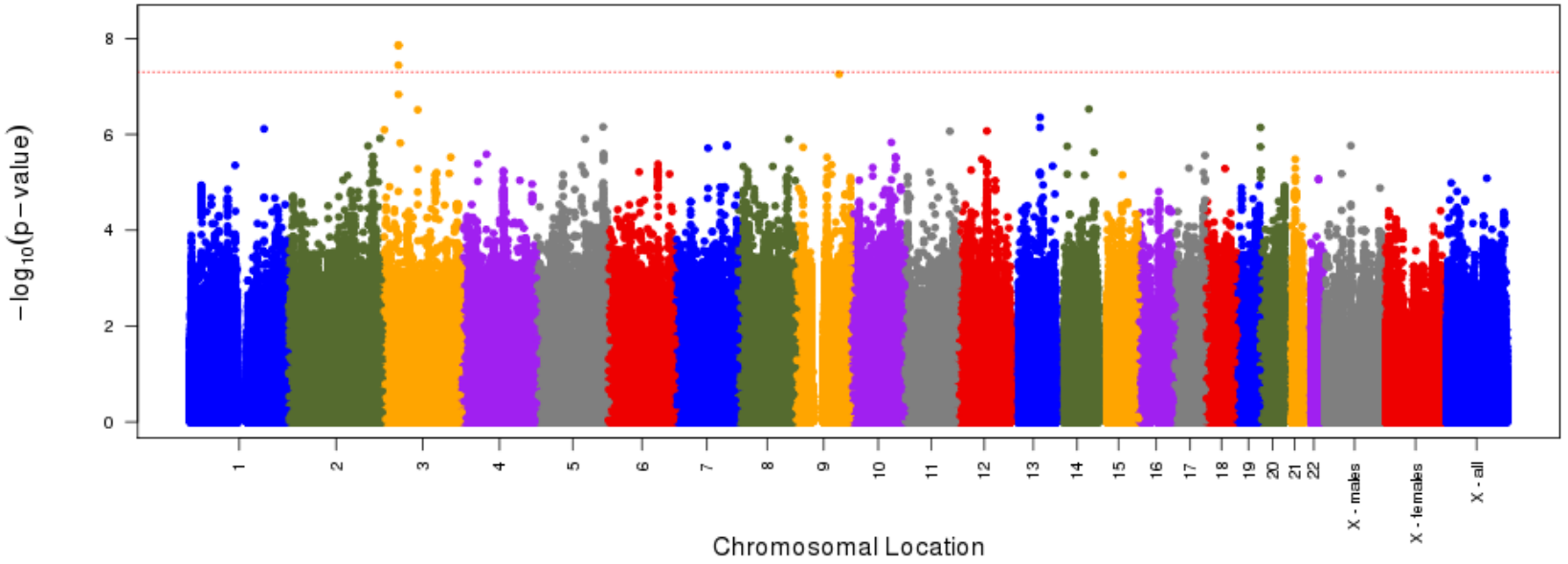
ESRD vs. ctrl - full



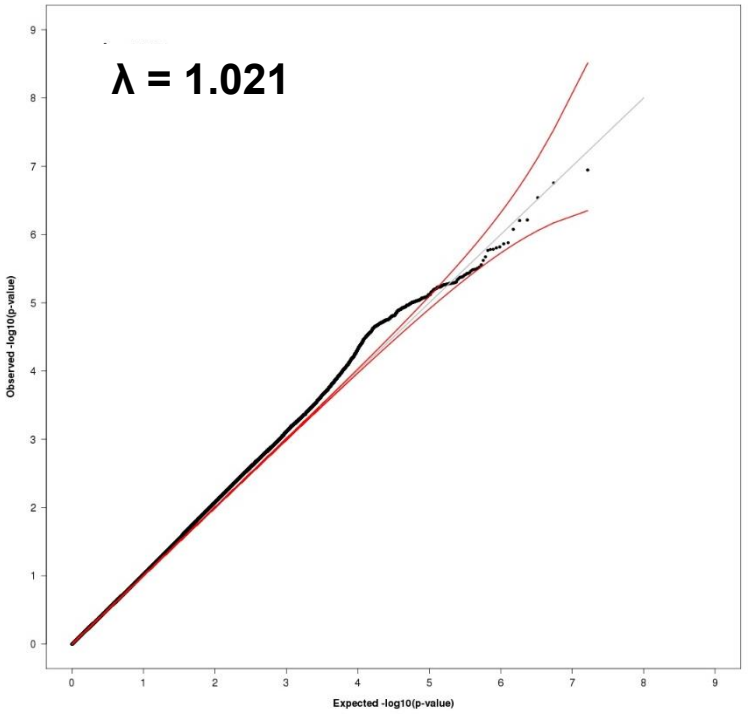


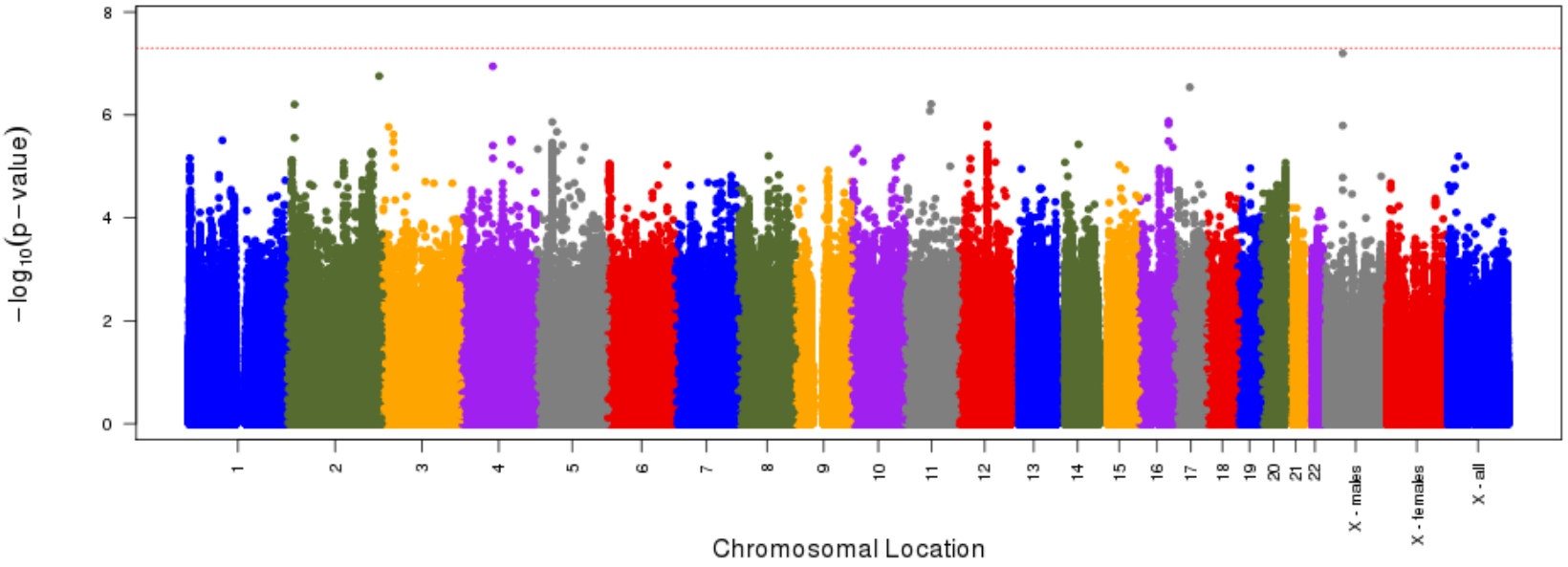
ESRD vs. non-ESRD -



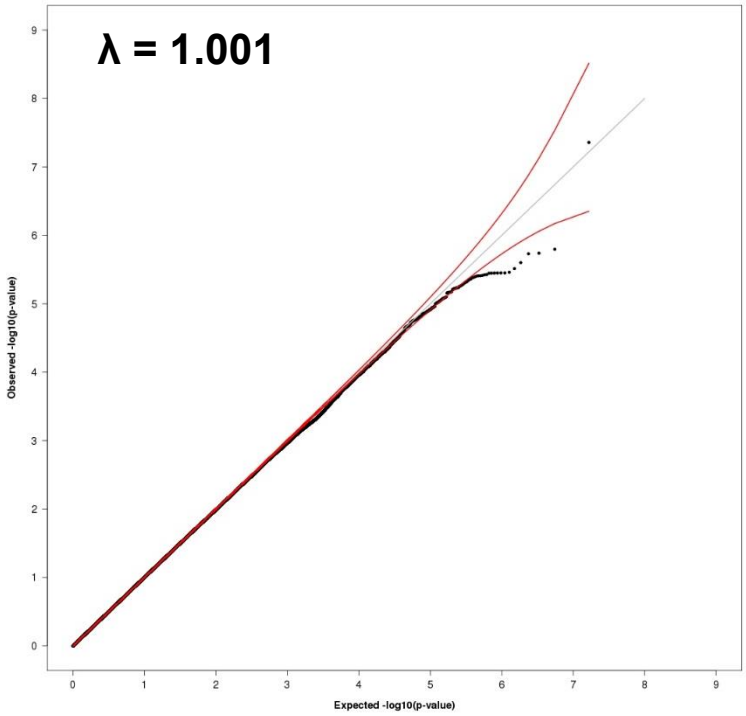


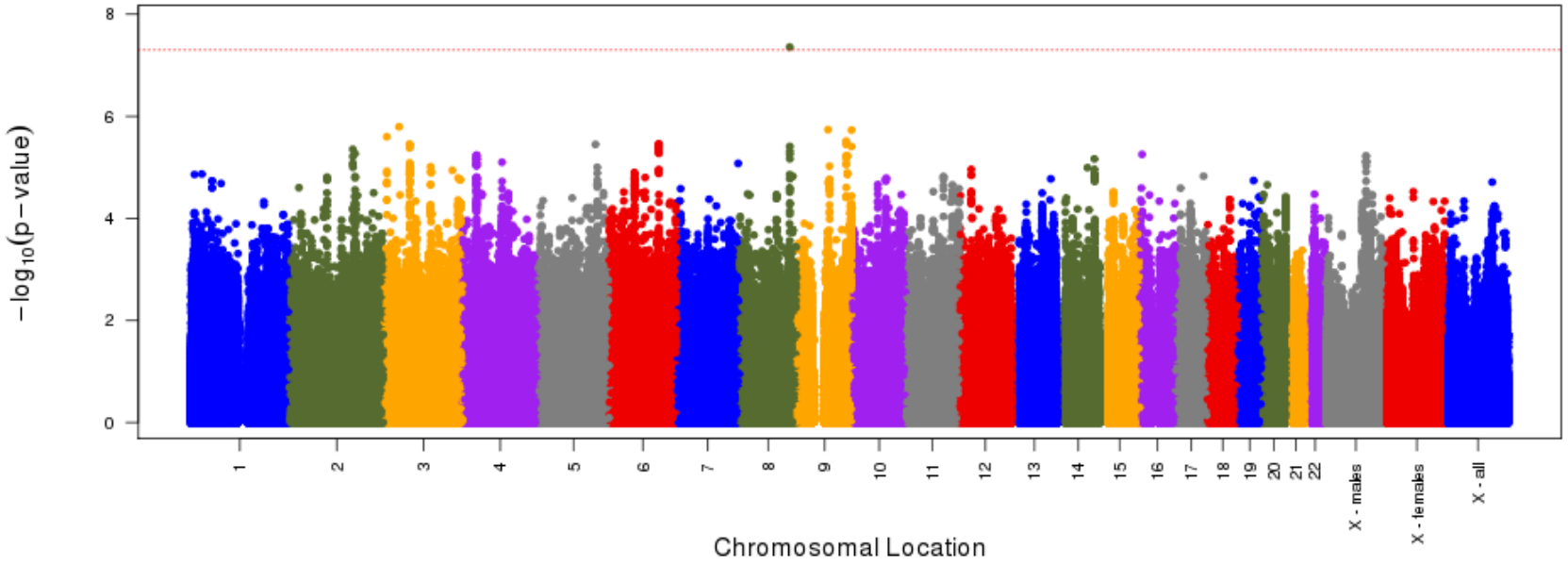
ESRD vs. non-ESRD -



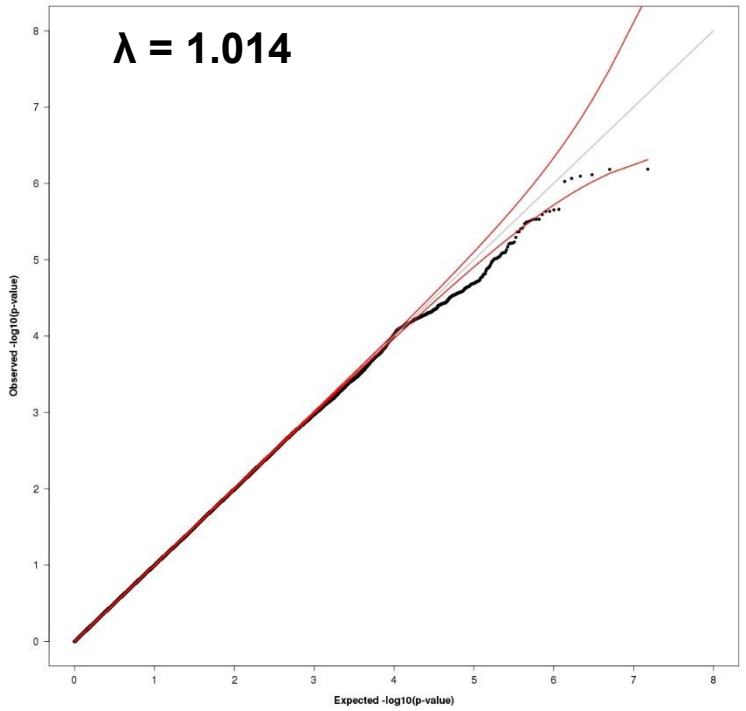


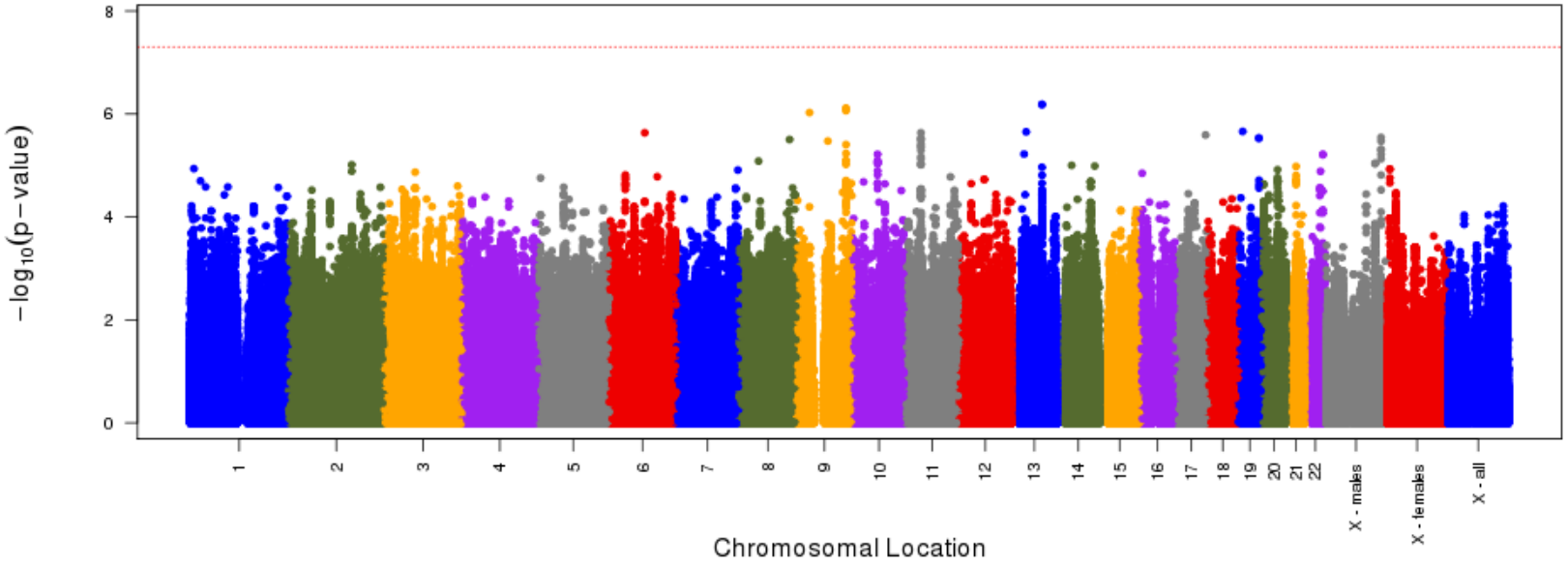
ESRD vs. macro - min



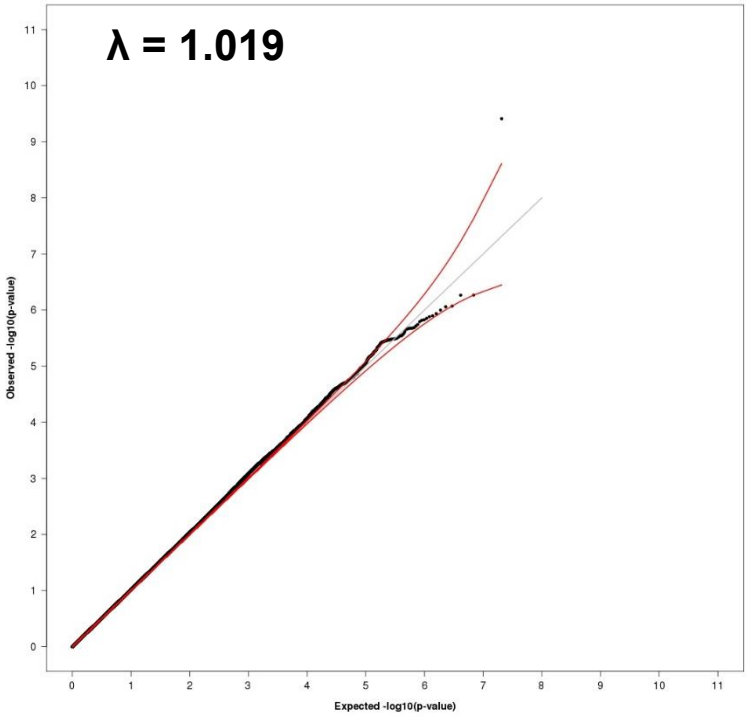


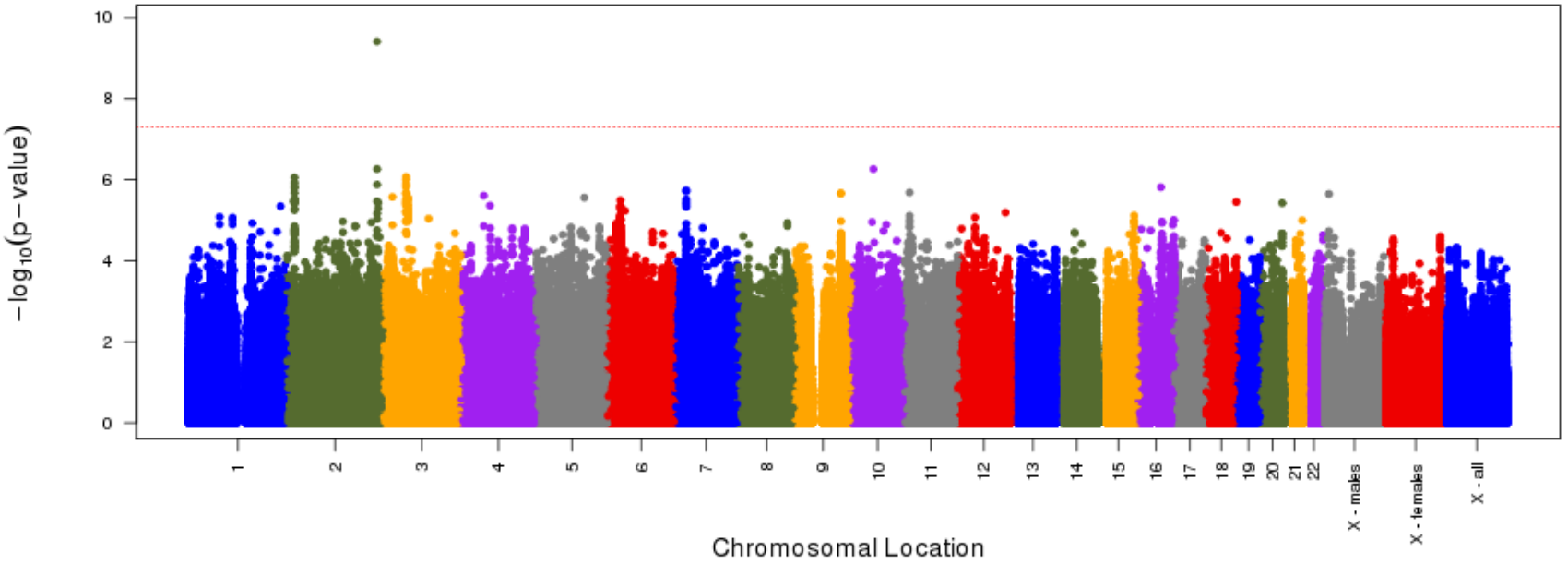
ESRD vs. macro - full



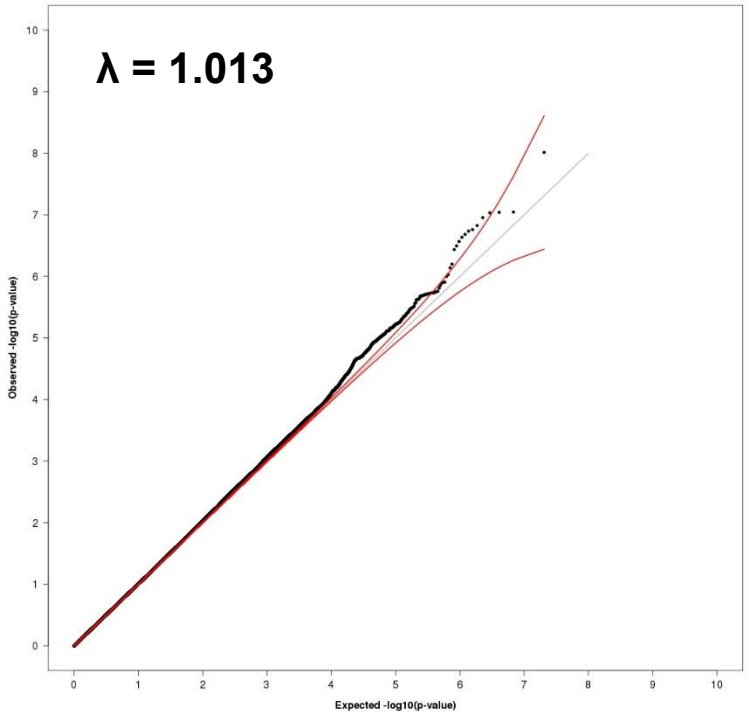


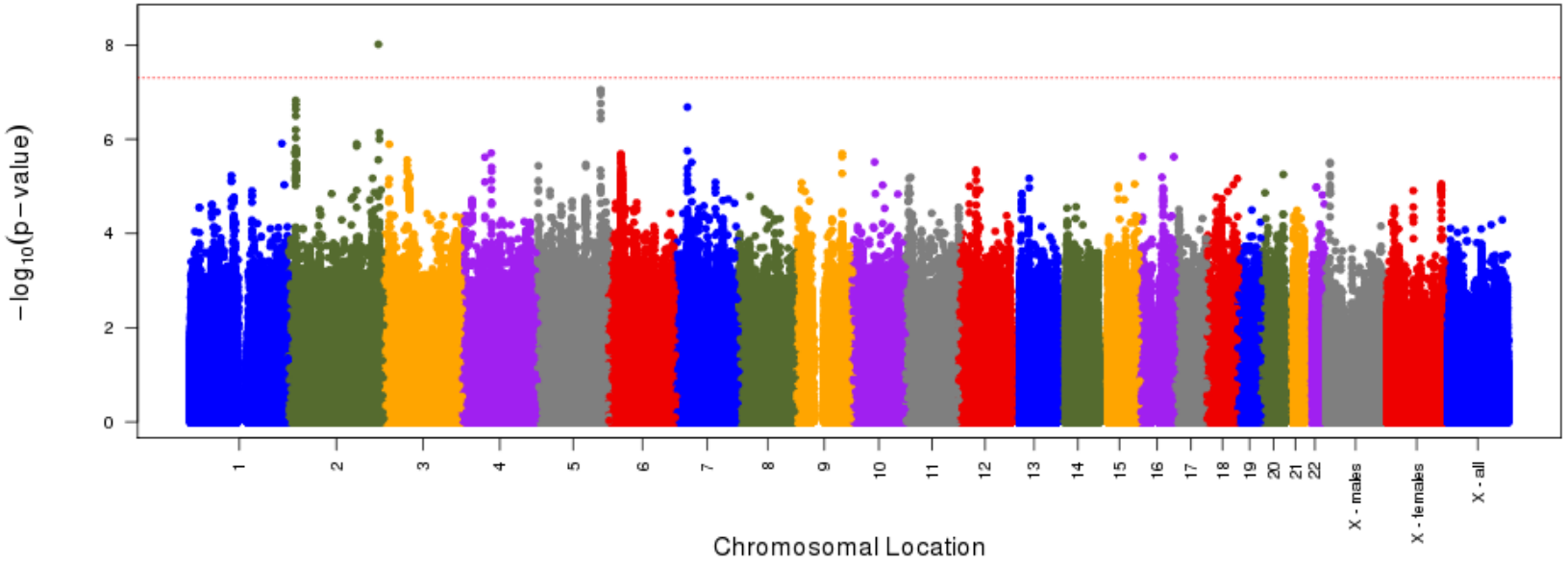
All vs. ctrl - min



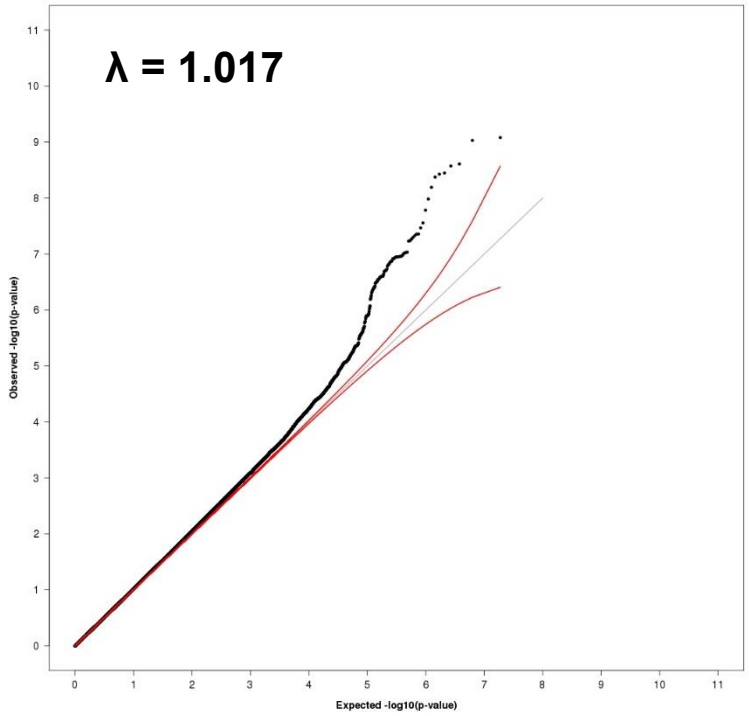


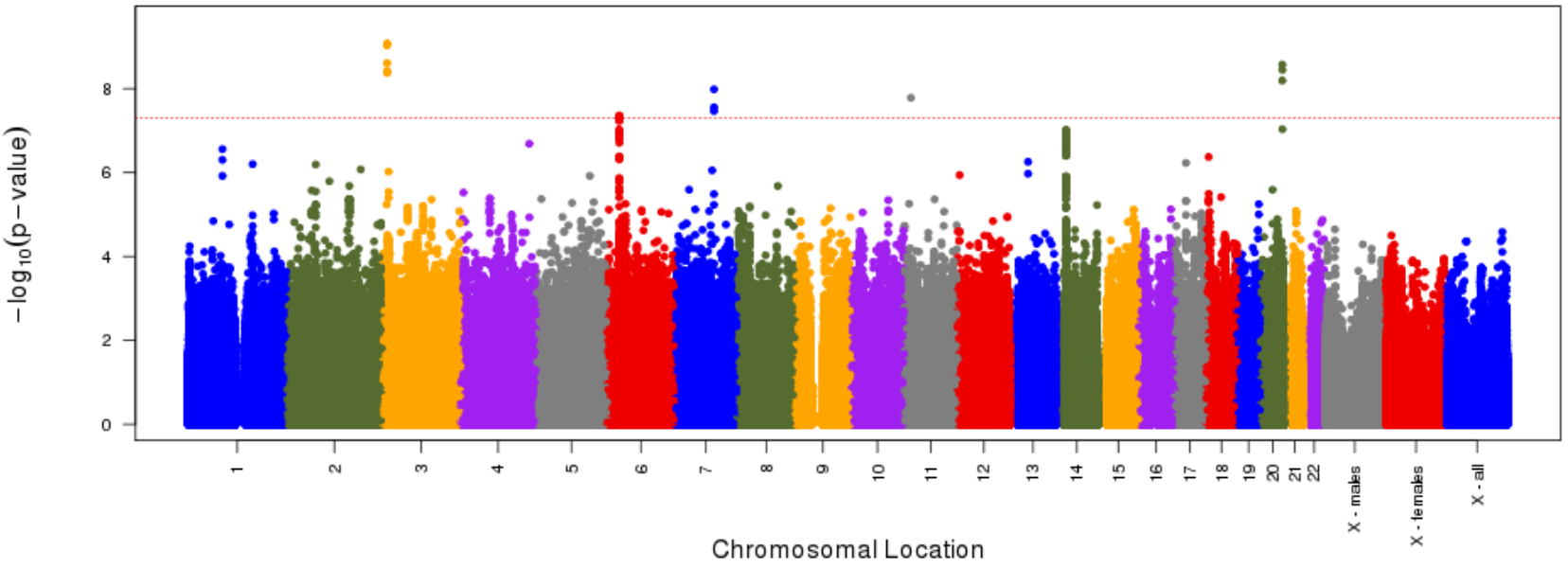
All vs. ctrl - full



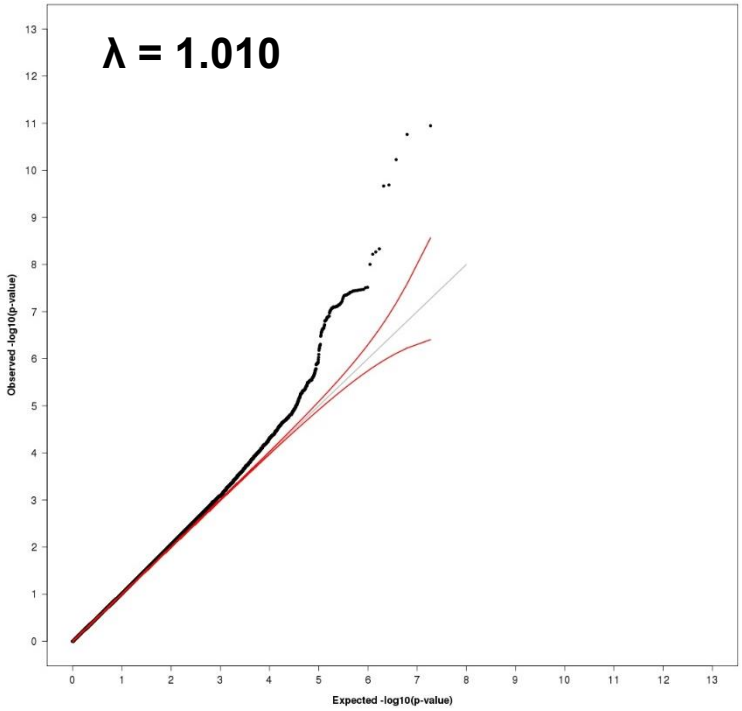


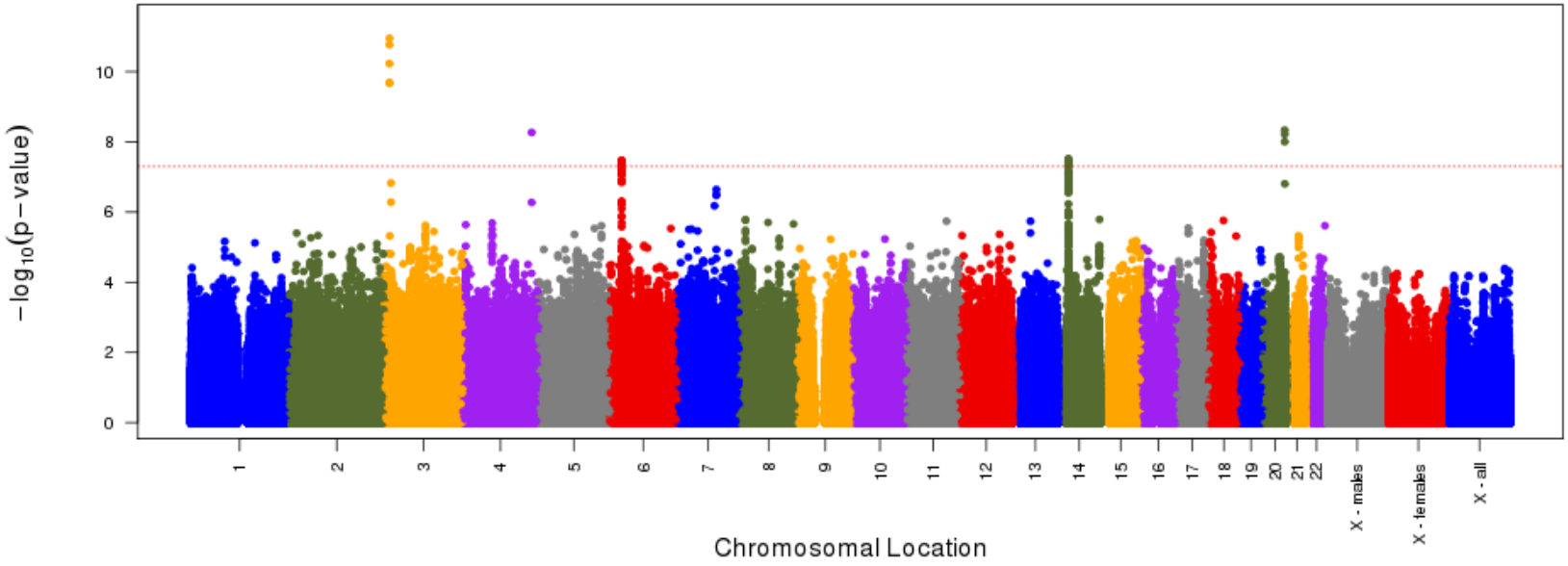
Micro - min


λ = 1.017
Observed -log10(p-value)
Expected -log10(p-value)

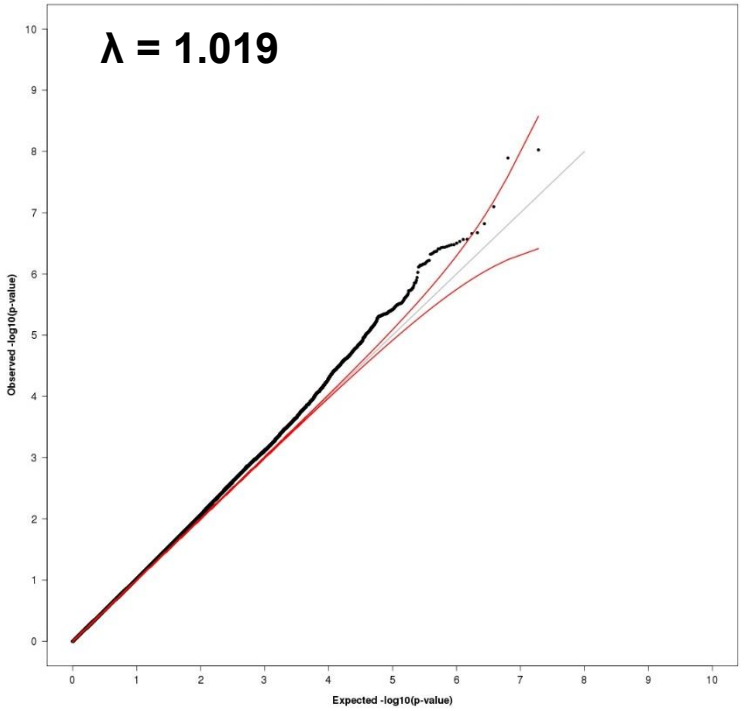

−log10(p−value)
Chromosomal Location
X - males
X - females
X - all

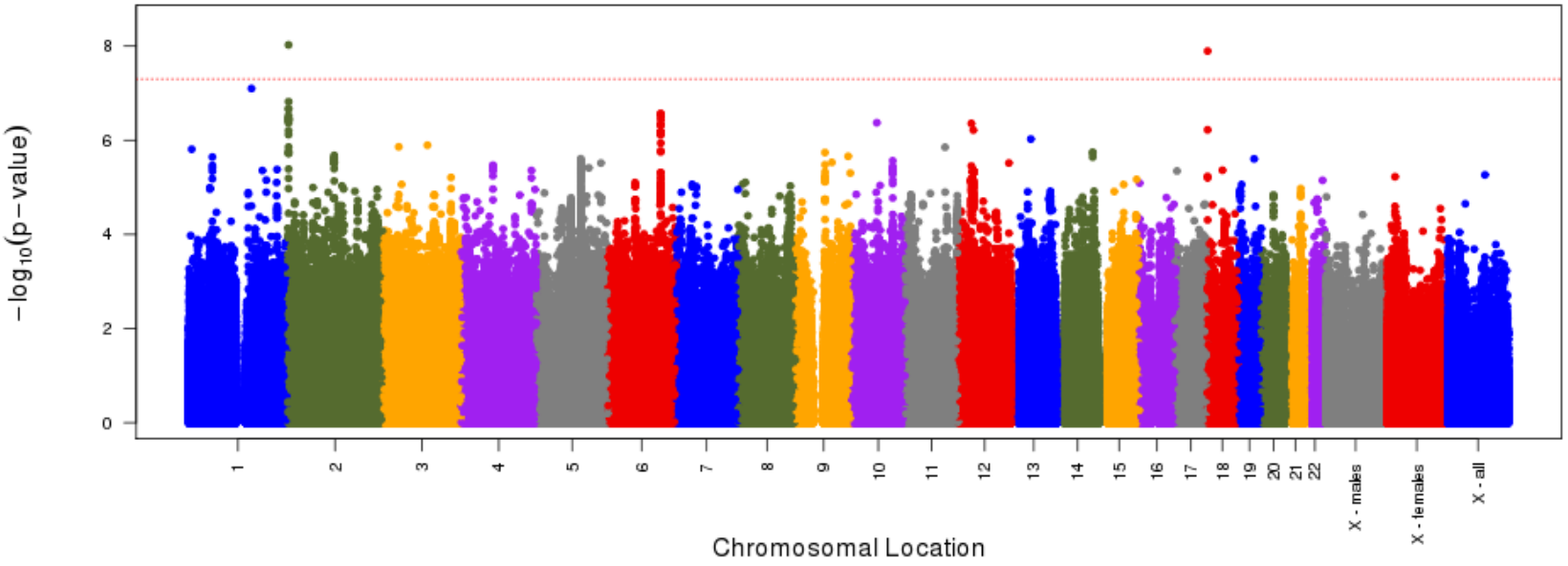
Micro - full


λ = 1.010
Observed -log10(p-value)
Expected -log10(p-value)

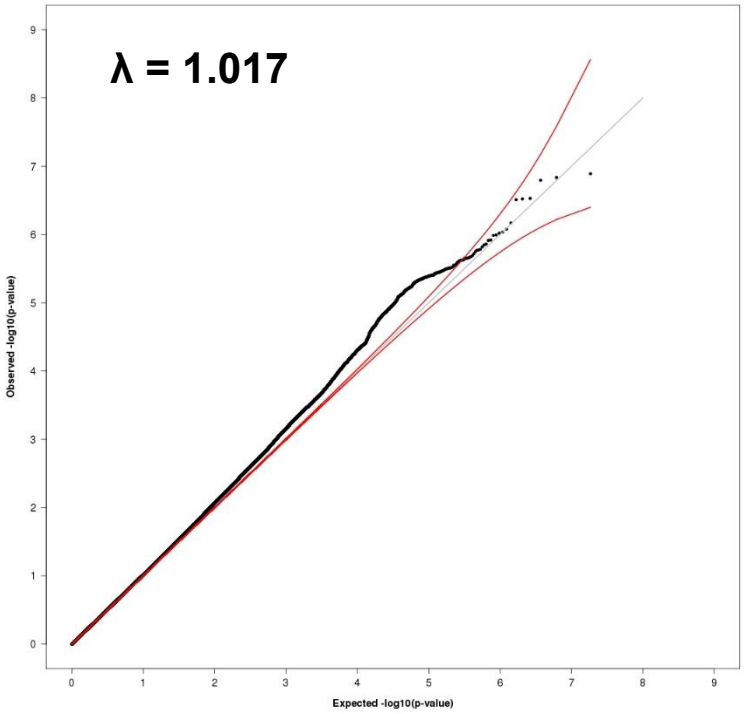

−log10(p−value)
Chromosomal Location
X - males
X - females
X - all

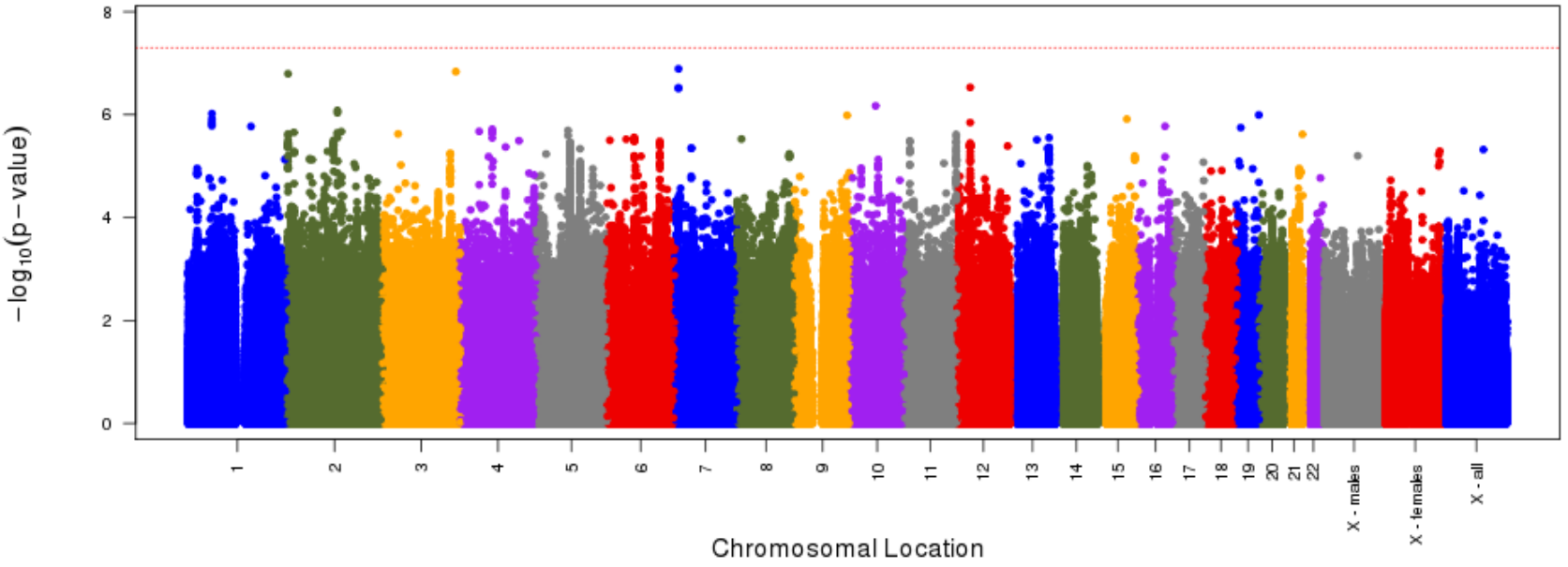
CKD - min


λ = 1.019
Observed -log10(p-value)
Expected -log10(p-value)

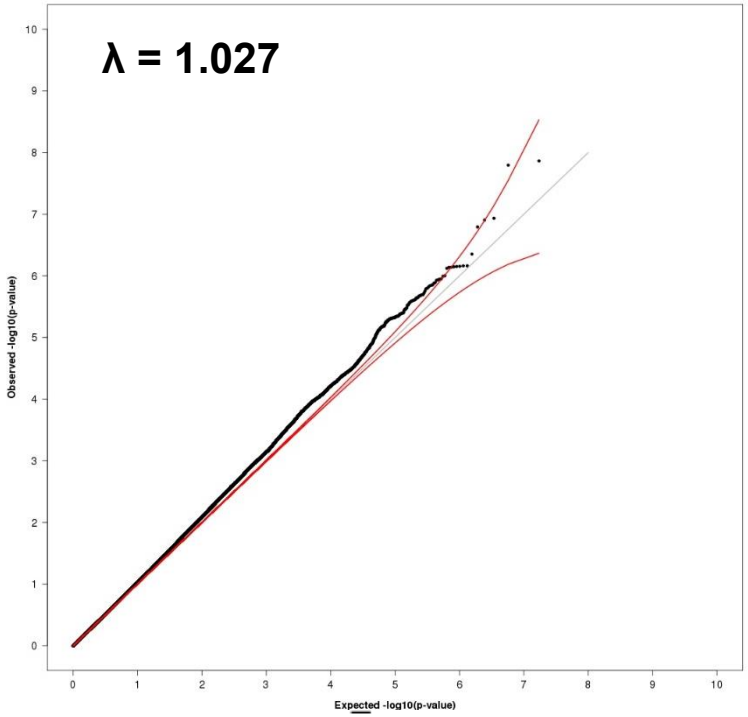

−log10(p−value)
Chromosomal Location
X - males
X - females
X - all

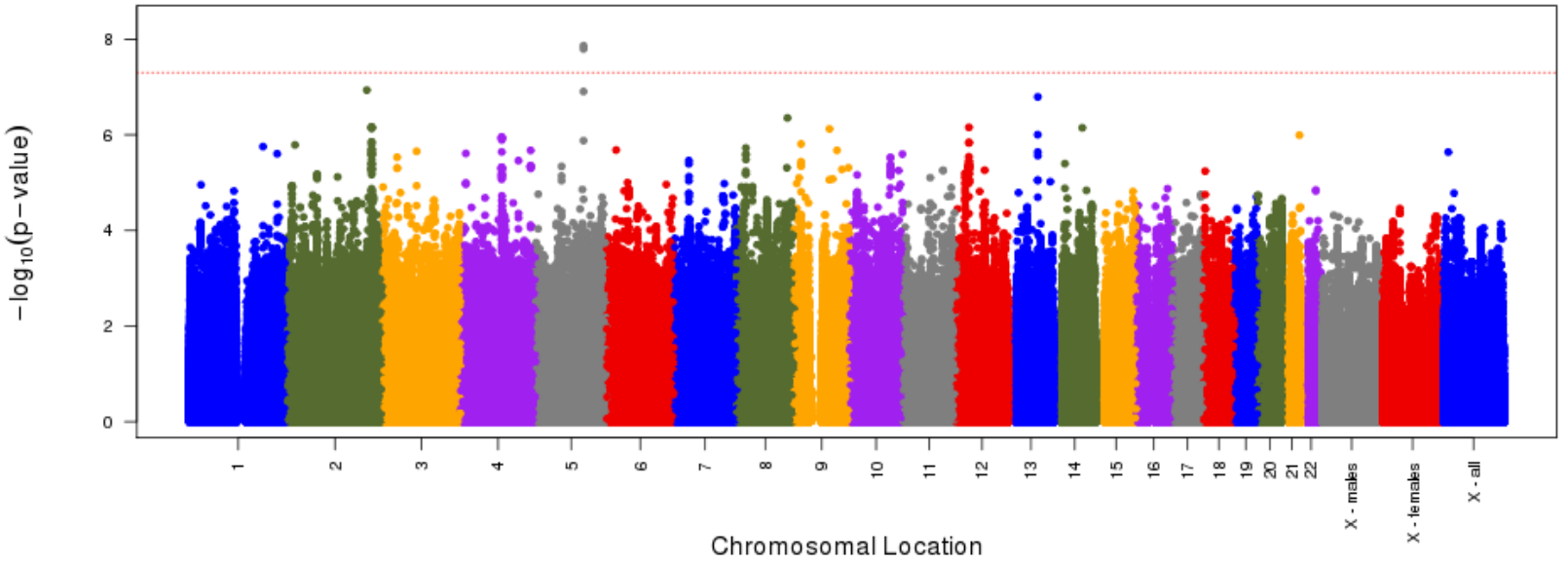
CKD - full


λ = 1.017
Observed -log10(p-value)
Expected -log10(p-value)

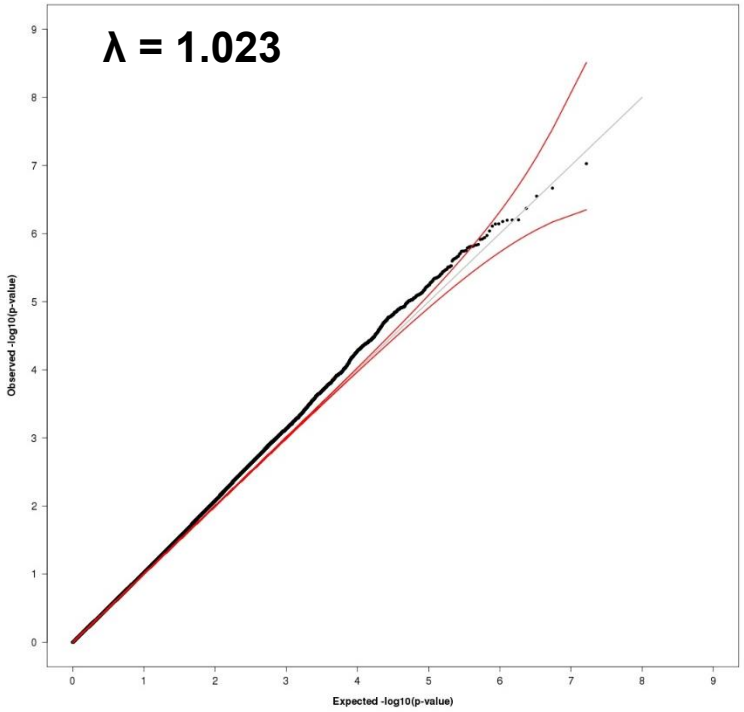

−log10(p−value)
Chromosomal Location
X - males
X - females
X - all

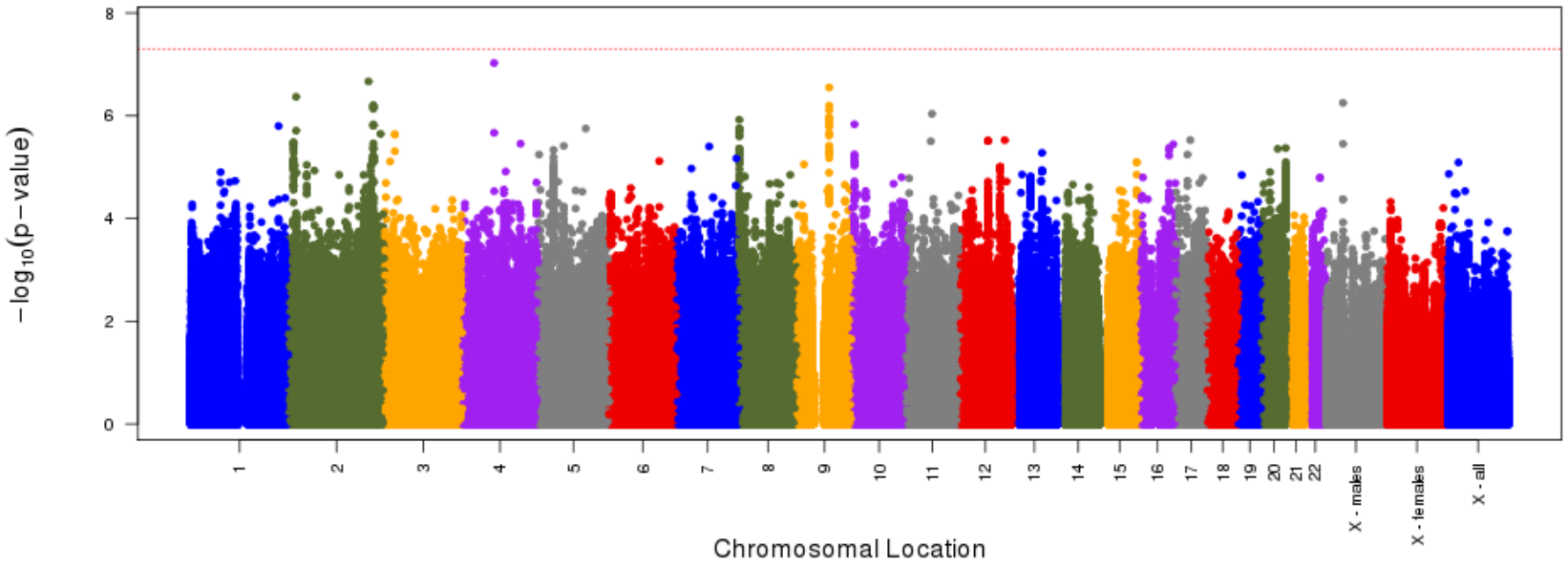
CKD extreme - min



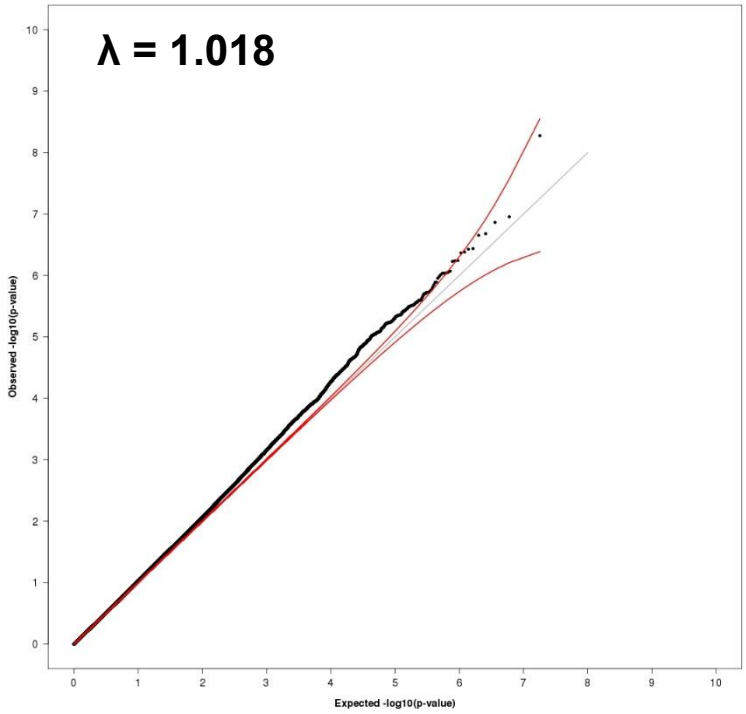


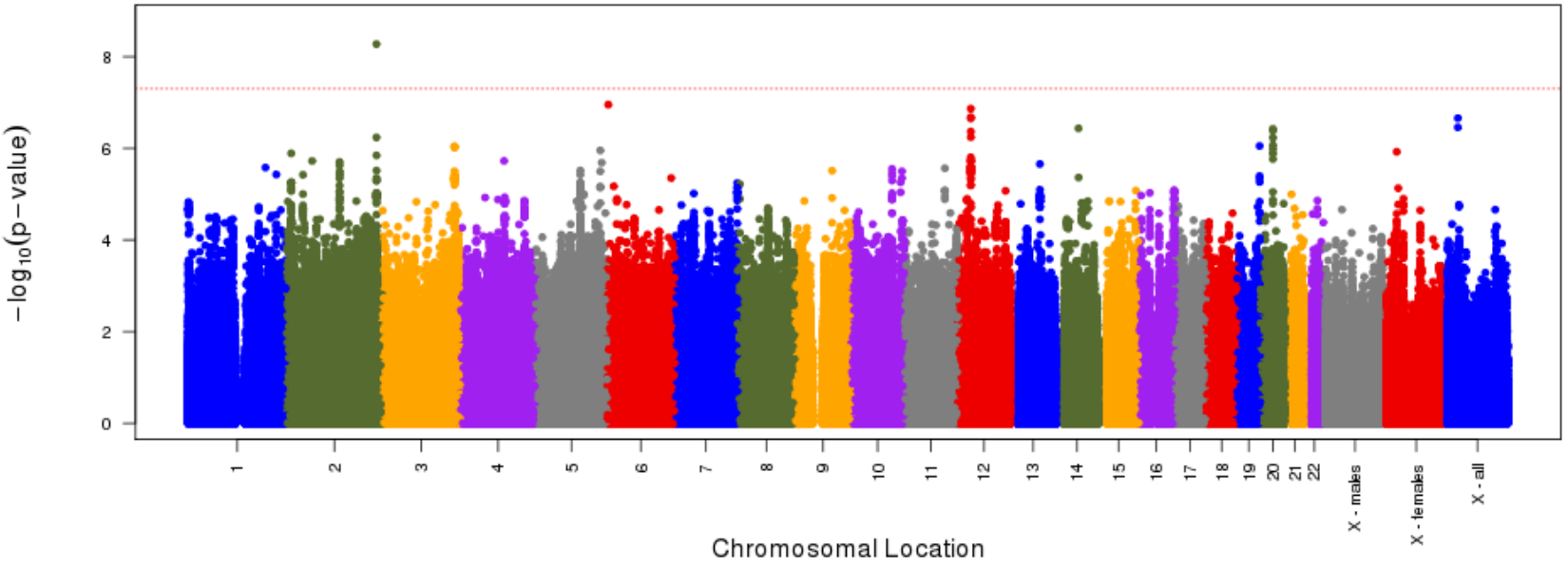
CKD extreme - full



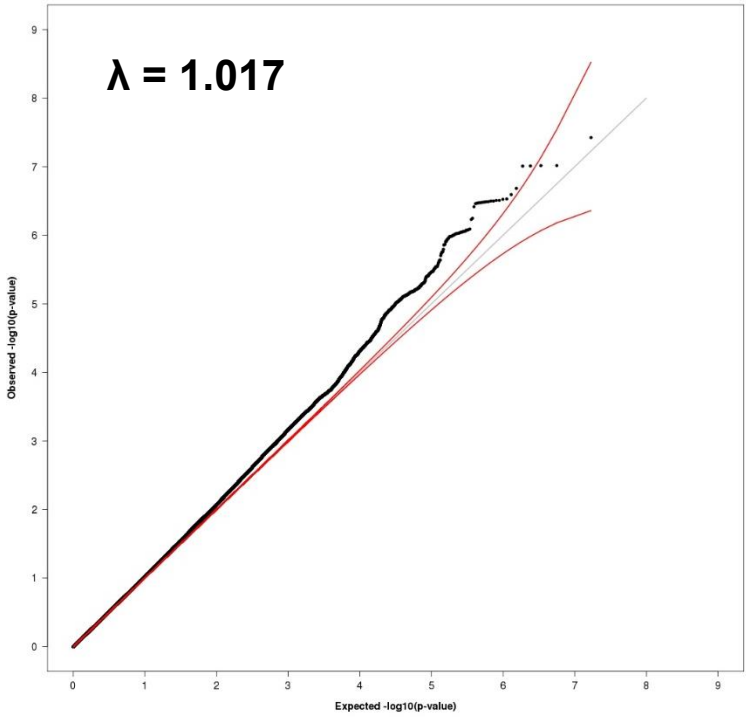


CKD-DN - min


λ = 1.018
Observed -log10(p-value)
Expected -log10(p-value)


−log10(p−value)
Chromosomal Location
X - males
X - females
X - all

CKD-DN - full


λ = 1.017
Observed -log10(p-value)
Expected -log10(p-value)

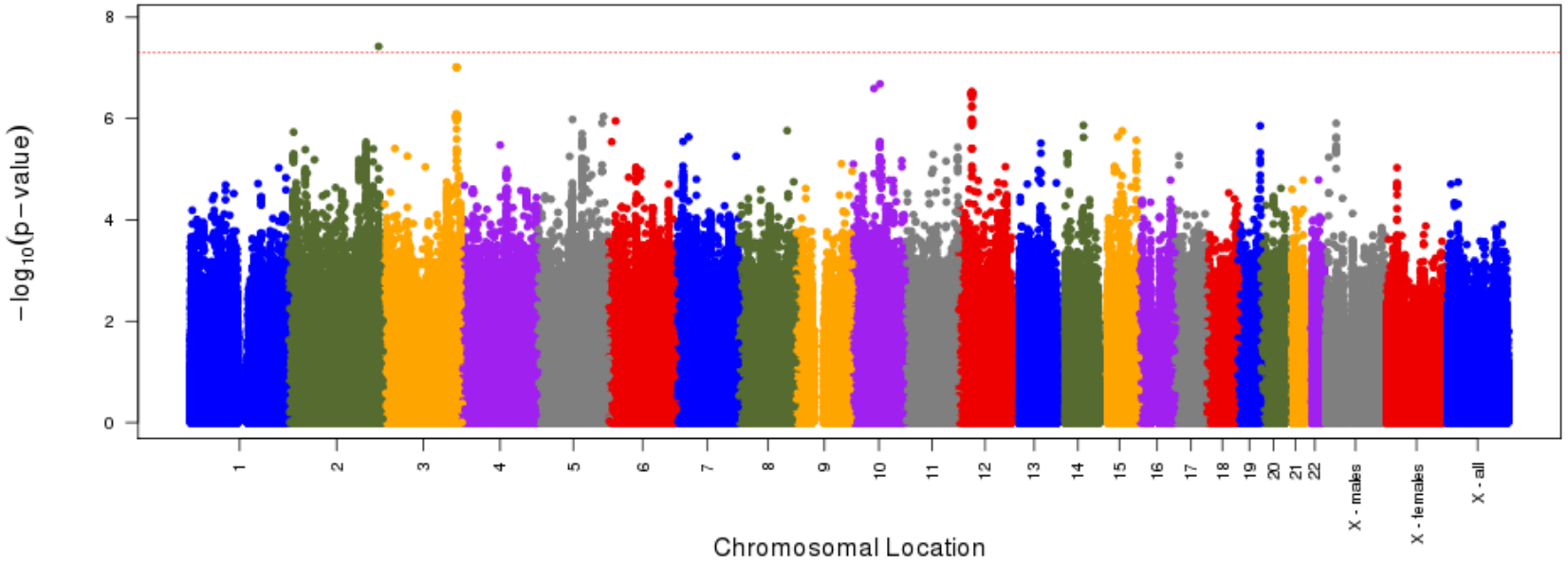
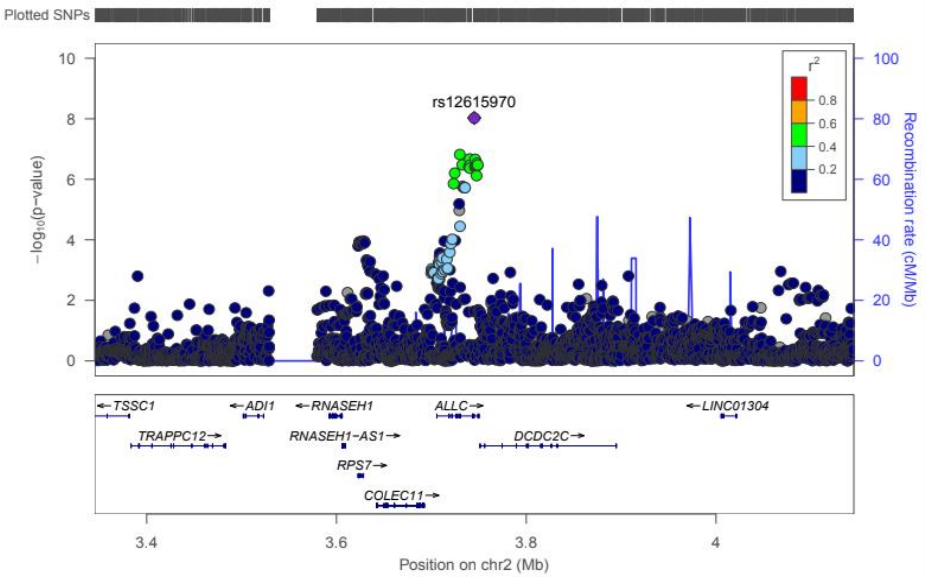
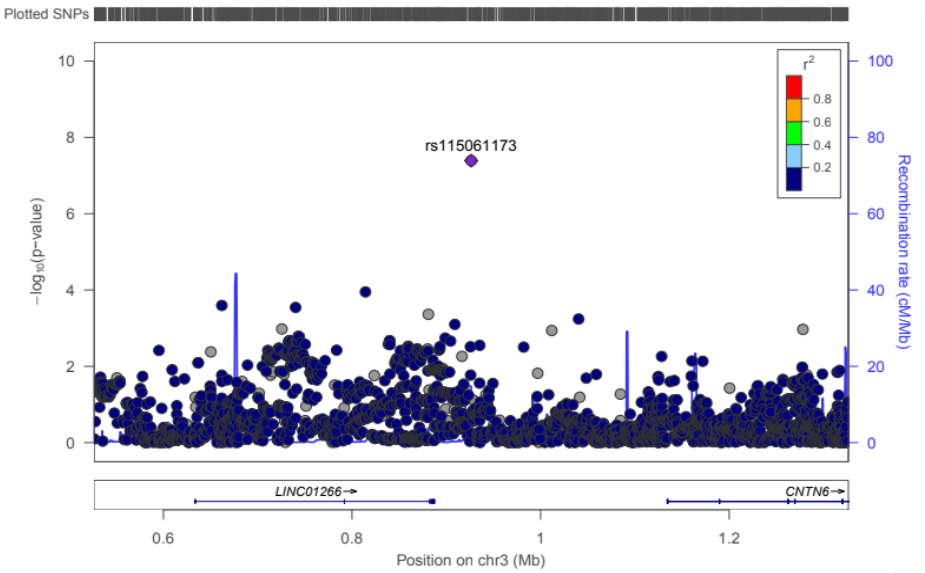

−log10(p−value)
Chromosomal Location
X - males
X - females
X - all

Figure S2. Regional chromosomal location plots and forest plots by cohort of newly discovered DKD associations

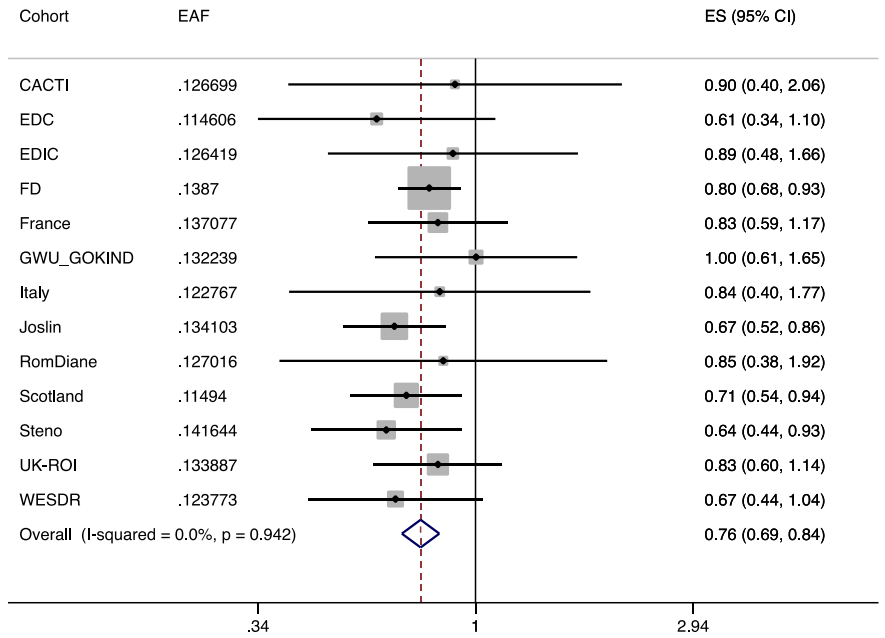
chr2:3745215 – rs12615970 – COLEC11 – CKD min



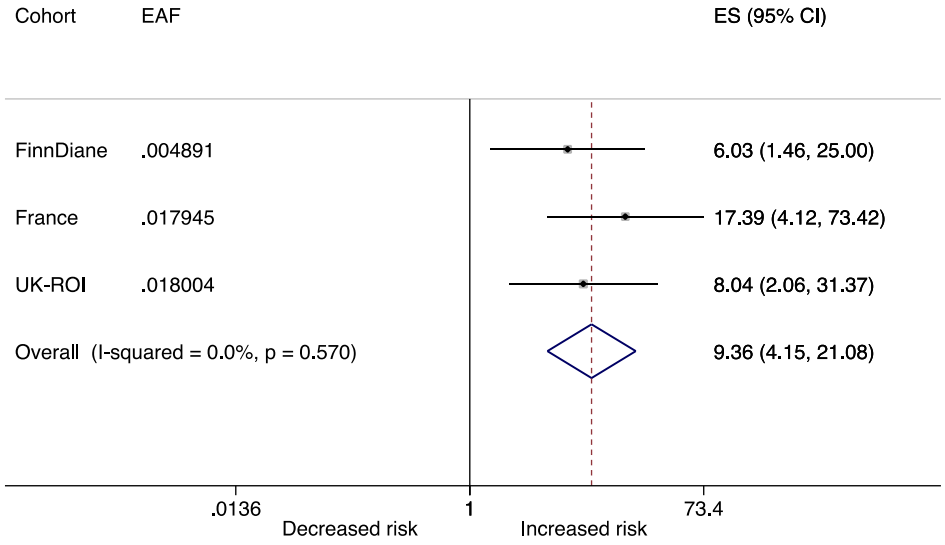
chr3:926345 – rs115061173 – *LINC01266* – ESRD vs ctrl min



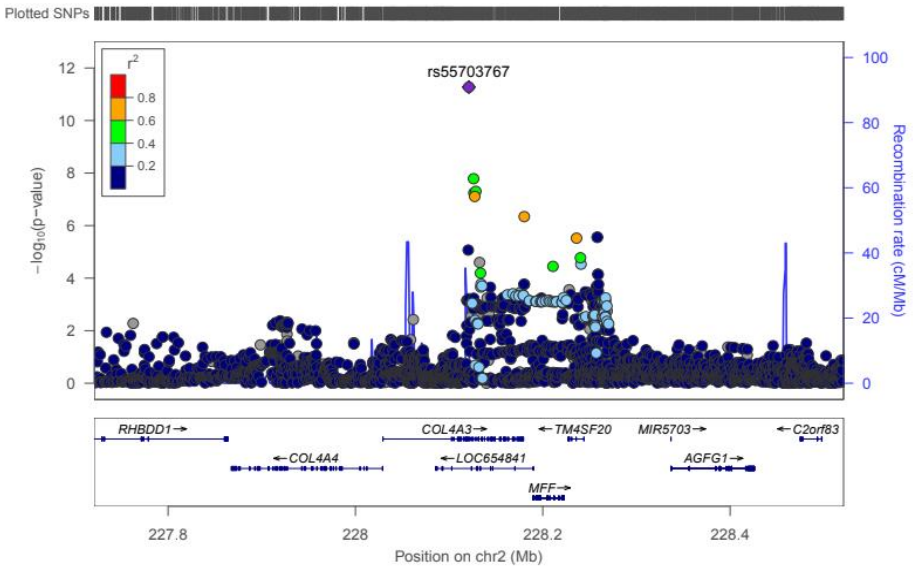
rs12615970 – CKD min

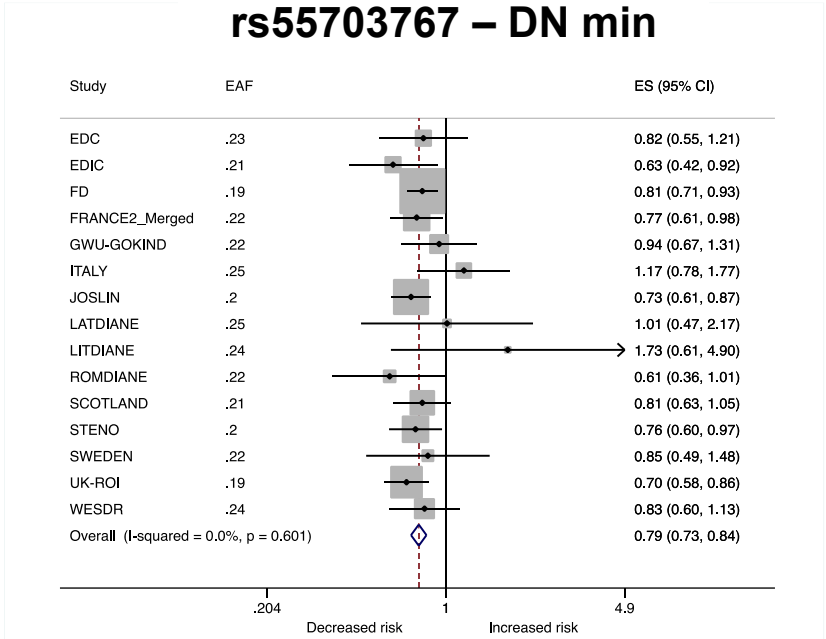


rs115061173 – ESRD vs. ctrl min

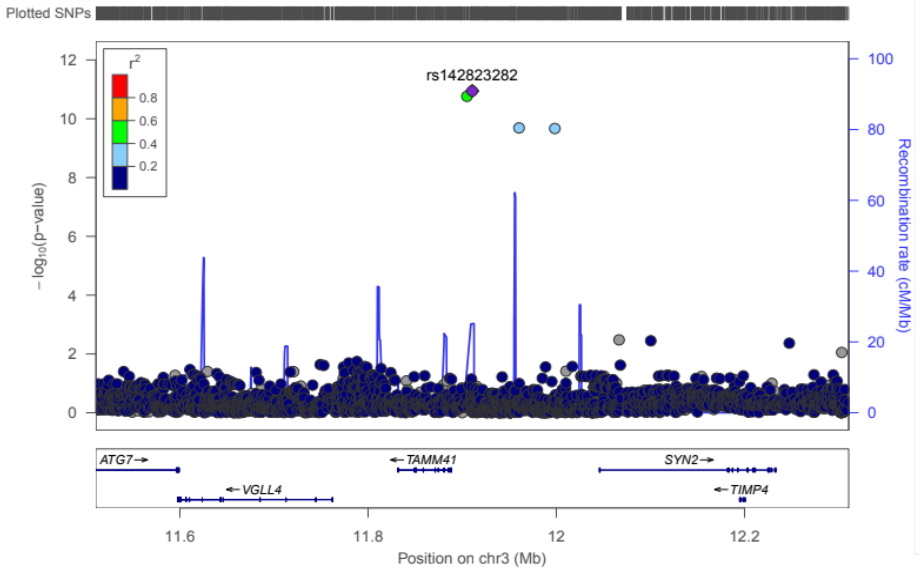


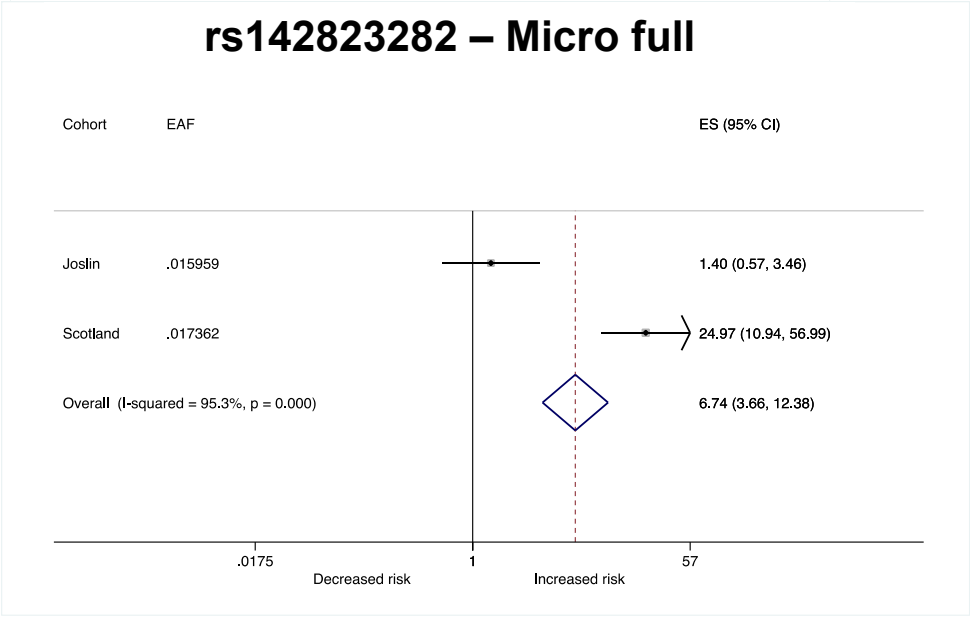
chr2:228121101 – rs55703767 – *COL4A3* – DN min



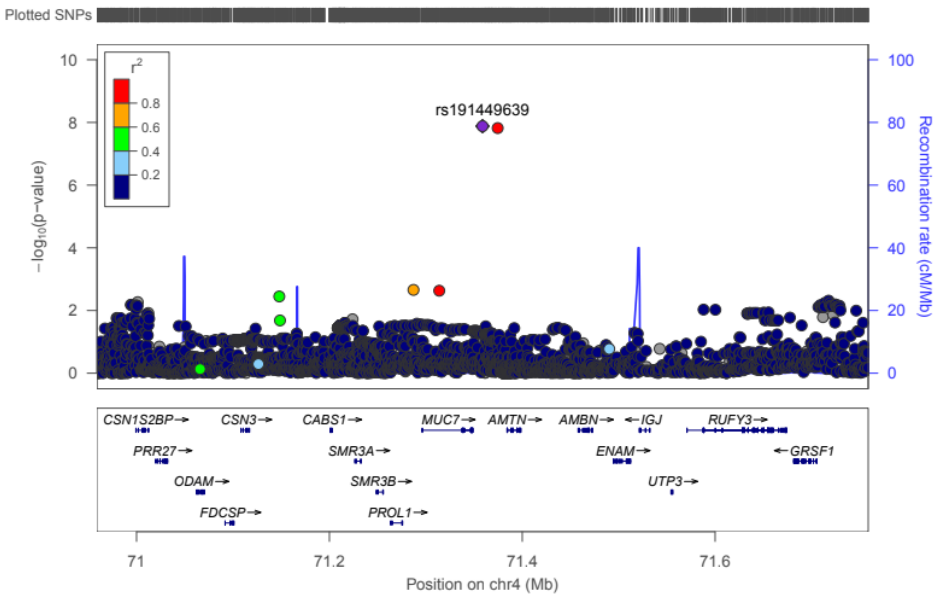


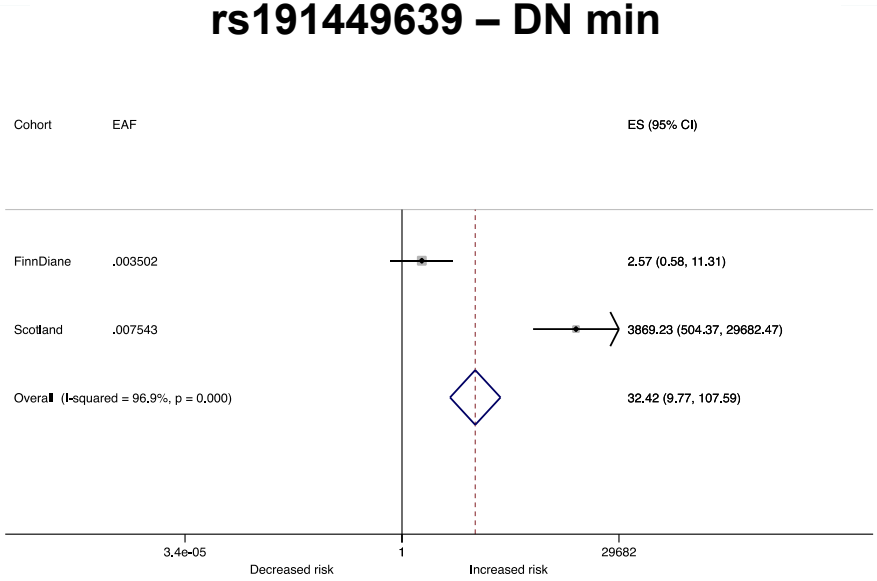
chr3:11910635 – rs142823282 – *TAMM41* – Micro full



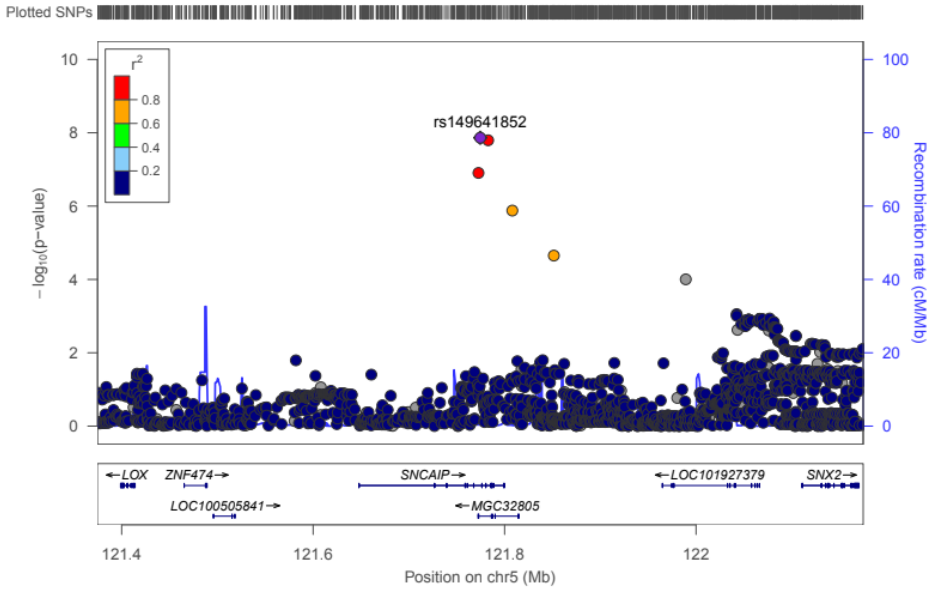


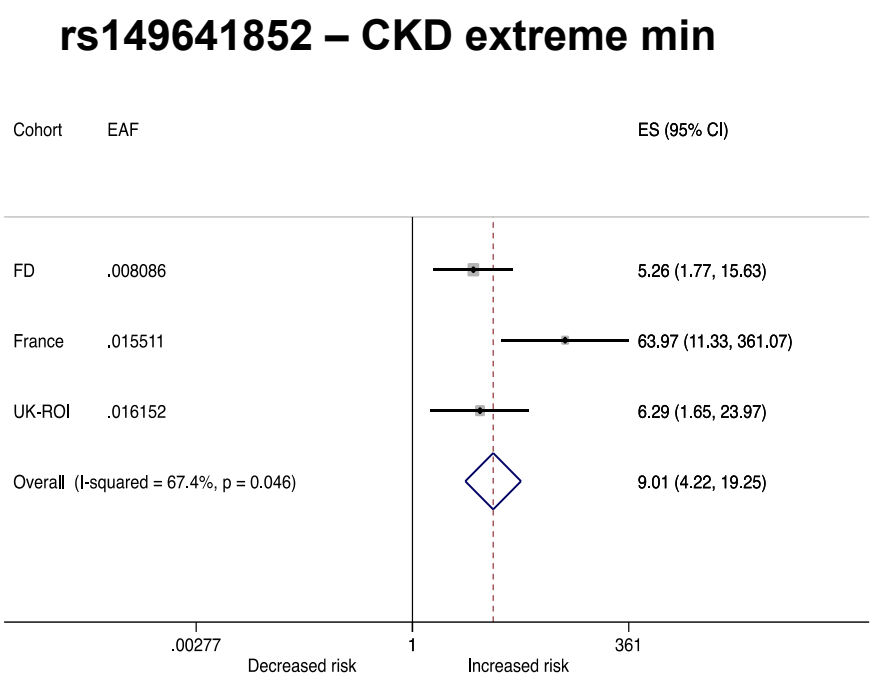
chr4:71358776 – rs191449639 – *MUC7* – DN min



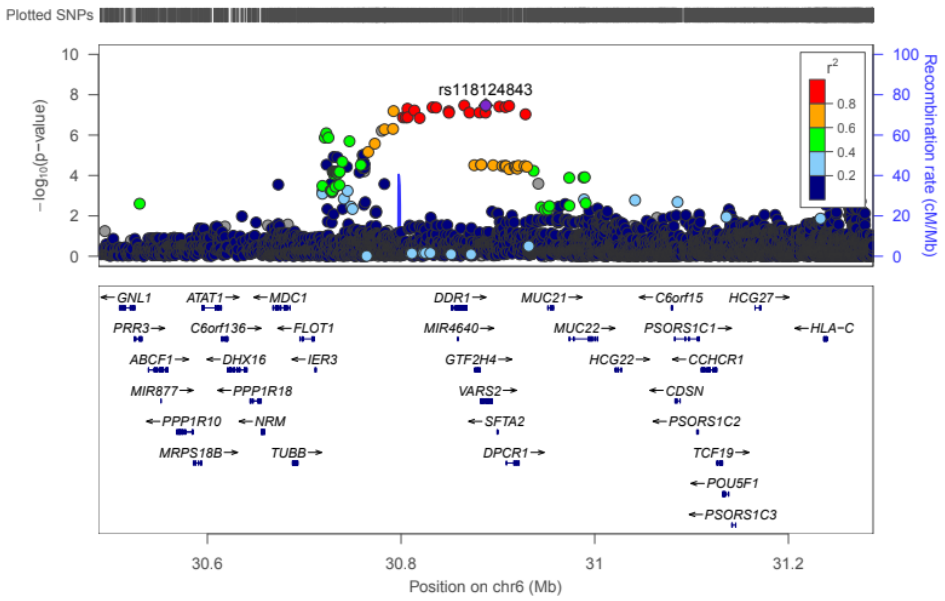


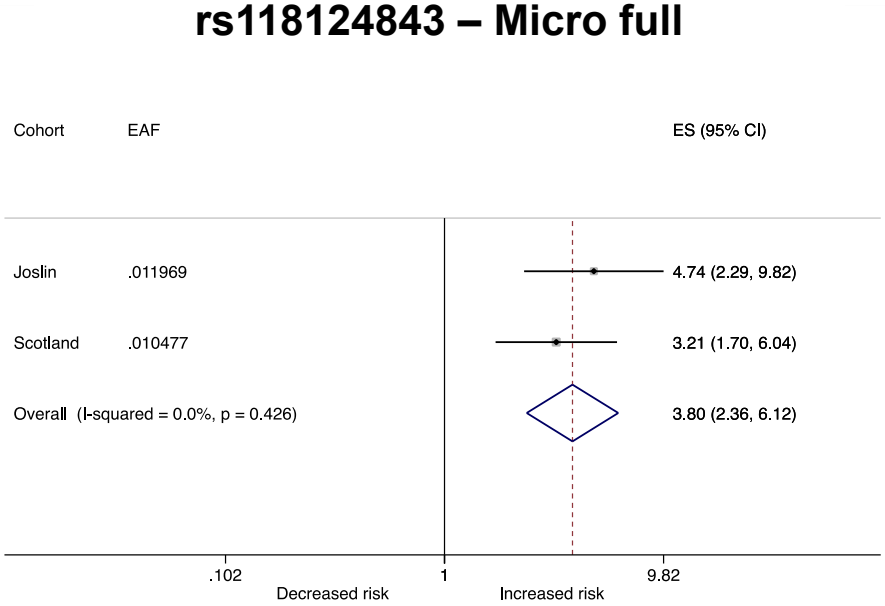
chr5:121774582 – rs149641852 – *SNCAIP* – CKD extreme min



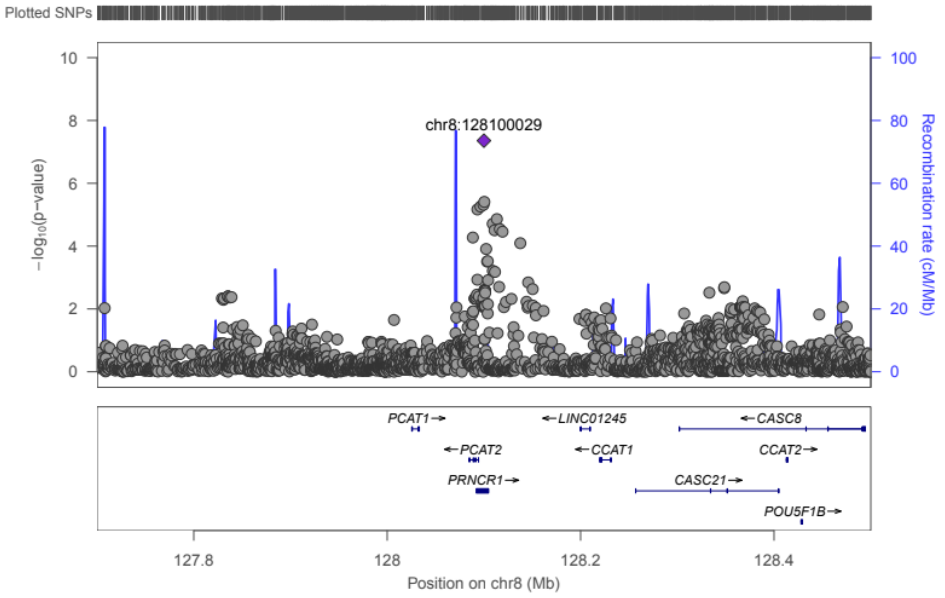


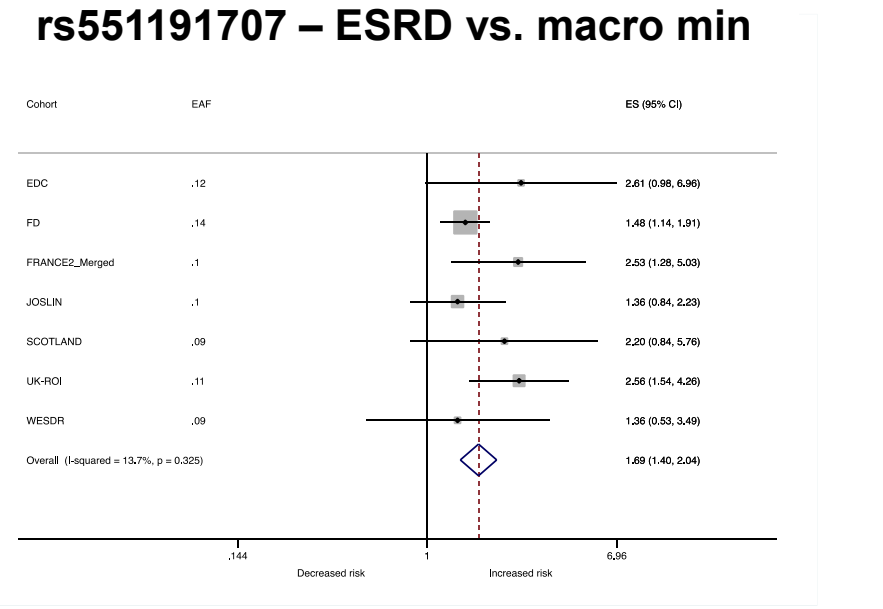
chr6:30865279 – rs118124843 – *DDR1* – Micro full



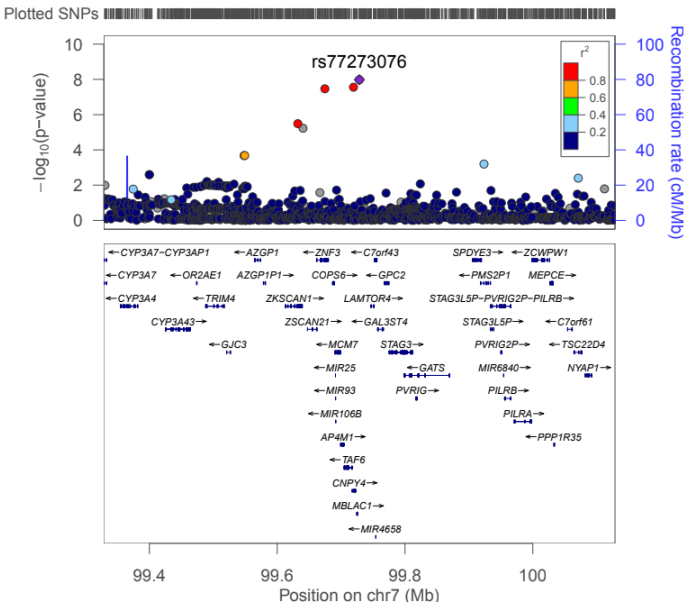


chr8:128100029 – rs551191707 – *PRNCR1* – ESRD vs macro min

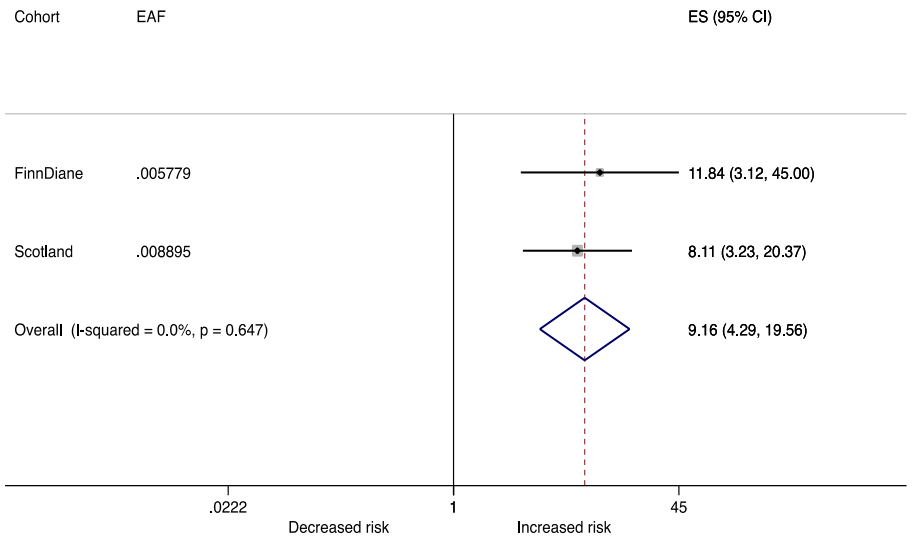




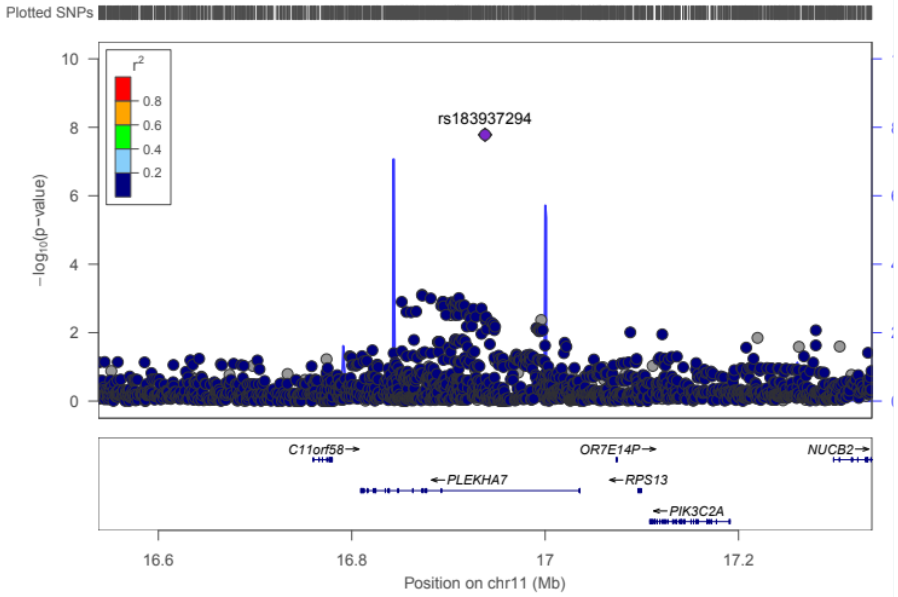
chr7:99728546 – rs77273076 – *MBLAC1* – Micro min



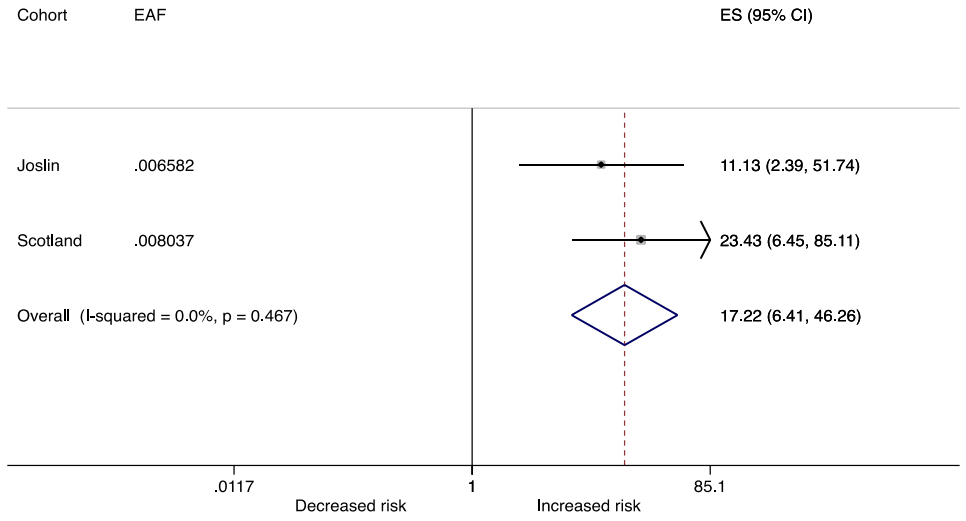
rs77273076 – Micro full



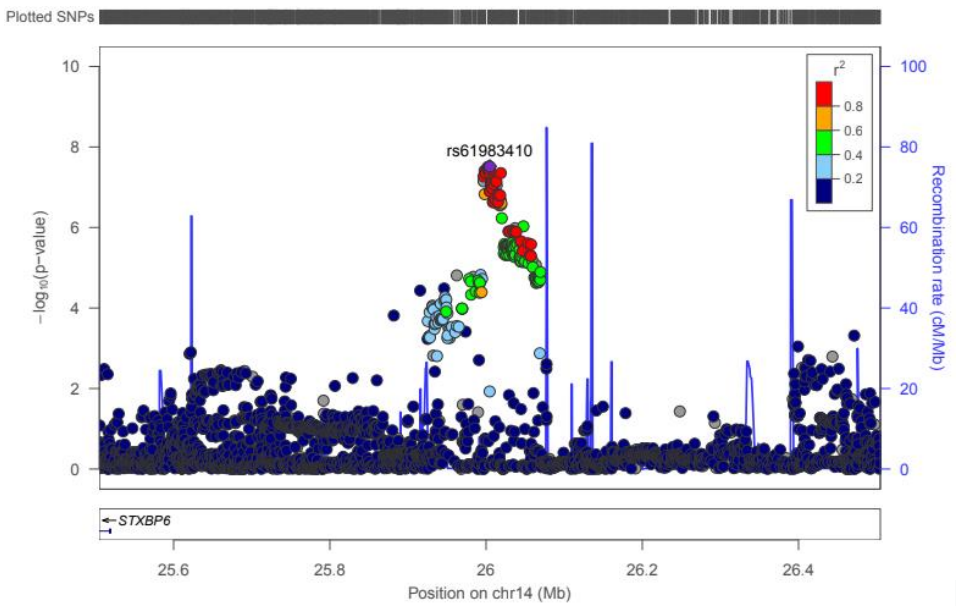
chr11:16937846 – rs183937294 – *PLEKHA7* – Micro min

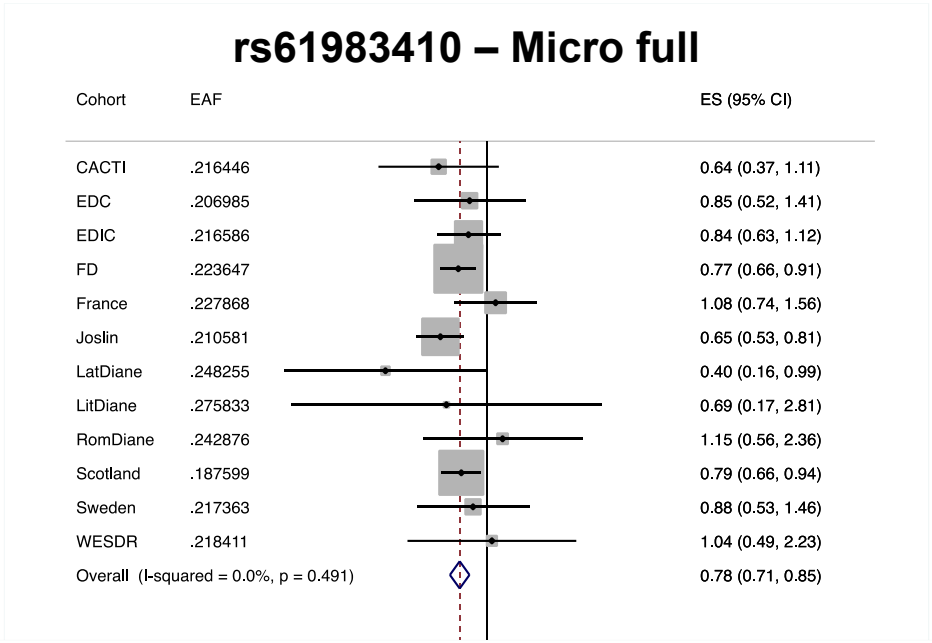


rs183937294 – Micro min

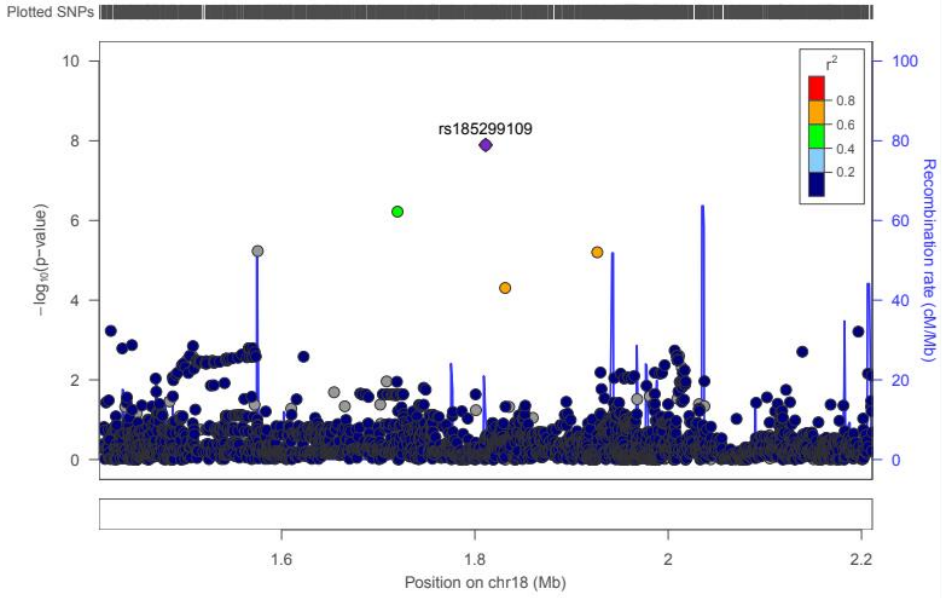


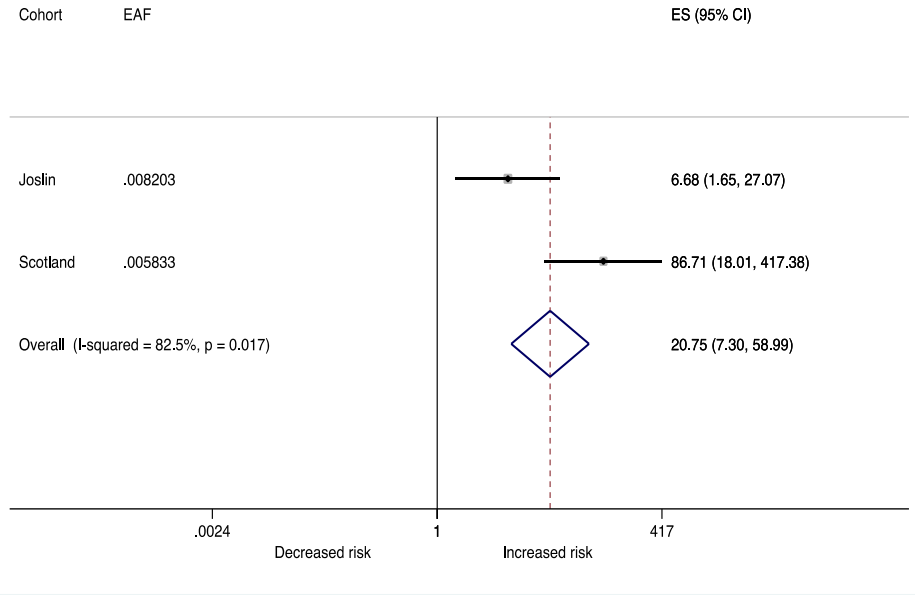
chr14:26004712 – rs61983410 – *STXBP6* – Micro full



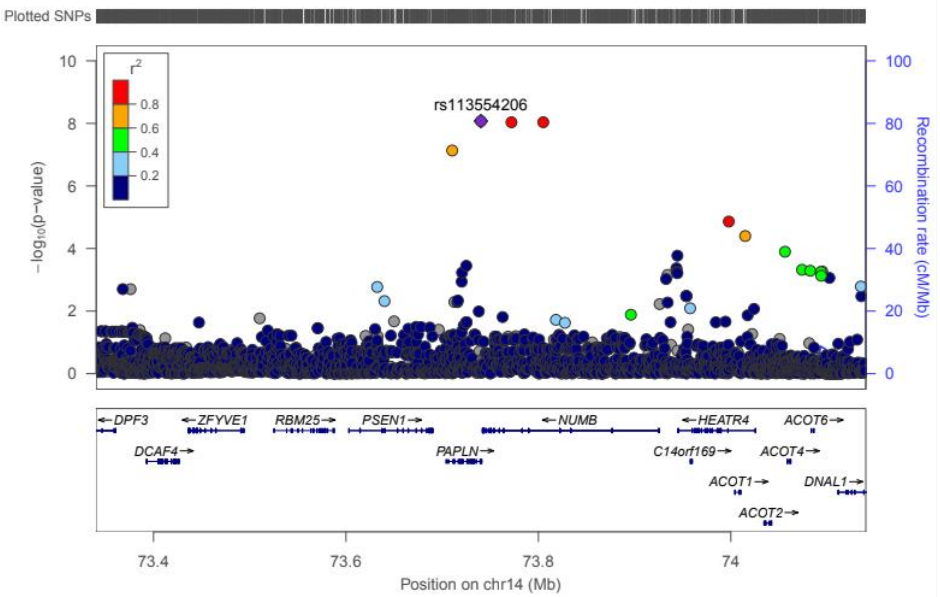


chr18:1811108 – rs185299109 – 18p11 – CKD min

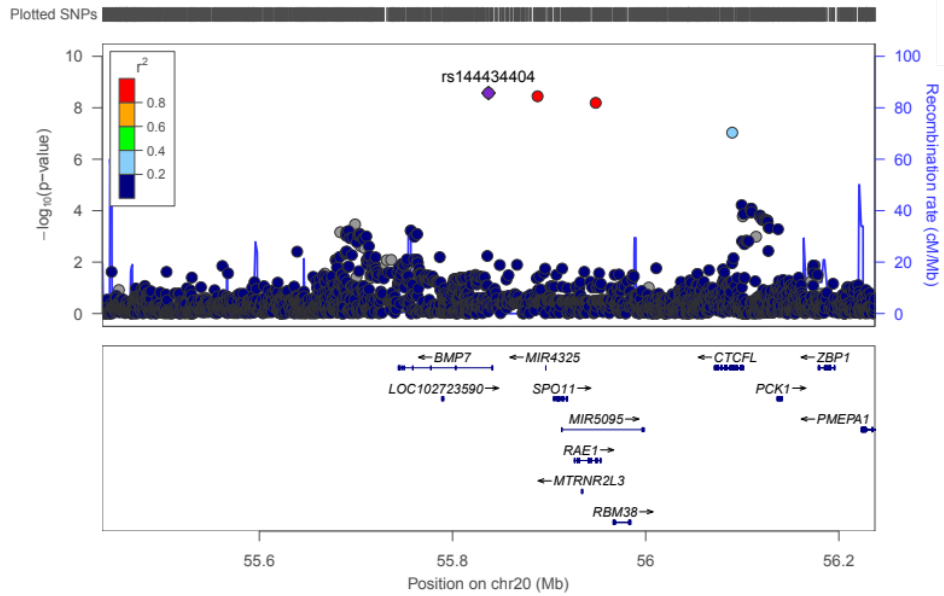




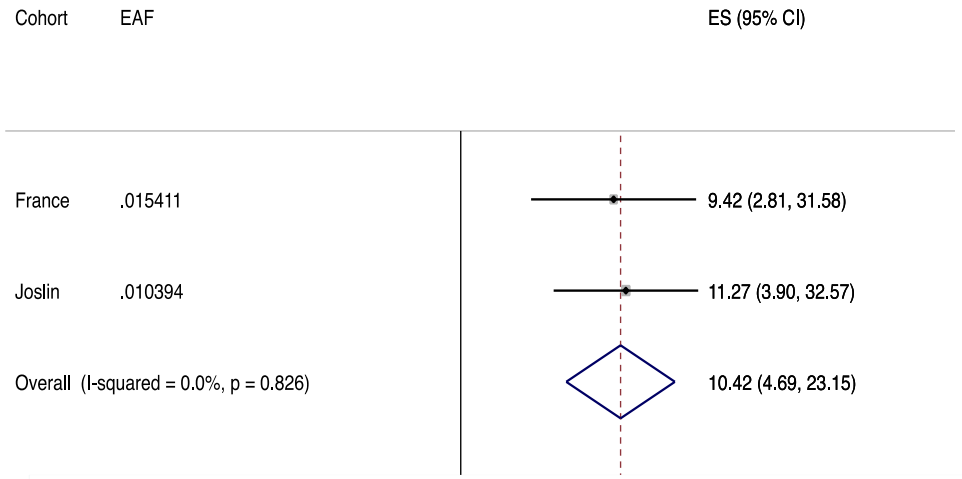
chr14:73740250 – rs113554206 – *PAPLN* – Macro full



chr20:55837263 – rs144434404 – *BMP7* – Micro min



rs113554206 – Macro full



rs144434404 – Micro min

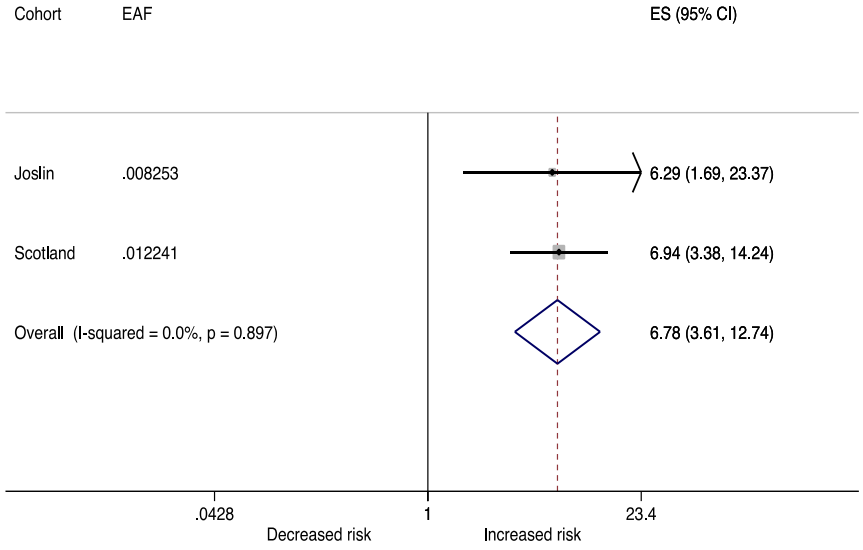


Figure S3. Correlation of expression of *COL4A3* with degree of fibrosis and eGFR in microdissected kidney samples.

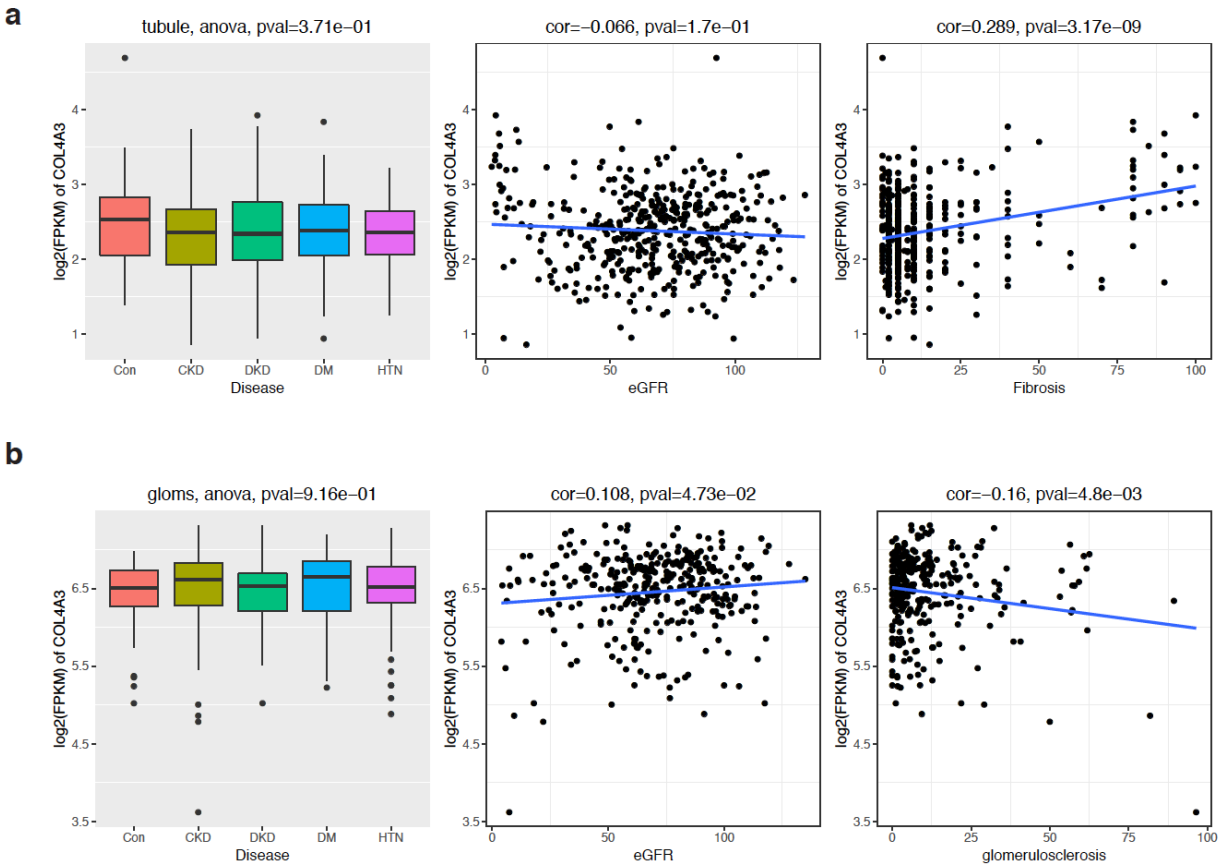


Figure S4. Genotype – phenotype associations at the lead loci when stratified by mean HbA_{1c} <7.5% in the FinnDiane study.
Only loci with a minor allele count ≥10 in each stratum are shown.

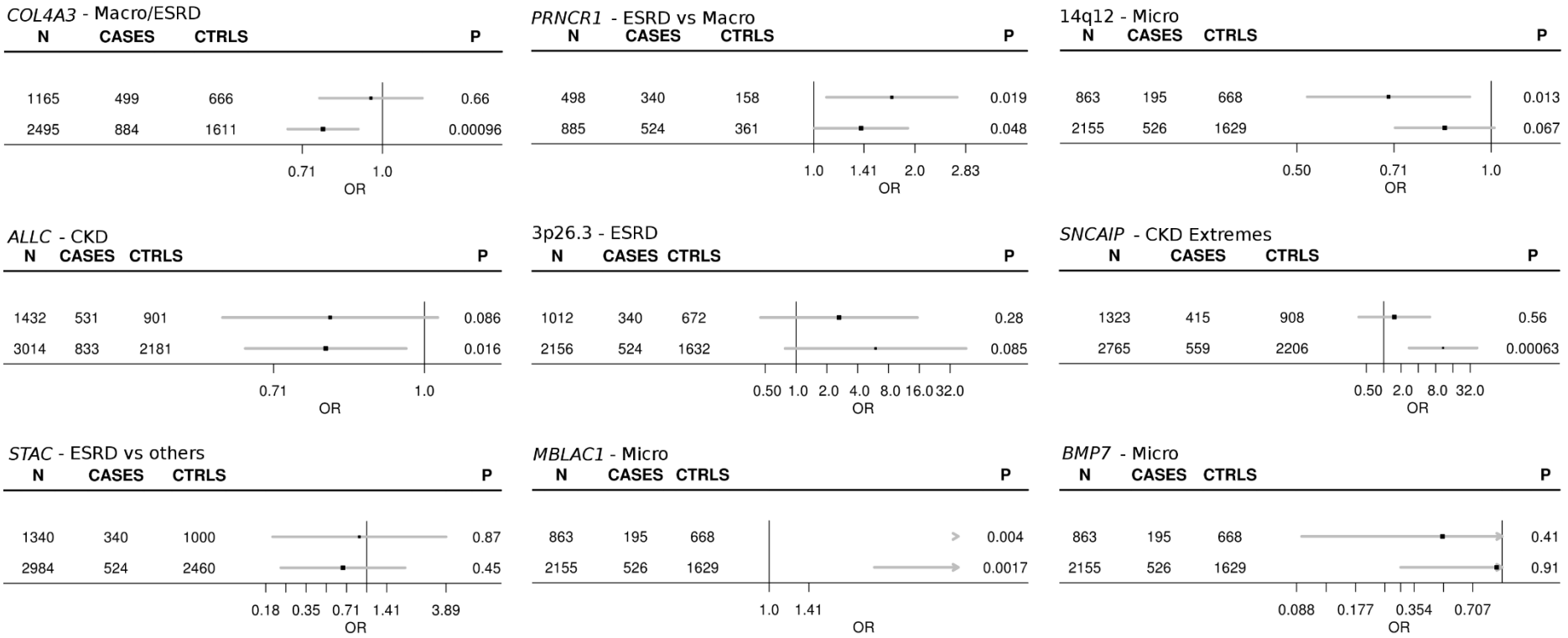


Figure S5. Genotype – phenotype associations at the lead rs55703767 (COL4A3) locus when stratified by mean HbA1c <7.5% in up to 3226 individuals with type 2 diabetes (T2D) from the GoDARTS.

For All vs. ctrl phenotype, 1632 individuals (848 cases, 784 controls) had HbA1c<7.5%, and 1572 individuals (874 cases, 698 controls) had HbA1c>=7.5%.

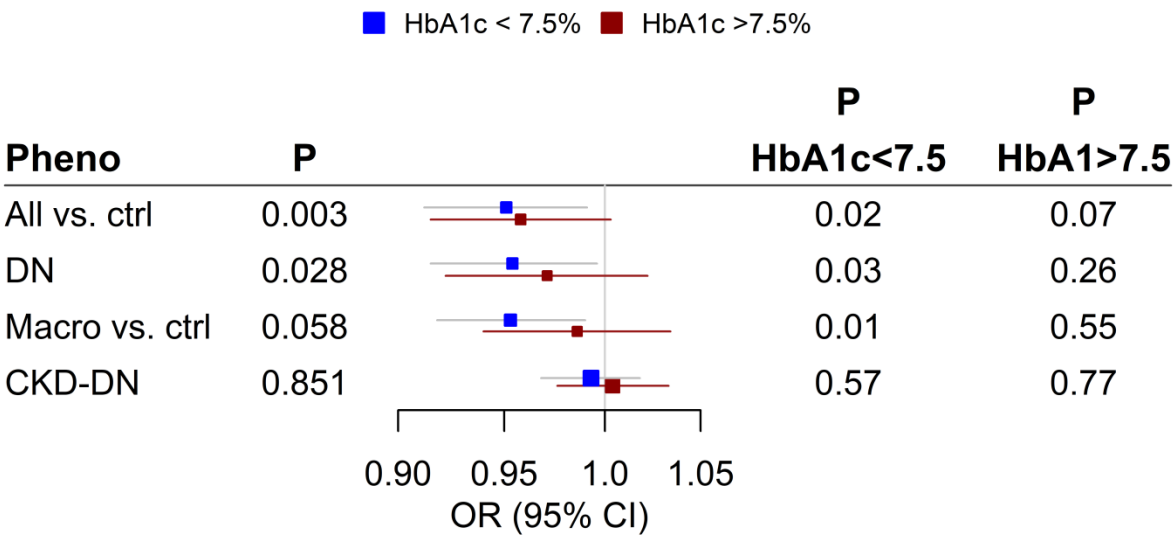
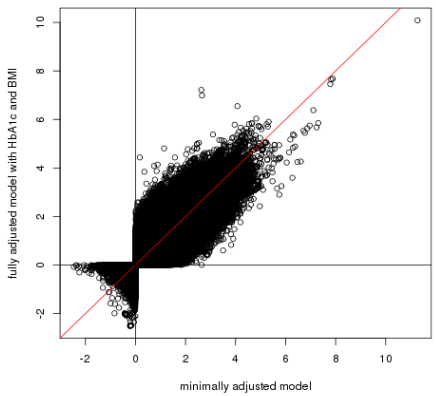
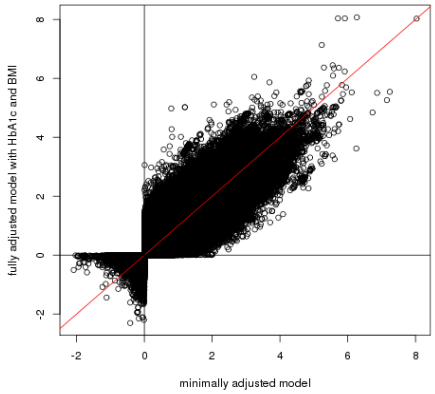


Figure S6. Fishplots comparing significance and directionality between minimal and fully adjusted models for each of the 10 phenotype definitions. Fishplots comparing the significance and directionality between the minimal and fully adjusted models for each of the 10 phenotype definitions. P-values are signed according to consistency in the direction of effect between the two GWAS under comparison, such that the –log(*P*) of SNPs with effect sizes in the same direction are plotted on quadrant 1 (the head and body of the fish), and the –log(*P*) of SNPs with effect sizes in opposite directions are plotted in quadrant 3 (the tail of the fish).

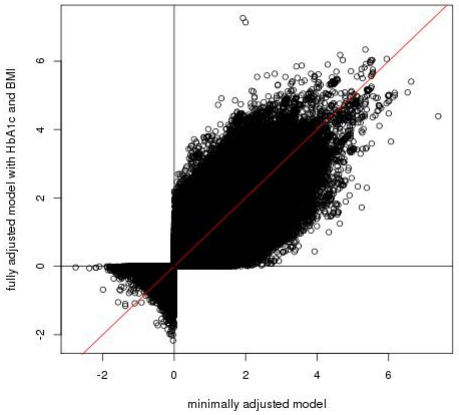
DN



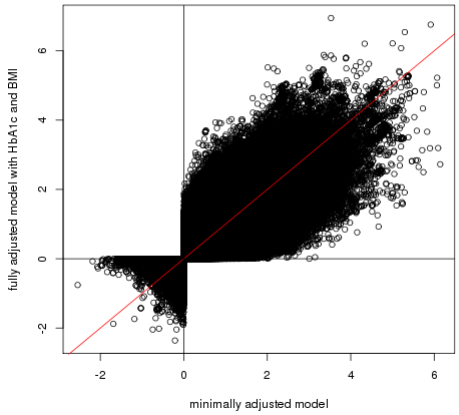
macro



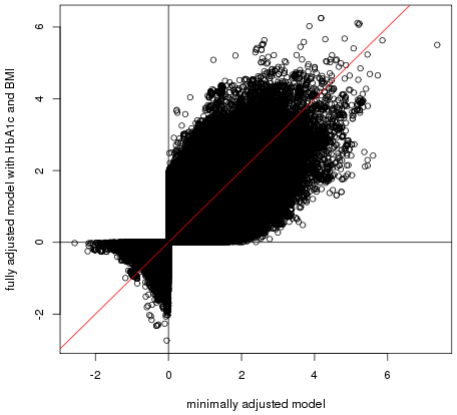
ESRD vs. ctrl



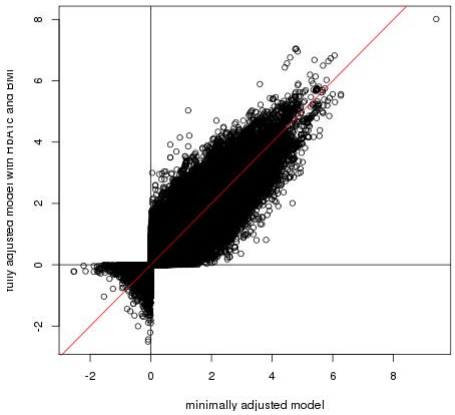
ESRD vs. non-ESRD



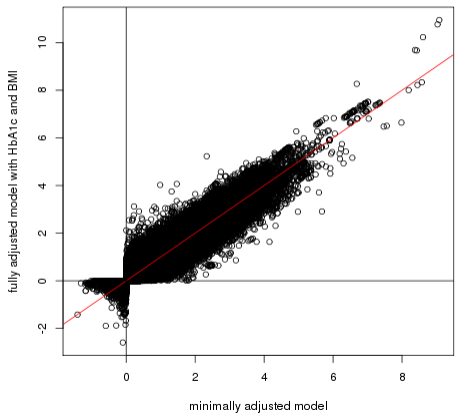
ESRD vs. macro



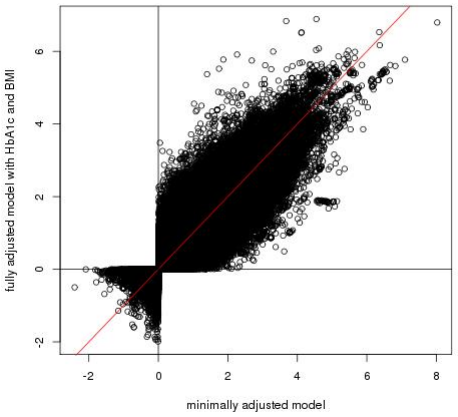
All vs. ctrl



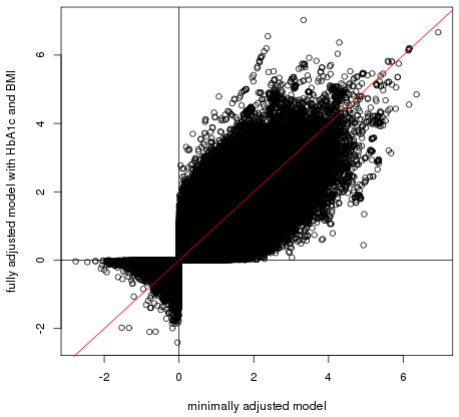
micro



CKD



CKD extreme



CKD-DN

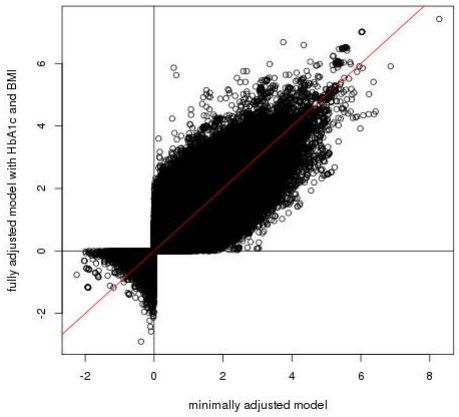


Figure S7: Association at previously reported loci ($p<5\times10^{-8}$) for renal complications in individuals with diabetes. *AFF3 and RGMA-MCTP2* were originally reported for ESRD (T1D) (Sandholm et al., 2012); *CDCA7/SP3* for ESRD in women (T1D) (Sandholm et al., 2013); *ERBB4* for DN (T1D) (Sandholm et al., 2012); *GABRR1* for microalbuminuria (T2D)(Van Zuydam et al., 2018); *GLRA3* for albuminuria (T1D) (Sandholm et al., 2014); *PRKAG2* and *UMOD* for eGFR (Pattaro et al., 2016; Van Zuydam et al., 2018); and *SCAF8/CNKSR3* for DN (T2D) (Iyengar et al., 2015).

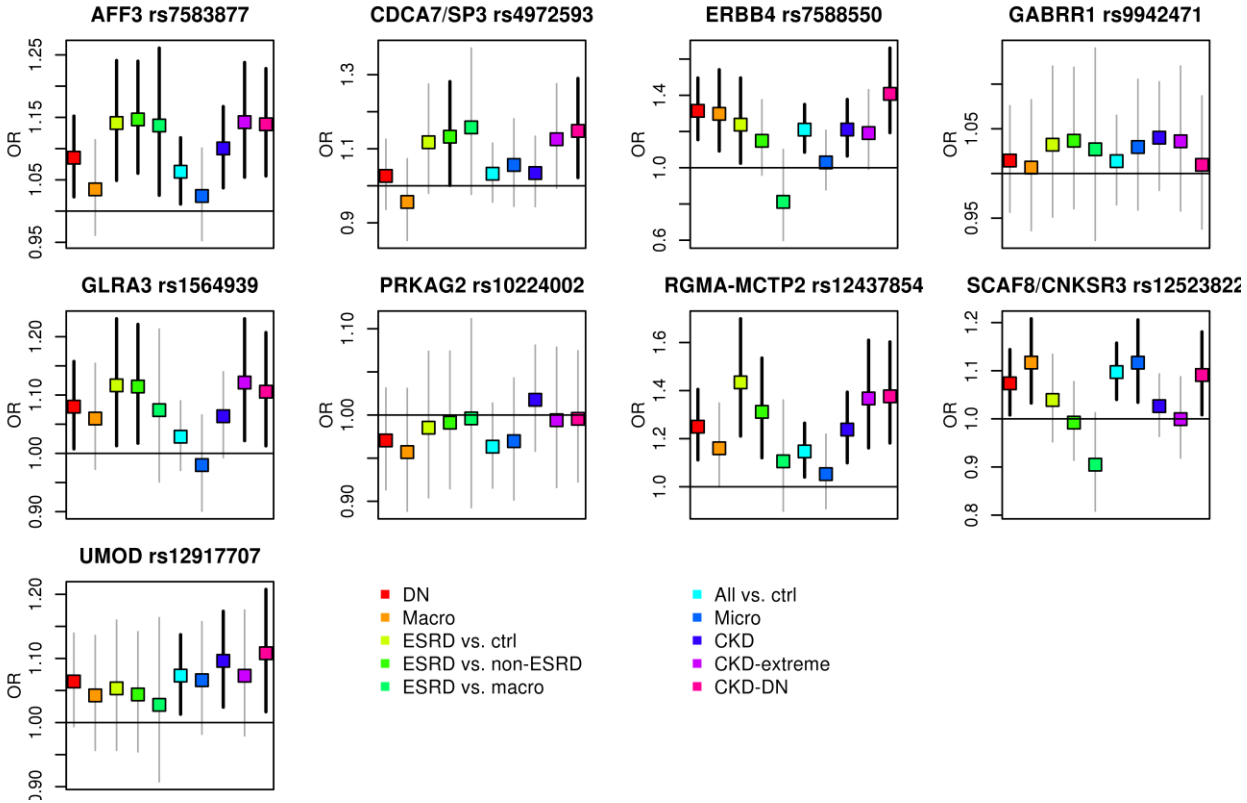


Figure S8: Forest plots of the associations at the previously reported lead loci from the GENIE consortium with largely overlapping studies. A: *RGMA-MCTP2* rs12437854. **B:** *AFF3* rs7583877. **C:** *ERBB4* rs7588550. Meta-analysis results for *RGMA-MCTP2*: Previous $P = 2.0\times10^{-9}$, OR = 1.80 (95% confidence interval 1.48, 2.17), Current $P = 7.4\times10^{-4}$, OR = 1.31 (1.12, 1.54); Meta-analysis results for *AFF3*: Previous $p=1.20\times10^{-8}$, OR = 1.29 (1.18, 1.40), Current p=5.97x10-4, OR=1.15 (1.06, 1.24). Meta-analysis results for *ERBB4*: Previous $P = 2.1\times10^{-7}$, OR = 0.66 (0.56, 0.77), Current $P = 3.5\times10^{-5}$, OR = 0.76 (0.67, 0.87).

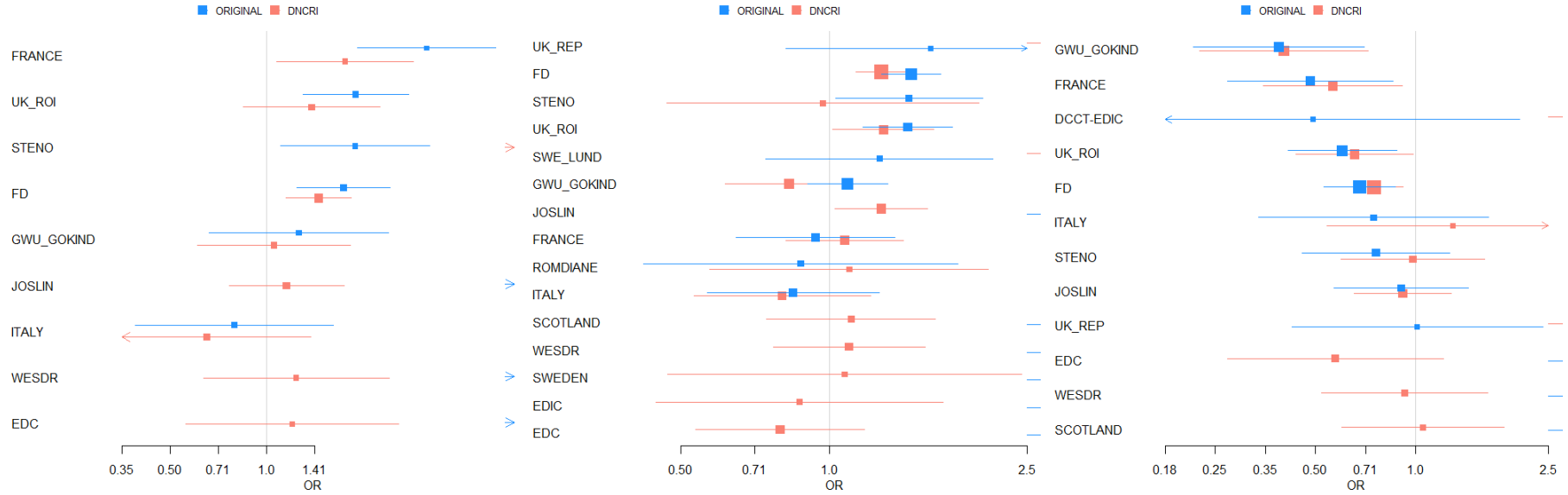


Figure S9: Meta-analysis results for the loci that have previously been associated with DKD, or with eGFR or AER in the general population. Figure shows OR [95% CI] for the 25 loci with $p<0.05$ for at least one sub-phenotype; associations with $p<0.05$ are indicated with black confidence intervals. Results are plotted so that odds ratio (OR)>1 indicates association in the same direction with the original report (for eGFR, this means that the allele associated with higher risk of DN is associated with lower eGFR). A total of 69 loci were evaluated, including loci for DKD (5 loci: *AFF3*, *RGMA-MCTP2*, *ERBB4* (Sandholm 2012), *CDCA7/SP3* (Sandholm2014), *SCAF8/CNKSR3* (Iyengar 2015)), for albuminuria in individuals with diabetes (*GLRA3* (Sandholm 2013), 3 suggestive loci *CUBN, HST6ST1* and *RAB38* (Teumer 2016)), for eGFR in individuals with diabetes (*UMOD*, Pattaro et al. 2016 and Van Zuydam et al. 2018, *PRKAG2* Van Zuydam et al. 2018) or without diabetes (61 loci, Gorski 2017). Associations at *AFF3, RGMA-MCTP2, ERBB4, SCAF8/CNKSR3*, and *UMOD* remained significant after correction for 69 tested loci ($p<7\times10^{-4}$).

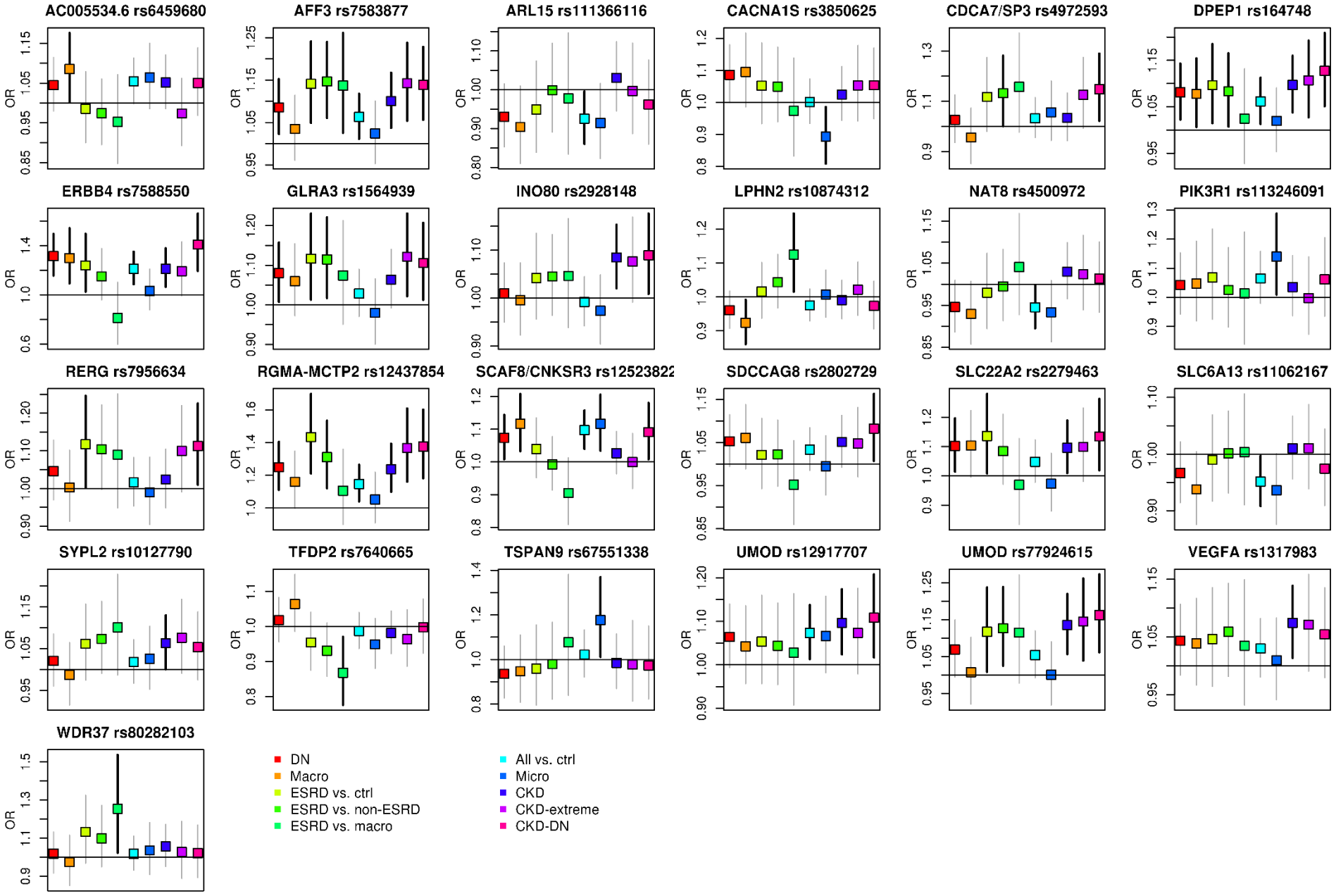

AC005534.6 rs6459680
AFF3 rs7583877
ARL15 rs111366116
CACNA1S rs3850625
CDCA7/SP3 rs4972593
DPEP1 rs164748
ERBB4 rs7588550
GLRA3 rs1564939
INO80 rs2928148
LPHN2 rs10874312
NAT8 rs4500972
PIK3R1 rs113246091
RERG rs7956634
RGMA-MCTP2 rs12437854
SCAF8/CNKSR3 rs12523822
SDCCAG8 rs2802729
SLC22A2 rs2279463
SLC6A13 rs11062167
SYPL2 rs10127790
TFDP2 rs7640665
TSPAN9 rs67551338
UMOD rs12917707
UMOD rs77924615
VEGFA rs1317983
WDR37 rs80282103
OR
DN
Macro
ESRD vs. ctrl
ESRD vs. non-ESRD
ESRD vs. macro
All vs. ctrl
Micro
CKD
CKD-extreme
CKD-DN

Figure S10. Expression of quantitative trait loci (eQTL) analysis in microdissected tubule samples. Boxplots showing normalized gene expression by stratified by homozygous common (red), heterozygous (green), and homozygous rare (blue) genotype. We identified nominal associations for rs55703767 in tubule samples with *IRS1* (a) and in glomerular samples with *RP11-395N3.2* and *AGFG1* (b). We also found nominal associations of rs61983410 with the gene encoding Cathepsin G, *CTSG*, in both eQTL analysis of whole kidney samples (c) and microdissected tubule samples (d).

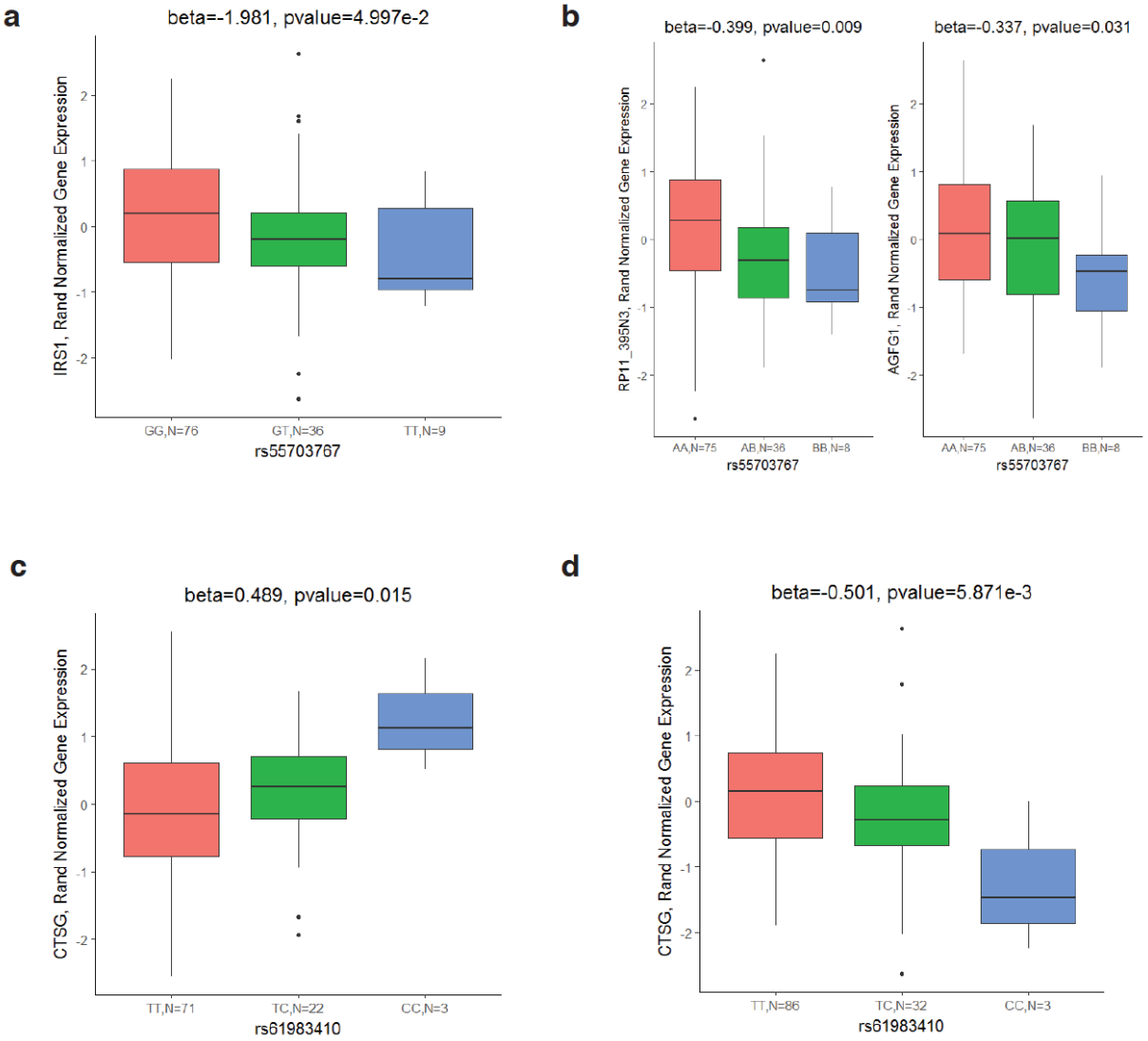
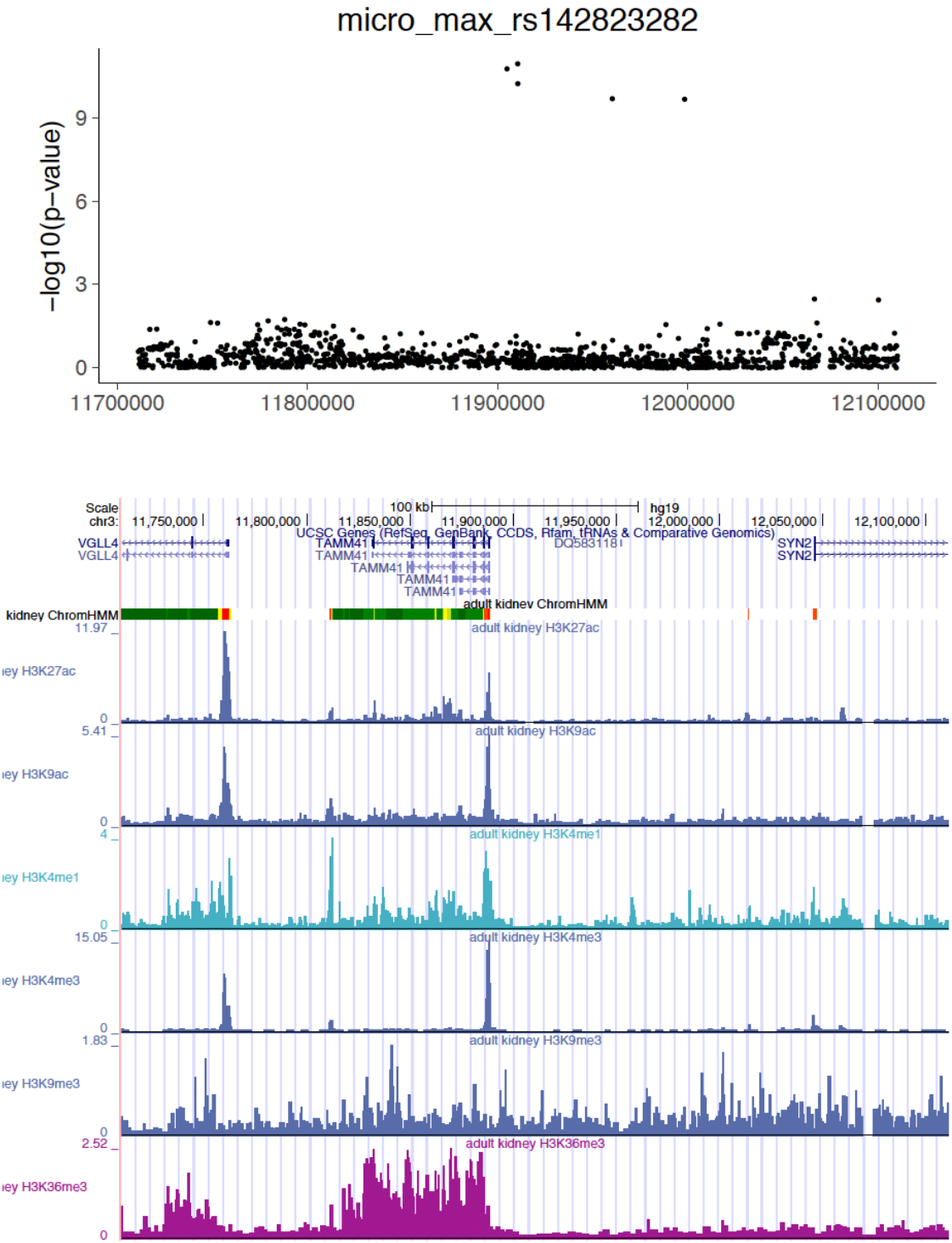


Figure S11. Functional annotation of *TAMM41*. ChIP-seq data derived from healthy adult human kidney samples (Bernstein et al., 2010) shows that variants associated with microalbuminuria are located close to H3K27ac, H3K9ac, H3K4me1, and H3K4me3 signals, suggesting that this locus is an active regulator of *TAMM41*.



Supplemental Methods: Cohort descriptions

CACTI: The Coronary Artery Calcification in Type 1 Diabetes (CACTI) study enrolled 656 subjects with diabetes diagnosed before age 30 years, treated with insulin within 1 year of diagnosis, and diabetes duration of at least 10 years on enrollment.[1]

DCCT/EDIC: The Diabetes Control and Complications Trial (DCCT) was a multi-center randomized clinical trial to compare intensive and conventional insulin therapy on the development and progression of early vascular and neurological complications of type 1 diabetes (T1D). Renal outcomes were defined as time in years from DCCT baseline until the event. AERs were measured annually in DCCT and every other year in the post-study Epidemiology of Diabetes Interventions and Complications (EDIC) cohort. Persistent microalbuminuria was defined as the time to two consecutive AER >30 mg/24 hours (>20.8 µg/min); severe nephropathy was the time to AER >300 mg/24 hours (>208 µg/min) with prior persistent microalbuminuria, or ESRD. 22% developed persistent microalbuminuria during follow-up (268 events, 976 censored), while 10% developed severe nephropathy (132 events, 1,172 censored).[2, 35]

EDC: The Pittsburgh Epidemiology of Diabetes Complications (EDC) is a historical cohort study based on incident cases of childhood onset (prior to age 17 years) T1D, diagnosed or seen within one year of diagnosis (1950-80) at Children's Hospital of Pittsburgh.[4] The cohort, which has been shown to be epidemiologically representative of the Allegheny County, Pennsylvania, T1D population,[36] was first assessed for the EDC study between 1986 and 1988 (mean participant age and diabetes duration were 28 and 19 years, respectively). Subsequently, biennial examinations were conducted for 10 years, with a further detailed examination at 18 and 25 years from enrollment. All EDC study participants provided informed consent, and all study procedures were approved by the University of Pittsburgh Institutional Review Board (IRB). Microalbuminuria was defined as albumin excretion rate (AER) 20-200 µg/min (30-300 mg/24 hours), overt nephropathy as AER >200 µg/min (>300 mg/24 hours) and albuminuria as >20 µg/min (>30 mg/24 hours) in at least two of three validated timed urine collections. End-stage renal disease was defined as receiving dialysis or renal transplantation.

FinnDiane: Finnish Diabetic Nephropathy Study (FinnDiane) is an ongoing nationwide Finnish multicenter study of adult participants with T1D described previously.[5, 6] The participants were invited to the study by their attending physician who filled a questionnaire on the medical status of the patient and performed a clinical examination. A subset of the patients participated at one or more follow-up visits with a similar setting. Additional health related information was obtained from Finnish hospital discharge registry and from the patients' medical records. Further patients were included to the FinnDiane study through collaboration with the Finnish National Institute for Health and Welfare; for these participants, health related data was obtained from the hospital discharge registry and from the medical records. For this study, participants were limited to those with T1D diagnosed prior to age 40 years and with insulin treatment begun within 2 calendar years from diabetes onset. Disease status was defined by urine albumin excretion rate (AER) or urine albumin to creatinine ratio (ACR) in at least two out of three consecutive urine collections at local centers: microalbuminuria was defined as AER 20-200 µg/min or 30-300 mg/24h or an ACR of 2.5-25 mg/mmol for men and 3.5-35 mg/mmol for women in overnight, 24-hour or spot urine collections, respectively. Similarly, the limit for macroalbuminuria was AER >200 µg/min or >300 mg/24h or ACR > 25 mg/mmol for men and >35 mg/mmol for women. ESRD was defined as ongoing dialysis treatment or receipt of transplanted kidney. Control patients with normal AER were required to have T1D duration of at least 15 years.[5, 6]

France-Belgium: The GENEDIAB ('Génétique de la Néphropathie Diabétique, Genetics of Diabetic Nephropathy) and Genesis subjects were recruited in France, and in France-Belgium, respectively. Patients with T1D were selected on the following criteria: 1) age at diabetes onset before age 35 years, and 2) definitive insulin use within one year after diagnosis. Diabetic nephropathy was classified according to the highest three AER measurements within the last 5 years. Categories included: 1) controls (normoalbuminuria), 2) incipient nephropathy (microalbuminuria), 3) established nephropathy (proteinuria), and 4) advanced nephropathy (serum creatinine >150 mol/L and/or renal replacement therapy).[7, 8]

GoKinD US: Genetics of Kidneys in Diabetes US Study (GoKinD): The GoKinD study consists of a DKD case-control cohort of individuals diagnosed with T1D prior to 31 years of age who began insulin treatment within 1 year of T1D diagnosis. Controls were 18-59 years of age, with T1D for at least 15 years but without DKD. DKD definition includes individuals with end-state renal disease (ESRD), dialysis or kidney transplant and persistent macroalbuminuria (at least 2 out of 3 tests positive for albuminuria by dipstick ≥1+, or ACR >300 µg albumin/mg of urine creatinine). Cases were defined as people 18-54 years of age, with T1D for at least 10 years and DKD. Individuals were recruited at two study centers, George Washington University and the Joslin Diabetes Center using differing methods.[9] The Joslin GoKinD subjects were analyzed jointly with subjects from the Joslin Microalbuminuria and 50-years medalists (see below).

The InterDiane Consortium: The International Diabetic Nephropathy Consortium (InterDiane) was initiated in 2010 based on the protocol of the FinnDiane Study. The aim of the study is to identify risk factors for diabetic nephropathy and other chronic complications in patients with T1D. The participating studies follow the main protocol of the FinnDiane Study and use the same standardized questionnaires for data acquisition. T1D was defined as diabetes onset <40 years with insulin treatment initiated within one year of diagnosis. The main renal phenotype information has been collected at a baseline visit but in some countries prospective patient visits have been performed and additional phenotype information has been gathered. The last available phenotype information has been used in the analyses. Patients included fulfil the harmonized case and control criteria of the present study. InterDiane centers included in this study come from Romania, Austria, Latvia and Lithuania.

- **AusDiane: The Austrian Diabetic Nephropathy Study (AusDiane)** was initiated in 2012 in the state of Salzburg in Austria, and is part of the InterDiane Consortium (please see also the InterDiane cohort description). The patients have been studied during a regular visit at two hospitals (Department of Internal Medicine 1, Paracelsus Medical University Hospital Salzburg and Diakonissen-Wehrle Hospital Salzburg). Recruitment was done consecutively in the outpatient departments of these two hospitals. Clinical data were collected mainly as part of

the Type 1 diabetes Registry of the state of Salzburg. Patients have been studied repeatedly every 1 to 1.5 years to improve the phenotype. The last available phenotype is used for the analysis. This study comprises 71 patients with normal AER and diabetes duration ≥15 years, 13 with microalbuminuria, 4 with macroalbuminuria and 2 with ESRD and with GWAS data available and passing the inclusion criteria. Renal status was assessed by morning urine samples at least once every year. The study received ethical approval from the local ethics committee (Ethikkommission Salzburg). Written consent was obtained prior to participation in the study.

- **The Latvian Diabetic Nephropathy Study (LatDiane)** was initiated in 2012 and is part of the InterDiane Consortium (please see also the InterDiane cohort description). Recruitment of patients took place in Pauls Stradins University Hospital (Riga). The patients were recruited from the Endocrinology department of Pauls Stradins University Hospital and from out-patient clinics of Riga and Riga district (cities Jelgava, Jurmala, Ogre, Salaspils ect). The study comprises 80 patients with normal AER and diabetes duration ≥15 years, 33 with microalbuminuria, 18 with macroalbuminuria and 7 with ESRD and with GWAS data available and passing the inclusion criteria. Patients from out-patients clinics of Riga and Riga district were invited for a separate recruitment visit following the invitation of their endocrinologist. Patients undergoing treatment or correction of therapy in Endocrinology department of Pauls Stradins University Hospital were recruited in the department. Renal status was assessed based on available data of albuminuria (albumin content in 24-hour urine or albumin/creatinine in morning spot urine). In addition, during the recruitment visit, morning spot urine was collected from all patients, and sent for albumin/creatinine measurement. For patients without available data on measurements of albuminuria before recruitment to the LatDiane Study, albumin/creatinine determination in morning spot urine was repeated also several weeks after recruitment. Follow-up visits are planned for 2018. The study received ethical approval from the Latvian Central Ethics Committee. Written consent was obtained prior to participation in the study.[11]

- **The Lithuanian Diabetic Nephropathy Study (LitDiane)** was initiated in 2013 and is part of the InterDiane Consortium (please see also the InterDiane cohort description). Patients with T1D have been collected in a single center at the Hospital of Lithuanian University of Health Sciences (HLUHS) in Kaunas. Patients were included in the study from out-patient and inpatient departments of Endocrinology clinic of HLUHS during separate study visit. Medical records were reviewed for each patient and prospective visits are performed once a year. Renal status was classified based on the urinary albumin excretion rate (AER) in at least two out of three consecutive urine collections as: normal AER (<30mg/24h in a 24-hour urine collection), incipient diabetic nephropathy (microalbuminuria; AER ≥30 and <300mg/24h) or overt diabetic nephropathy (macroalbuminuria; AER ≥300mg/24h). Patients on dialysis or with a kidney transplant were considered to have end-stage renal disease (ESRD). As a measure of renal function estimated GFR (eGFR) was calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. At the time of analysis, the study comprised 39 patients with normal AER, 32 with microalbuminuria, 9 with macroalbuminuria and 10 with ESRD and with GWAS data available and passing the inclusion criteria. The study received ethical approval from the Kaunas Regional Biomedical Research Ethics Committee (No. BE-2-16, 13-March-2013). Written consent was obtained prior to participation in the study.
- **The Romanian Diabetic Nephropathy Study (RomDiane)** was initiated in 2010 in Romania as the pilot study of the InterDiane Consortium. Patients have been studied in a cross-sectional manner in two centers in Bucharest and one in Craiova between 2010 and 2012. Renal status was assessed based on the AER or ACR in two out of three consecutive urine collections at local centers. This study comprises 89 patients with normal AER and diabetes duration ≥15 years, 48 with microalbuminuria, 70 with macroalbuminuria and 28 with ESRD, and with GWAS data available and passing the inclusion criteria. The study received ethical approval from the local ethics committee. Written consent was obtained prior to participation in the study.[12]

Italy: Subjects with T1D were recruited at the Complications of Diabetes Unit of the San Raffaele Scientific Institute, Milan, Italy. Diabetic nephropathy was defined as a median AER >200 µg min-1 in three overnight collections of sterile urine in patients with T1D for at least 10 years, concomitant diabetic retinopathy and absence of clinical or laboratory evidence of cardiac failure or other renal or urinary tract disease. Patients without nephropathy had a median AER <20 µg/min.[5]

Joslin Cohort: There were 2,271 Joslin patients with T1D included in this study. These patients were derived from three cohorts included in the ongoing Joslin Kidney Study.[10] Recruitment of 1,600 patients into the 1st Joslin Kidney Study on Natural History of Microalbuminuria in T1D took place between 1991 and 1993, and the cohort was followed through 2004. Recruitment of 1,108 patients into the 2nd Joslin Kidney Study on Natural History of Early Renal Decline in T1D took place between 2003 and 2012 and the follow-up of this cohort is still ongoing. The Joslin Proteinuria Cohort that included 630 patients was assembled from among those who developed proteinuria while attending the Joslin Clinic between 1991 and 2004. The follow-up of this cohort is still ongoing. In the analysis of data for this study, the kidney phenotypes of patients at the enrollment into the Joslin Kidney Study were considered. Genotyping data were available for 244 patients with ESRD, 475 patients with proteinuria, 470 patients with microalbuminuria and 1,189 patients with normoalbuminuria.

SDRNT1BIO: The Scottish Diabetes Research Network Type 1 Bioresource is a prospective cohort study of 6,127 individuals from across Scotland. Participants aged 16 years and over with a clinical diagnosis of T1D and insulin use within a year of onset were recruited from primary and secondary care across Scotland between 2010 and 2013. Serum, plasma, whole blood and urine samples were collected at study day allowing eGFR and albuminuria status to be obtained. Further retrospective and prospective biochemistry, co-morbidity and lifestyle data were linked from routine electronic health care records, providing serial estimates of renal status.[13]

Steno: Patients with T1D attending the outpatient clinic at Steno Diabetes Center were invited to participate in a study of genetic risk factors for diabetes complications. T1D was

considered present if the age at onset of diabetes was ≤35 years and time to definite insulin therapy ≤1 year. DKD was defined by persistent albuminuria (>300 mg/24 h) in two out of three consecutive measurements, presence of retinopathy, and absence of other kidney or urinary tract disease. Absence of DKD (controls) was defined as persistent normoalbuminuria (<30 mg/24 h) after more than 15 years of T1D in patients not treated with ACE inhibitors or angiotensin-II receptor blockers. ESRD was defined as chronic dialysis or kidney transplantation.[15]

Sweden: All patients with T1D were Swedish and diagnosed before 30 years of age. The patients with macroalbuminuria (urinary AER ≥ 200 µg min-1 in at least two consecutive overnight samples) were defined as case. The patients with AER <20 µg min-1 were considered as control.[16]

UK-ROI: In the United Kingdom (UK) GoKinD, Warren 3 and All Ireland (UK-ROI) study, data were collected under a parallel protocol to that of the GoKinD study in the United States (see above). Briefly, all individuals are white with parents and grandparents born in the UK or Ireland and who had T1D diagnosed before 31 years of age. Cases have DKD diagnosed by the onset of proteinuria (>0.5 g/24 hr) >10 years since diagnosis of diabetes; controls are diabetic individuals without evidence of proteinuria (or microalbuminuria) >15 years after onset of diabetes.[18]

WESDR: The Wisconsin Epidemiologic Study of Diabetic Retinopathy was an epidemiologic study of subjects with diabetes diagnosed before 30 years of age and taking insulin. Outcomes collected included proteinuria on a urine dipstick test.[19]

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