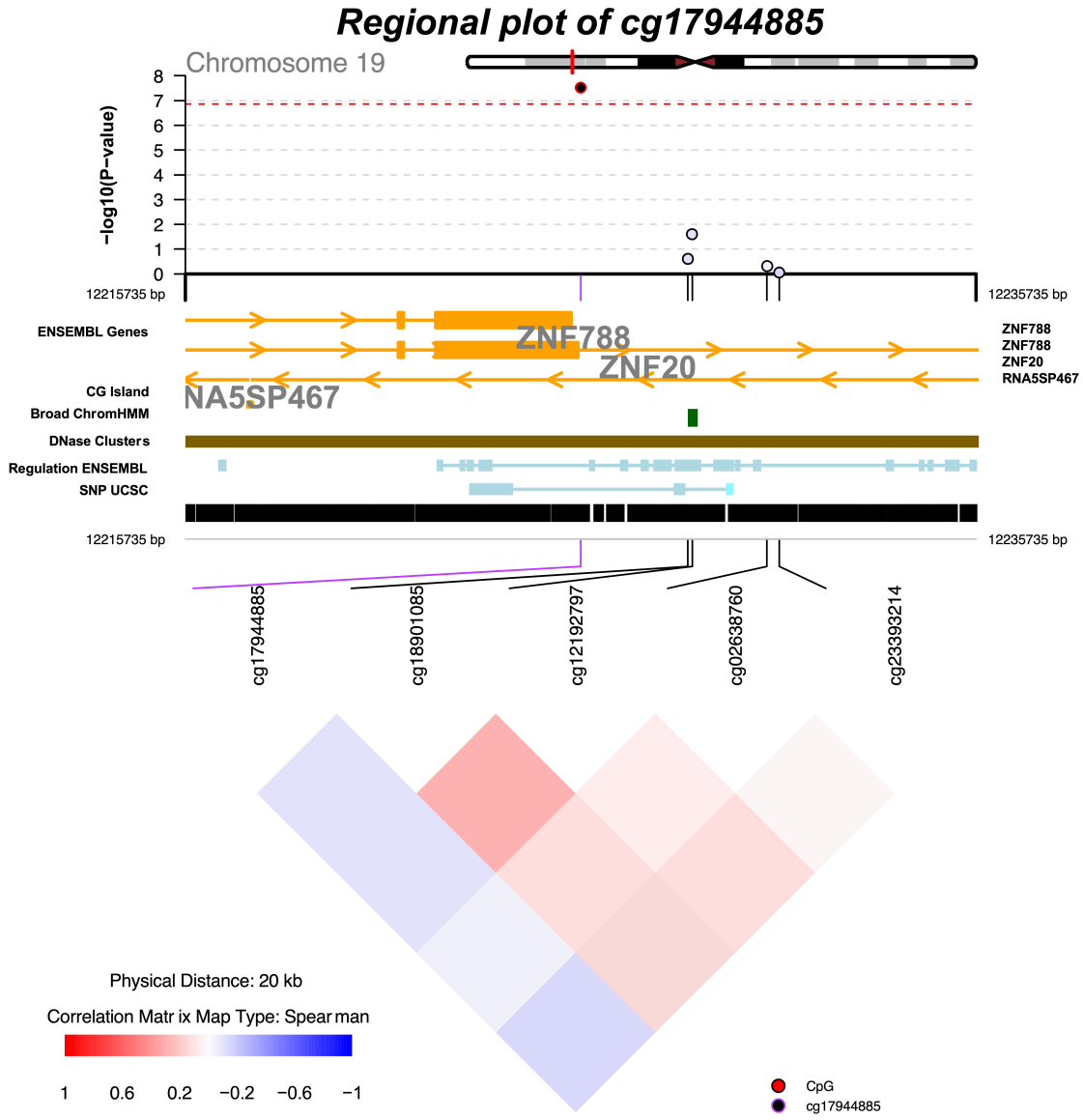
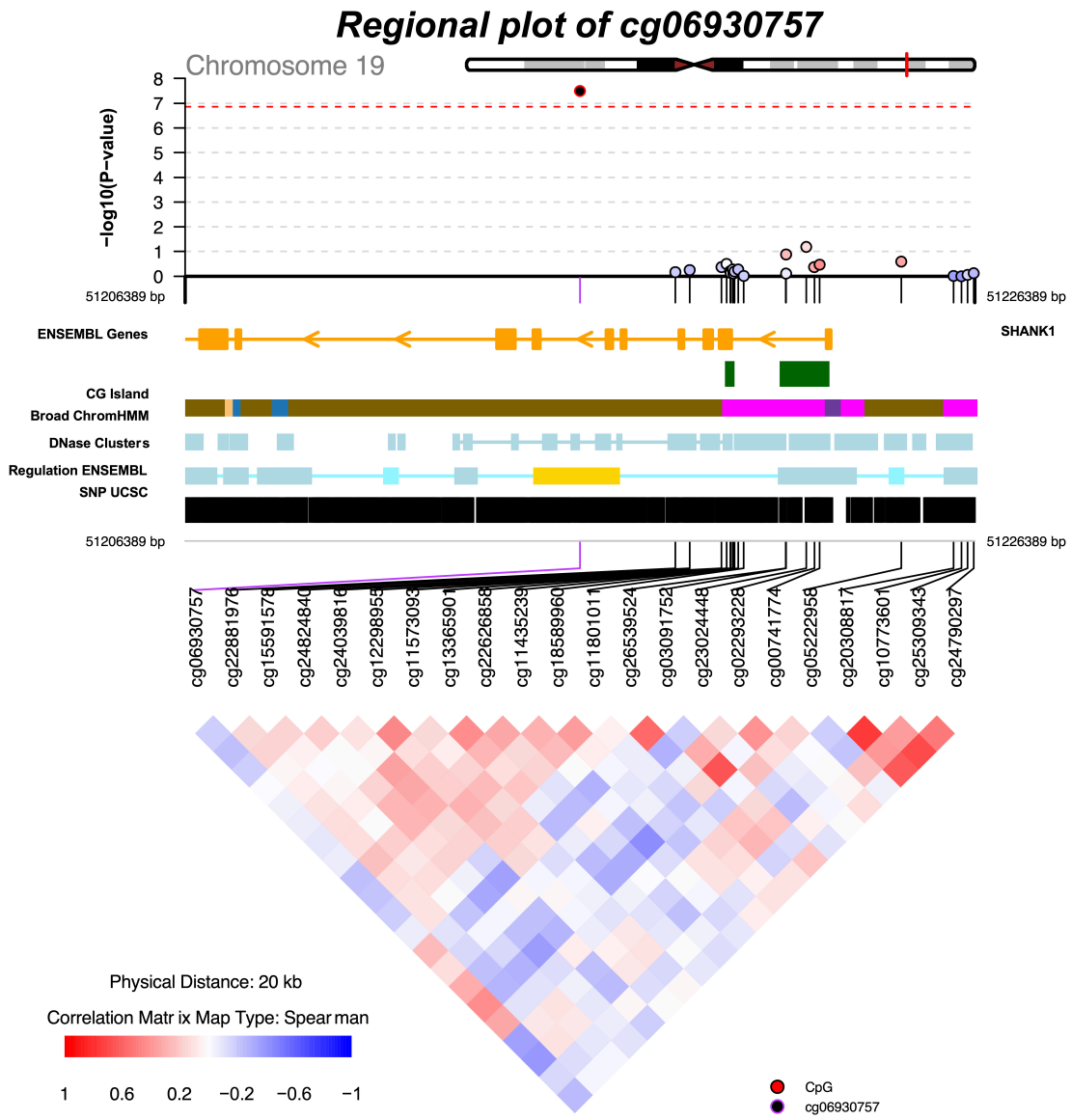
Supplement Figure 1. Regional plots of significant CpG sites associated with estimated glomerular filtration rate calculated using Chronic Kidney Disease Epidemiology Collaboration 2021 equation from meta-analysis among African American in Veteran Aging Cohort Study. A. Regional plot of CpG site cg17944885; B. Regional plot of CpG site cg06930757.

A.



B.


Regional plot of cg06930757
Chromosome 19
−log10(P−value)
8
7
6
5
4
3
2
1
0
51206389 bp
51226389 bp
ENSEMBL Genes
SHANK1
CG Island
Broad ChromHMM
DNase Clusters
Regulation ENSEMBL
SNP UCSC
51206389 bp
51226389 bp
cg06930757
cg22881976
cg15591578
cg24824840
cg24039816
cg12298955
cg11573093
cg13365901
cg22626858
cg11435239
cg18589960
cg11801011
cg26539524
cg03091752
cg23024448
cg02293228
cg00741774
cg05222958
cg20308817
cg10773601
cg25309343
cg24790297
Physical Distance: 20 kb
Correlation Matr ix Map Type: Spear man
1
0.6
0.2
−0.2
−0.6
−1
CpG
cg06930757

Supplement table 1. Replication in Veteran Aging Cohort Study (VACS) participants of CpG associations with eGFR discovered and successfully replicated by meta-analysis among multi-ancestry population in Breeze et al, 2021 (MA META).

		Position		MA META			EWAS of eGFR2021 in VACS				EWAS of eGFR2006 in VACS			
CpG sites	Chr	(bp)	Gene	Beta-coefficient	SE	P-value	Beta-coefficient	SE	P-value	FDR-q	Beta-coefficient	SE	P-value	FDR-q
cg13235761	1	203592452	-	-0.30	0.05	1.88E-09	-0.50	0.37	0.18	0.32	-0.84	0.55	0.13	0.27
cg26099045	2	64064666	-	0.13	0.02	3.26E-09	0.57	0.14	7.56E-05	9.46E-04	0.83	0.21	1.04E-04	8.68E-04
cg04428662	4	2932461	MFSD10	-0.33	0.05	5.51E-12	-1.04	0.28	2.04E-04	1.70E-03	-1.61	0.41	1.04E-04	8.68E-04
cg23174201	5	151674695	SPARC	-0.35	0.05	4.02E-12	0.08	0.45	0.86	0.90	-0.16	0.67	0.81	0.88
cg17170437	6	44229461	SLC29A1	-0.24	0.04	3.80E-08	-0.94	0.34	6.70E-03	0.04	-1.43	0.51	4.95E-03	0.02
cg26277237	9	631910	KANK1	-0.16	0.04	1.94E-05	-0.61	0.26	0.02	0.06	-0.76	0.38	0.05	0.17
cg13692082	9	133582278	FAM163B	-0.26	0.05	2.32E-07	0.17	0.49	0.73	0.87	0.46	0.72	0.52	0.69
cg14507845	9	134526223	RP11-473E2.4	-0.23	0.04	1.26E-07	-0.15	0.30	0.61	0.76	-0.05	0.44	0.91	0.95
cg14871770	10	96658622	CYP2C9;CYP2C19	-0.33	0.06	1.23E-08	-0.53	0.39	0.17	0.32	-0.38	0.57	0.51	0.69
cg23845009	11	34302131	ABTB2	0.16	0.03	6.54E-08	-0.22	0.26	0.40	0.56	-0.33	0.39	0.40	0.59
cg02157636	11	68709367	MTL5	-0.33	0.05	8.58E-10	-0.99	0.42	0.02	0.06	-1.03	0.62	0.10	0.23
cg09074338	11	70817424	SHANK2	-0.27	0.05	4.00E-07	-0.56	0.47	0.23	0.39	-0.73	0.69	0.29	0.48
cg26039141	11	75402116	RPS3	-0.36	0.06	2.90E-10	-0.09	0.42	0.83	0.90	-0.25	0.61	0.68	0.82
cg11777890	11	119334337	RNF26	0.14	0.02	7.68E-09	0.03	0.33	0.92	0.92	-0.03	0.49	0.95	0.95
cg11224251	12	6226111	CD9	-0.16	0.04	3.47E-05	0.63	0.45	0.16	0.32	1.10	0.67	0.10	0.23
cg22593432	13	32001768	NA	-0.23	0.04	4.61E-10	-0.53	0.30	0.08	0.19	-0.59	0.44	0.18	0.35
cg11789371	14	102085048	HSP90AA1	-0.28	0.05	1.41E-08	-0.84	0.37	0.02	0.06	-1.29	0.53	0.02	0.07
cg13408344	15	31339037	KLF13	-0.20	0.04	3.60E-07	-0.14	0.24	0.56	0.73	-0.18	0.36	0.61	0.77
cg03297731	16	30112972	GDPD3	-0.26	0.04	1.05E-08	-0.77	0.30	0.01	4.86E-02	-1.30	0.45	3.63E-03	0.02
cg04983687	16	88491815	ZFPM1	0.12	0.03	2.52E-06	0.30	0.12	0.01	4.86E-02	0.32	0.17	0.06	0.19
cg23712458	17	339211	RPH3AL	-0.19	0.04	4.55E-07	-0.04	0.25	0.86	0.90	0.09	0.36	0.81	0.88
cg13734658	17	73482882	SDK2	-0.24	0.05	1.54E-07	-0.45	0.31	0.14	0.32	-0.49	0.46	0.28	0.48
cg05796561	18	57128273	NA	-0.29	0.05	1.41E-08	-0.37	0.37	0.31	0.48	-0.48	0.54	0.37	0.58
cg17944885	19	12114920	ZNF20/ZNF788P	-0.21	0.03	1.24E-13	-1.30	0.24	3.01E-08	7.53E-07	-1.69	0.35	1.20E-06	3.00E-05
cg15787712	19	13837429	CTD-3252C9.4/MIR23	-0.33	0.05	9.01E-13	-0.29	0.31	0.35	0.52	-0.76	0.46	0.10	0.23

Abbreviations: CpG site (cytosine-phosphate-guanine dinucleotide sites), eGFR (estimated glomerular filtration rate), Chr (Chromosome), bp (base-pair), SE (Standard error), EWAS (Epigenome-wide association study), eGFR2021 (estimated glomerular filtration rate calculated using Chronic Kidney Disease Epidemiology Collaboration 2021 equation).

In MA META, eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration 2009 equation. Beta-coefficient refers to the changes in eGFR with 1% changes in DNA methylation b value. Beta-coefficients, standard error and p-values reported by M META were obtained from a final meta-analysis of EWAS results in the discovery and replication dataset and were located in Additional file 3: Supplementary Tables, Table S3a in their paper.

Supplement table 2. Replication in Veteran Aging Cohort Study (VACS) participants of CpG associations with eGFR discovered and successfully replicated by EWAS among multi-ancestry population in Chu et al, 2017 (Chu 2017).

		Position		Chu 2017			EWAS of eGFR2021 in VACS				EWAS of eGFR2006 in VACS			
CpG sites	Chr	(bp)	Gene	Beta-coefficient	SE	P-value	Beta-coefficient	SE	P-value	FDR-q	Beta-coefficient	SE	P-value	FDR-q
cg11950754	1	53782077	LRP8	-0.029	0.005	2.00E-10	-0.02	0.25	0.95	0.95	0.02	0.37	0.95	0.97
cg12065228	1	19652788	PQLC2	0.033	0.005	2.20E-10	0.44	0.15	3.50E-03	0.01	0.72	0.22	9.86E-04	0.01
cg19497511	2	238609807	LRRFIP1	-0.025	0.005	3.50E-08	-0.04	0.23	0.86	0.91	0.01	0.34	0.97	0.97
cg00501876	3	39193251	CSRNP1	-0.044	0.006	3.60E-15	-0.65	0.31	0.04	0.07	-0.66	0.45	0.15	0.22
cg04460609	4	16532808	LDB2	-0.028	0.005	7.80E-09	-0.49	0.18	7.14E-03	0.02	-0.56	0.27	0.04	0.08
cg09022230	7	5457225	TNRC18	-0.033	0.005	5.20E-10	0.17	0.21	0.42	0.47	0.17	0.31	0.59	0.66
cg23597162	7	28102341	JAZF1	-0.064	0.007	2.80E-19	-0.63	0.18	4.63E-04	2.20E-03	-0.81	0.26	2.10E-03	7.98E-03
cg02059849	8	142437898	PTP4A3	0.032	0.005	7.70E-10	0.57	0.40	0.16	0.20	0.55	0.60	0.35	0.42
cg10750182	10	73497514	C10orf105;CDH23	-0.041	0.007	5.00E-10	-0.37	0.36	0.30	0.36	-0.55	0.53	0.30	0.38
cg04036920	11	33562503	C11orf41	-0.068	0.009	2.40E-15	-0.40	0.20	4.59E-02	0.08	-0.46	0.30	0.12	0.22
cg19942083	12	7070562	PTPN6/PHB2	0.033	0.005	7.20E-10	0.68	0.16	2.82E-05	2.68E-04	0.78	0.24	1.25E-03	7.89E-03
cg06158227	15	43662311	TUBGCP4;ZSCAN29	-0.027	0.004	8.50E-10	-1.29	0.40	1.37E-03	0.01	-1.49	0.59	0.01	0.03
cg16428517	16	3317428	MEFV / ZNF263	-0.026	0.004	1.20E-10	-0.70	0.36	0.05	0.09	-0.78	0.53	0.14	0.22
cg27660627	16	89461803	ANKRD11	-0.052	0.008	9.90E-10	-0.77	0.28	5.77E-03	0.01	-1.00	0.41	0.02	0.04
cg12116137	17	1576449	PRPF8	-0.042	0.007	5.30E-09	0.23	0.13	0.08	0.10	0.29	0.19	0.13	0.22
cg22515589	17	79426432	BAHCC1	0.025	0.005	6.40E-08	0.62	0.33	0.06	0.09	0.55	0.49	0.26	0.36
cg00994936	19	1423902	DAZAP1	0.041	0.006	3.30E-11	0.67	0.25	6.30E-03	0.01	1.07	0.37	3.39E-03	1.07E-02
cg17944885	19	12225735	ZNF788/ZNF20	-0.044	0.004	1.20E-23	-1.30	0.24	3.01E-08	5.72E-07	-1.69	0.35	1.20E-06	2.28E-05

Abbreviations: CpG site (cytosine-phosphate-guanine dinucleotide sites), eGFR (estimated glomerular filtration rate), Chr (Chromosome), bp (base-pair), SE (Standard error), EWAS (Epigenome-wide association study), eGFR2021 (estimated glomerular filtration rate calculated using Chronic Kidney Disease Epidemiology Collaboration 2021 equation).

In Chu 2017, eGFR was calculated using the estimated glomerular filtration rate calculated using Modification of Diet in Renal Disease equation and log transformed before EWAS, thus interpretation of Beta-coefficients in Chu 2017 is in log scale. Beta-coefficient in EWAS of eGFR2021 in VACS refers to the changes in eGFR with 1% changes in DNA methylation b value. Beta-coefficients, standard error and p-values reported by Chu 2017 were obtained from a final meta-analysis of EWAS results in the ARIC and FHS dataset and were located in Table 2 in their paper.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6-7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	7-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-9
Bias	9	Describe any efforts to address potential sources of bias	9-10
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10-12
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	10-12
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	12
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	12
Outcome data	15*	Report numbers of outcome events or summary measures over time	12

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	12-14
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14-15
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	20

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.