

Supplemental Table 1. Genome-wide Significant SNPs for the Multi Ancestry Diabetic Retinopathy GWAS; CHR, build 38 chromosome; BP, build 38 position; EA, effect allele; OA, other allele; EAF, effect allele frequency; OR, odds ratio; LCI, lower 95% confidence interval; UCI, upper 95% confidence interval; *p*, two sided *p* value from the inverse variance-weighted meta-analysis.

rsID	CHR	BP	EA	OA	EAF	OR	LCI	UCI	P
rs1050828	23	154536002	T	C	0.0937	1.479	1.450	1.508	2.83E-90
rs7063597	23	154663327	T	C	0.0973	1.453	1.425	1.481	2.26E-82
rs185814586	23	154690417	C	G	0.8962	0.696	0.683	0.709	2.74E-81
rs141555380	23	154677735	T	C	0.1098	1.384	1.359	1.409	5.75E-73
rs782270174	23	154654332	C	G	0.0968	1.449	1.419	1.480	1.81E-68
rs146474788	23	154665129	A	G	0.1041	1.423	1.394	1.452	7.31E-66
rs201851580	23	154959385	CA	C	0.0938	1.397	1.370	1.424	1.17E-65
rs762516	23	154536448	T	C	0.1231	1.336	1.314	1.359	1.67E-65
rs116703563	23	154355802	T	C	0.1083	1.349	1.325	1.373	2.95E-62
rs149621038	23	154724850	T	C	0.1203	1.331	1.308	1.354	3.97E-61
rs138941436	23	154696029	A	G	0.8733	0.760	0.747	0.773	7.23E-59
rs115712917	23	154440632	A	C	0.8602	0.772	0.759	0.784	3.90E-58
rs201543735	23	154323411	CT	C	0.1068	1.334	1.310	1.358	5.79E-56
rs142342229	23	154368256	T	G	0.1355	1.286	1.266	1.308	1.16E-53
rs762517	23	154536519	A	G	0.1276	1.333	1.308	1.358	3.02E-53
rs2515905	23	154533860	A	G	0.128	1.330	1.306	1.355	1.16E-52
rs183132698	23	154353251	T	C	0.1396	1.279	1.258	1.300	3.11E-52
rs2515904	23	154534556	C	G	0.1254	1.331	1.306	1.357	1.56E-51
rs7885619	23	154732442	T	G	0.8749	0.750	0.736	0.765	5.96E-51
rs5987241	23	154307629	T	G	0.1018	1.329	1.304	1.355	2.13E-49
rs141235526	23	154476920	A	G	0.1293	1.321	1.296	1.346	1.01E-48
rs140657308	23	154979499	A	C	0.8676	0.794	0.781	0.807	1.43E-44
rs28370190	23	155023548	T	C	0.1333	1.257	1.237	1.278	2.82E-44
rs28370191	23	155023547	T	C	0.1333	1.257	1.236	1.278	3.47E-44
rs183182105	23	154426613	A	G	0.1439	1.283	1.260	1.306	1.16E-43
rs5987002	23	154649096	T	C	0.201	1.209	1.192	1.226	5.22E-42
rs116301817	23	154398354	A	G	0.1442	1.272	1.249	1.295	3.20E-41
rs151161250	23	155006140	T	G	0.8648	0.791	0.777	0.806	3.69E-37
rs112877021	23	155051464	C	G	0.1379	1.254	1.231	1.277	1.25E-35
rs28370215	23	154907163	C	G	0.797	0.842	0.830	0.854	2.32E-35
rs781911237	23	154939640	T	C	0.2084	1.178	1.162	1.194	7.45E-33
rs148368240	23	154910087	A	G	0.7925	0.850	0.838	0.861	1.41E-32
rs28370225	23	154895736	T	C	0.2102	1.174	1.158	1.190	4.00E-32
rs7066193	23	154849166	T	C	0.2078	1.173	1.157	1.189	1.86E-31
rs143727248	23	154834395	T	C	0.2089	1.172	1.156	1.188	3.23E-31
rs28370233	23	154835660	A	G	0.79	0.854	0.842	0.865	3.65E-31
rs28370232	23	154835737	A	C	0.7899	0.854	0.842	0.866	4.72E-31
rs28412378	23	154875225	A	G	0.7902	0.854	0.843	0.866	4.75E-31
rs145782678	23	154108537	C	G	0.9209	0.791	0.774	0.808	5.30E-29
rs5987043	23	154840653	A	G	0.7469	0.867	0.856	0.878	1.05E-28
rs146461515	23	154138628	T	G	0.9021	0.792	0.775	0.809	5.16E-28

rs148439175	23	154950309	T	C	0.7862	0.849	0.836	0.862	1.01E-26
rs139039414	23	154955449	A	G	0.2138	1.178	1.160	1.196	1.02E-26
rs188375209	23	154848779	C	G	0.217	1.173	1.155	1.191	3.71E-26
rs184832892	23	154839524	A	G	0.2153	1.174	1.156	1.191	3.86E-26
rs7879130	23	154851549	C	G	0.2176	1.172	1.155	1.190	4.07E-26
rs1104645	23	154920208	T	G	0.7767	0.854	0.841	0.867	1.31E-25
rs1800297	23	154860563	T	C	0.78	0.856	0.843	0.868	1.32E-25
rs189776248	23	154872360	T	C	0.7827	0.854	0.841	0.867	1.49E-25
rs12014480	23	154939013	A	G	0.2245	1.170	1.152	1.187	1.67E-25
rs138703929	23	154847980	A	C	0.2152	1.172	1.154	1.190	1.98E-25
rs146041456	23	154127943	A	G	0.8707	0.841	0.827	0.855	4.20E-25
rs143154790	23	154083577	A	C	0.9147	0.812	0.795	0.828	4.95E-25
rs1226429453	23	154941969	A	G	0.2229	1.167	1.150	1.185	2.07E-24
rs137875631	23	154115214	T	C	0.9077	0.804	0.787	0.822	3.75E-24
rs144536680	23	154047895	T	C	0.0848	1.225	1.201	1.250	8.51E-24
rs12393550	23	154530445	A	G	0.2827	1.140	1.124	1.155	4.88E-21
rs5986990	23	154533413	A	G	0.2849	1.139	1.123	1.155	5.69E-21
rs762515	23	154536313	T	C	0.6943	0.883	0.871	0.895	5.02E-20
rs2872737	23	154126885	A	G	0.8519	0.865	0.852	0.879	5.27E-20
rs28470352	23	154525272	A	T	0.2848	1.135	1.120	1.151	5.58E-20
rs3027902	23	154012020	T	C	0.1217	1.163	1.143	1.182	2.11E-19
rs3027936	23	154040393	T	C	0.1069	1.173	1.152	1.194	2.70E-19
rs140180287	23	153980959	A	G	0.0736	1.236	1.207	1.266	5.46E-19
rs147211339	23	153972972	T	C	0.0905	1.189	1.166	1.213	1.55E-18
rs1051151	23	153957032	T	G	0.0909	1.188	1.165	1.211	1.85E-18
rs146907766	23	154002307	A	G	0.1058	1.187	1.163	1.211	8.23E-18
rs150824159	23	153930729	T	C	0.0908	1.174	1.152	1.197	3.58E-17
rs140142141	23	154068513	T	C	0.8886	0.851	0.835	0.868	1.72E-16
rs189047640	23	153934563	T	C	0.0925	1.174	1.151	1.197	2.28E-16
rs138880088	23	153977587	A	G	0.0904	1.192	1.166	1.218	2.89E-16
rs149235100	23	154061285	T	C	0.8881	0.853	0.837	0.870	4.25E-16
rs3027906	23	154013520	A	G	0.1258	1.162	1.140	1.184	7.57E-16
rs150536778	23	153949894	A	G	0.0919	1.187	1.162	1.213	8.29E-16
rs192306384	23	154038686	A	C	0.8759	0.875	0.860	0.890	1.37E-15
rs7889328	23	153946435	A	G	0.0923	1.185	1.160	1.210	1.65E-15
rs7903146	10	112998590	T	C	0.3278	1.069	1.060	1.078	1.88E-15
rs7889967	23	153946892	A	G	0.0923	1.184	1.159	1.210	1.98E-15
rs12009271	23	154830834	A	G	0.6523	0.913	0.902	0.923	3.05E-15
rs149446642	23	154007184	A	G	0.1241	1.159	1.138	1.181	3.18E-15
rs143302326	23	153947699	A	G	0.0837	1.186	1.159	1.213	8.09E-14
rs191116415	23	153905288	A	G	0.8933	0.876	0.860	0.892	2.92E-13
rs138183490	23	153984500	A	T	0.1084	1.157	1.134	1.180	3.14E-13
rs72826075	10	112990741	A	G	0.7648	0.931	0.922	0.941	6.51E-13
rs55972445	10	113023031	T	G	0.227	1.075	1.064	1.085	6.77E-13
rs12244851	10	113014167	T	C	0.35	1.069	1.059	1.079	8.66E-13

rs4267006	10	112999020	T	G	0.2298	1.074	1.063	1.085	1.25E-12
rs56087297	10	113039413	A	G	0.7237	0.938	0.929	0.946	1.62E-12
rs55899248	10	113013849	A	G	0.7732	0.932	0.923	0.941	1.70E-12
rs10659211	10	113022822	G	GCT	0.7043	0.941	0.932	0.949	1.82E-12
rs149290876	23	153870301	C	G	0.9177	0.870	0.852	0.888	5.58E-12
rs143092299	23	153874665	T	C	0.0888	1.138	1.116	1.160	2.33E-11
rs75619922	23	153789757	A	G	0.0727	1.172	1.144	1.200	2.46E-11
rs2734643	23	154025736	T	C	0.1432	1.110	1.092	1.127	2.47E-11
rs181208874	23	153724433	T	C	0.0638	1.169	1.141	1.197	5.14E-11
rs36090025	10	113014674	A	C	0.6984	0.946	0.938	0.954	7.25E-11
rs73640842	23	153941449	A	G	0.1242	1.128	1.107	1.150	1.02E-10
rs187927063	23	153775752	A	G	0.0717	1.167	1.139	1.195	1.27E-10
rs2269371	23	153941572	T	C	0.8759	0.887	0.870	0.904	1.34E-10
rs181218840	23	153742928	A	G	0.0675	1.173	1.144	1.203	2.25E-10
rs7883522	23	153760577	A	G	0.0704	1.168	1.139	1.196	2.35E-10
rs76624501	8	101415496	T	C	0.0626	1.221	1.183	1.260	2.70E-10
rs11196211	10	113057250	A	C	0.7172	0.944	0.936	0.953	2.72E-10
rs1042512	23	153870192	A	G	0.086	1.152	1.127	1.179	3.26E-10
rs4506565	10	112996282	A	T	0.6129	0.951	0.943	0.958	4.62E-10
rs56299331	10	113028677	T	C	0.207	1.065	1.054	1.076	9.44E-10
rs72826094	10	113041729	A	T	0.791	0.938	0.928	0.948	9.91E-10
rs7881265	23	153925787	T	C	0.8843	0.888	0.871	0.906	1.26E-09
rs181597230	23	153979851	T	C	0.1777	1.091	1.076	1.107	2.24E-09
rs2229241	23	153943036	T	C	0.8485	0.902	0.886	0.917	2.30E-09
rs11950268	5	167825696	T	C	0.0533	0.811	0.783	0.840	2.55E-09
rs4077527	10	113053282	T	C	0.4787	1.055	1.046	1.065	6.39E-09
rs138848380	23	153837718	T	G	0.0907	1.124	1.102	1.147	6.69E-09
rs3027937	23	154041209	A	T	0.1467	1.106	1.087	1.125	7.06E-09
rs12718338	10	113053288	T	C	0.4817	1.055	1.045	1.065	7.08E-09
rs3027922	23	154028630	T	C	0.0763	1.076	1.062	1.090	7.19E-09
rs7059306	23	154049539	A	G	0.1524	1.102	1.083	1.121	1.35E-08
rs7054174	23	153827002	A	G	0.0869	1.136	1.111	1.161	1.38E-08
rs140855390	23	153919362	A	G	0.201	1.091	1.075	1.108	1.46E-08
rs114926776	12	116914542	T	C	0.0698	0.838	0.812	0.864	1.62E-08
rs11196200	10	113042179	C	G	0.5225	0.950	0.941	0.958	2.13E-08
rs2070821	23	154398956	T	C	0.5099	1.065	1.053	1.077	2.39E-08
rs2076085	22	37074001	A	C	0.5671	1.046	1.037	1.054	2.52E-08
rs4820268	22	37073551	A	G	0.5668	1.045	1.037	1.054	2.56E-08
rs12260037	10	113031731	T	C	0.3025	1.049	1.040	1.058	2.75E-08
rs306908	23	155731842	T	C	0.1478	1.095	1.077	1.113	3.03E-08
rs73995757	17	75092906	C	G	0.8883	1.144	1.116	1.172	3.81E-08
rs186986494	23	153901088	A	C	0.8674	0.912	0.897	0.928	3.99E-08
rs115170237	1	205573079	A	G	0.9324	1.193	1.155	1.232	4.00E-08
rs76980457	12	116908685	T	C	0.0656	0.843	0.818	0.870	4.01E-08
rs2072860	22	37074564	A	G	0.5619	1.044	1.036	1.053	4.09E-08

rs7333159	13	110248596	A	G	0.8706	1.134	1.108	1.160	4.83E-08
rs3935958	12	116916099	A	C	0.9316	1.190	1.152	1.228	4.92E-08

Supplemental Table 2. Genome-wide Significant SNPs for the NH-African Ancestry Diabetic Retinopathy GWAS; CHR, build 38 chromosome; BP, build 38 position; EA, effect allele; OA, other allele; EAF, effect allele frequency; OR, odds ratio; LCI, lower 95% confidence interval; UCI, upper 95% confidence interval; p, two sided p value from the inverse variance-weighted meta-analysis.

rsID	CHR	BP	EA	OA	EAF	OR	LCI	UCI	P
rs1050828	23	154536002	T	C	0.0942	1.466	1.436	1.498	1.45E-73
rs782270174	23	154654332	C	G	0.0968	1.449	1.419	1.480	1.81E-68
rs7063597	23	154663327	T	C	0.0978	1.443	1.413	1.474	1.01E-67
rs185814586	23	154690417	C	G	0.8957	0.701	0.687	0.716	2.23E-66
rs146474788	23	154665129	A	G	0.1041	1.423	1.394	1.452	7.31E-66
rs141555380	23	154677735	T	C	0.1134	1.382	1.355	1.410	9.69E-60
rs201851580	23	154959385	CA	C	0.097	1.400	1.370	1.431	1.68E-54
rs762517	23	154536519	A	G	0.1276	1.333	1.308	1.358	3.02E-53
rs762516	23	154536448	T	C	0.1276	1.333	1.308	1.358	3.04E-53
rs2515905	23	154533860	A	G	0.128	1.330	1.306	1.355	1.16E-52
rs2515904	23	154534556	C	G	0.1254	1.331	1.306	1.357	1.56E-51
rs7885619	23	154732442	T	G	0.8749	0.750	0.736	0.765	5.96E-51
rs149621038	23	154724850	T	C	0.1244	1.331	1.306	1.357	2.25E-50
rs141235526	23	154476920	A	G	0.1293	1.321	1.296	1.346	1.01E-48
rs138941436	23	154696029	A	G	0.8689	0.760	0.746	0.775	1.84E-48
rs116703563	23	154355802	T	C	0.1135	1.337	1.310	1.363	4.56E-48
rs201543735	23	154323411	CT	C	0.111	1.326	1.299	1.353	1.84E-44
rs115712917	23	154440632	A	C	0.8531	0.780	0.766	0.794	5.01E-44
rs183182105	23	154426613	A	G	0.1439	1.283	1.260	1.306	1.16E-43
rs116301817	23	154398354	A	G	0.1442	1.272	1.249	1.295	3.20E-41
rs142342229	23	154368256	T	G	0.1424	1.273	1.250	1.297	1.07E-40
rs5987241	23	154307629	T	G	0.1027	1.317	1.289	1.344	1.57E-39
rs183132698	23	154353251	T	C	0.1466	1.265	1.243	1.288	1.93E-39
rs151161250	23	155006140	T	G	0.8648	0.791	0.777	0.806	3.69E-37
rs140657308	23	154979499	A	C	0.8629	0.792	0.778	0.807	3.83E-37
rs28370190	23	155023548	T	C	0.1378	1.256	1.234	1.279	3.73E-36
rs28370191	23	155023547	T	C	0.1379	1.256	1.233	1.279	4.54E-36
rs112877021	23	155051464	C	G	0.1379	1.254	1.231	1.277	1.25E-35
rs5987002	23	154649096	T	C	0.2094	1.203	1.184	1.222	1.14E-32
rs28370215	23	154907163	C	G	0.7896	0.842	0.829	0.855	3.17E-29
rs146461515	23	154138628	T	G	0.9021	0.792	0.775	0.809	5.16E-28
rs781911237	23	154939640	T	C	0.216	1.178	1.160	1.196	3.60E-27
rs148368240	23	154910087	A	G	0.7851	0.850	0.837	0.863	6.76E-27
rs148439175	23	154950309	T	C	0.7862	0.849	0.836	0.862	1.01E-26
rs139039414	23	154955449	A	G	0.2138	1.178	1.160	1.196	1.02E-26
rs28370225	23	154895736	T	C	0.2178	1.175	1.157	1.192	1.26E-26
rs143727248	23	154834395	T	C	0.2164	1.174	1.157	1.192	2.20E-26
rs7066193	23	154849166	T	C	0.2153	1.174	1.156	1.192	2.67E-26
rs188375209	23	154848779	C	G	0.217	1.173	1.155	1.191	3.71E-26
rs28370233	23	154835660	A	G	0.7824	0.853	0.840	0.866	3.80E-26
rs184832892	23	154839524	A	G	0.2153	1.174	1.156	1.191	3.86E-26

rs7879130	23	154851549	C	G	0.2176	1.172	1.155	1.190	4.07E-26
rs28370232	23	154835737	A	C	0.7823	0.853	0.840	0.866	4.78E-26
rs28412378	23	154875225	A	G	0.7826	0.854	0.841	0.866	6.66E-26
rs1104645	23	154920208	T	G	0.7767	0.854	0.841	0.867	1.31E-25
rs1800297	23	154860563	T	C	0.78	0.856	0.843	0.868	1.32E-25
rs189776248	23	154872360	T	C	0.7827	0.854	0.841	0.867	1.49E-25
rs12014480	23	154939013	A	G	0.2245	1.170	1.152	1.187	1.67E-25
rs138703929	23	154847980	A	C	0.2152	1.172	1.154	1.190	1.98E-25
rs1226429453	23	154941969	A	G	0.2229	1.167	1.150	1.185	2.07E-24
rs137875631	23	154115214	T	C	0.9077	0.804	0.787	0.822	3.75E-24
rs145782678	23	154108537	C	G	0.9204	0.793	0.775	0.812	3.95E-24
rs5987043	23	154840653	A	G	0.736	0.868	0.856	0.881	3.35E-23
rs143154790	23	154083577	A	C	0.9142	0.813	0.795	0.831	4.76E-21
rs12393550	23	154530445	A	G	0.2827	1.140	1.124	1.155	4.88E-21
rs5986990	23	154533413	A	G	0.2849	1.139	1.123	1.155	5.69E-21
rs144536680	23	154047895	T	C	0.0853	1.224	1.197	1.251	4.27E-20
rs762515	23	154536313	T	C	0.6943	0.883	0.871	0.895	5.02E-20
rs28470352	23	154525272	A	T	0.2848	1.135	1.120	1.151	5.58E-20
rs140180287	23	153980959	A	G	0.0736	1.236	1.207	1.266	5.46E-19
rs146041456	23	154127943	A	G	0.866	0.849	0.834	0.865	1.29E-18
rs146907766	23	154002307	A	G	0.1058	1.187	1.163	1.211	8.23E-18
rs140142141	23	154068513	T	C	0.8886	0.851	0.835	0.868	1.72E-16
rs3027936	23	154040393	T	C	0.1104	1.174	1.152	1.198	2.45E-16
rs138880088	23	153977587	A	G	0.0904	1.192	1.166	1.218	2.89E-16
rs149235100	23	154061285	T	C	0.8881	0.853	0.837	0.870	4.25E-16
rs147211339	23	153972972	T	C	0.0911	1.190	1.165	1.216	4.47E-16
rs1051151	23	153957032	T	G	0.0915	1.188	1.163	1.213	7.50E-16
rs3027906	23	154013520	A	G	0.1258	1.162	1.140	1.184	7.57E-16
rs3027902	23	154012020	T	C	0.1261	1.160	1.139	1.182	8.21E-16
rs150536778	23	153949894	A	G	0.0919	1.187	1.162	1.213	8.29E-16
rs7889328	23	153946435	A	G	0.0923	1.185	1.160	1.210	1.65E-15
rs7889967	23	153946892	A	G	0.0923	1.184	1.159	1.210	1.98E-15
rs2872737	23	154126885	A	G	0.8469	0.871	0.856	0.886	2.58E-15
rs149446642	23	154007184	A	G	0.1241	1.159	1.138	1.181	3.18E-15
rs150824159	23	153930729	T	C	0.0943	1.178	1.154	1.204	7.14E-15
rs189047640	23	153934563	T	C	0.0931	1.178	1.153	1.203	1.13E-14
rs192306384	23	154038686	A	C	0.8706	0.868	0.852	0.885	3.34E-14
rs3027922	23	154028630	T	C	0.1157	1.156	1.134	1.178	4.82E-14
rs143302326	23	153947699	A	G	0.0837	1.186	1.159	1.213	8.09E-14
rs138183490	23	153984500	A	T	0.1084	1.157	1.134	1.180	3.14E-13
rs12009271	23	154830834	A	G	0.6348	0.915	0.903	0.927	4.50E-12
rs75619922	23	153789757	A	G	0.0727	1.172	1.144	1.200	2.46E-11
rs73640842	23	153941449	A	G	0.1242	1.128	1.107	1.150	1.02E-10
rs187927063	23	153775752	A	G	0.0717	1.167	1.139	1.195	1.27E-10
rs2269371	23	153941572	T	C	0.8759	0.887	0.870	0.904	1.34E-10

rs181208874	23	153724433	T	C	0.0637	1.180	1.150	1.211	1.75E-10
rs191116415	23	153905288	A	G	0.8889	0.879	0.861	0.897	1.82E-10
rs181218840	23	153742928	A	G	0.0675	1.173	1.144	1.203	2.25E-10
rs7883522	23	153760577	A	G	0.0704	1.168	1.139	1.196	2.35E-10
rs149290876	23	153870301	C	G	0.9141	0.867	0.847	0.887	2.36E-10
rs1042512	23	153870192	A	G	0.086	1.152	1.127	1.179	3.26E-10
rs2734643	23	154025736	T	C	0.1493	1.114	1.095	1.134	5.00E-10
rs143092299	23	153874665	T	C	0.0937	1.143	1.118	1.168	8.03E-10
rs306908	23	155731842	T	C	0.2171	1.154	1.127	1.182	1.05E-09
rs7881265	23	153925787	T	C	0.8843	0.888	0.871	0.906	1.26E-09
rs2229241	23	153943036	T	C	0.8485	0.902	0.886	0.917	2.30E-09
rs3027937	23	154041209	A	T	0.1467	1.106	1.087	1.125	7.06E-09
rs138848380	23	153837718	T	G	0.091	1.133	1.109	1.158	1.27E-08
rs915941	23	154398308	A	C	0.4987	1.074	1.061	1.088	1.28E-08
rs7059306	23	154049539	A	G	0.1524	1.102	1.083	1.121	1.35E-08
rs7054174	23	153827002	A	G	0.0869	1.136	1.111	1.161	1.38E-08
rs140855390	23	153919362	A	G	0.2039	1.090	1.073	1.107	2.79E-08
rs2070821	23	154398956	T	C	0.493	1.072	1.059	1.086	2.86E-08
rs60516219	23	154394242	A	C	0.4976	0.933	0.921	0.945	3.64E-08

Supplemental Table 3. Genome-wide Significant SNPs for the NH-European Ancestry Diabetic Retinopathy GWAS ; CHR, build 38 chromosome; BP, build 38 position; EA, effect allele; OA, other allele; EAF, effect allele frequency; OR, odds ratio; LCI, lower 95% confidence interval; UCI, upper 95% confidence interval; p, two sided p value from the inverse variance-weighted meta-analysis

rsID	CHR	BP	EA	OA	EAF	OR	LCI	UCI	P
rs7903146	10	112998590	T	C	0.3346	1.077	1.066	1.088	3.14E-13
rs36090025	10	113014674	A	C	0.6635	0.927	0.918	0.937	4.54E-13
rs10659211	10	113022822	G	GCT	0.6638	0.927	0.917	0.937	7.87E-13
rs12244851	10	113014167	T	C	0.3556	1.072	1.061	1.083	1.60E-11
rs4267006	10	112999020	T	G	0.2545	1.078	1.066	1.090	1.88E-11
rs55972445	10	113023031	T	G	0.2544	1.076	1.064	1.089	6.28E-11
rs4506565	10	112996282	A	T	0.6454	0.936	0.927	0.946	1.04E-10
rs55899248	10	113013849	A	G	0.7452	0.930	0.920	0.941	1.09E-10
rs72826075	10	112990741	A	G	0.7376	0.931	0.921	0.941	1.61E-10
rs56087297	10	113039413	A	G	0.6866	0.935	0.925	0.945	1.69E-10
rs12255372	10	113049143	T	G	0.3236	1.068	1.057	1.080	2.07E-10
rs11196211	10	113057250	A	C	0.6816	0.935	0.925	0.945	2.28E-10
rs12260037	10	113031731	T	C	0.3154	1.067	1.055	1.078	1.00E-09
rs72826094	10	113041729	A	T	0.7693	0.936	0.925	0.947	1.26E-08
rs56299331	10	113028677	T	C	0.2304	1.067	1.055	1.079	2.41E-08

Supplemental Table 4. Genome-wide Significant SNPs for the Multi Ancestry Proliferative Diabetic Retinopathy GWAS. CHR, build 38 chromosome; BP, build 38 position; EA, effect allele; OA, other allele; EAF, effect allele frequency; OR, odds ratio; LCI, lower 95% confidence interval; UCI, upper 95% confidence interval; p, two sided p value from the inverse variance-weighted meta-analysis.

<u>rsID</u>	<u>CHR</u>	<u>BP</u>	<u>EA</u>	<u>OA</u>	<u>EAF</u>	<u>N</u>	<u>OR</u>	<u>LCI</u>	<u>UCI</u>	<u>P</u>
rs28370190	23	155023548	T	C	0.1505	67093	1.210	1.169	1.252	2.62E-08
rs138941436	23	154696029	A	G	0.8554	67093	0.796	0.768	0.824	1.04E-10
rs149621038	23	154724850	T	C	0.1385	67093	1.268	1.223	1.314	3.07E-11
rs201851580	23	154959385	CA	C	0.1085	67093	1.289	1.238	1.342	2.91E-10
rs185814586	23	154690417	C	G	0.8817	67093	0.756	0.727	0.785	2.37E-13
rs201543735	23	154323411	CT	C	0.1236	67093	1.286	1.239	1.335	1.13E-11
rs1050828	23	154536002	T	C	0.1063	67093	1.362	1.309	1.416	3.28E-15
rs146041456	23	154127943	A	G	0.8583	67093	0.821	0.793	0.851	1.53E-08
rs143154790	23	154083577	A	C	0.9083	67093	0.791	0.759	0.824	7.76E-09
rs7063597	23	154663327	T	C	0.1103	67093	1.344	1.292	1.398	4.63E-14
rs144536680	23	154047895	T	C	0.0908	67093	1.270	1.219	1.323	4.20E-09
rs5987241	23	154307629	T	G	0.1133	67093	1.300	1.251	1.352	1.07E-11
rs5987002	23	154649096	T	C	0.2103	67093	1.184	1.150	1.218	4.46E-09
rs7903146	10	112998590	T	C	0.3294	67093	1.111	1.092	1.131	2.28E-09
rs116703563	23	154355802	T	C	0.1273	67093	1.268	1.223	1.316	9.33E-11
rs145782678	23	154108537	C	G	0.9137	67093	0.766	0.735	0.799	1.74E-10
rs5840289	20	8798197	G	GA	0.2515	67093	2.152	1.877	2.468	2.14E-08
rs141555380	23	154677735	T	C	0.1277	67093	1.294	1.247	1.342	3.34E-12
rs183132698	23	154353251	T	C	0.1608	67093	1.202	1.162	1.243	4.636E-08
rs28370191	23	155023547	T	C	0.1505	67093	1.209	1.169	1.251	2.715E-08
rs762516	23	154536448	T	C	0.1417	67093	1.275	1.231	1.320	4.657E-12

Supplemental Table 5. Genome-wide Significant SNPs for the NH-African Ancestry Proliferative Diabetic Retinopathy GWAS. CHR, build 38 chromosome; BP, build 38 position; EA, effect allele; OA, other allele; EAF, effect allele frequency; OR, odds ratio; LCI, lower 95% confidence interval; UCI, upper 95% confidence interval; p, two sided p value from the inverse variance-weighted meta-analysis.

rsID	CHR	BP	EA	OA	EAF	N	OR	LCI	UCI	P
rs143154790	23	154083577	A	C	0.9083	28382	0.79	0.76	0.82	7.76E-09
rs7063597	23	154663327	T	C	0.1103	28382	1.34	1.29	1.40	4.63E-14
rs144536680	23	154047895	T	C	0.0908	28382	1.27	1.22	1.32	4.20E-09
rs5987241	23	154307629	T	G	0.1133	28382	1.30	1.25	1.35	1.07E-11
rs28370190	23	155023548	T	C	0.1505	28382	1.21	1.17	1.25	2.62E-08
rs116703563	23	154355802	T	C	0.1273	28382	1.27	1.22	1.32	9.33E-11
rs138941436	23	154696029	A	G	0.8554	28382	0.80	0.77	0.82	1.04E-10
rs149621038	23	154724850	T	C	0.1385	28382	1.27	1.22	1.31	3.07E-11
rs145782678	23	154108537	C	G	0.9137	28382	0.77	0.73	0.80	1.74E-10
rs201851580	23	154959385	CA	C	0.1085	28382	1.29	1.24	1.34	2.91E-10
rs141555380	23	154677735	T	C	0.1277	28382	1.29	1.25	1.34	3.34E-12
rs183132698	23	154353251	T	C	0.1608	28382	1.20	1.16	1.24	4.64E-08
rs185814586	23	154690417	C	G	0.8817	28382	0.76	0.73	0.79	2.37E-13
rs201543735	23	154323411	CT	C	0.1236	28382	1.29	1.24	1.33	1.13E-11
rs1050828	23	154536002	T	C	0.1063	28382	1.36	1.31	1.42	3.28E-15
rs146041456	23	154127943	A	G	0.8583	28382	0.82	0.79	0.85	1.53E-08
rs28370191	23	155023547	T	C	0.1505	28382	1.21	1.17	1.25	2.72E-08
rs762516	23	154536448	T	C	0.1417	28382	1.27	1.23	1.32	4.66E-12

Supplemental Table 6. Genome-wide Significant SNPs for the NH-European Ancestry Proliferative Diabetic Retinopathy GWAS.; CHR, build 38 chromosome; BP, build 38 position; EA, effect allele; OA, other allele; EAF, effect allele frequency; OR, odds ratio; LCI, lower 95% confidence interval; UCI, upper 95% confidence interval; p, two sided p value from the inverse variance-weighted meta-analysis.

rsID	CHR	BP	EA	OA	EAF	N	OR	LCI	UCI	P
rs5840289	20	8798197	G	GA	0.2515	38711	2.15	1.88	2.47	2.14E-08

Supplemental Table 7. λ_{GC} and LDSC Intercepts for Multi, NH-African, and NH-European Ancestry Analyses of Diabetic Retinopathy and Proliferative Diabetic Retinopathy

Outcome	Ancestry	λ_{GC}	LDSC Intercept	h^2
DR	Multi	1.0772	1.0468 (0.0083)	0.0234 (0.0057)
PDR	Multi	1.0957	1.0519 (0.0055)	0.0060 (0.0116)
DR	African	1.0225	0.9817 (0.0059)	0.0802 (0.0224)
PDR	African	1.1238	1.0555 (0.0067)	-0.0012 (0.0302)
DR	European	1.0405	0.9841 (0.0077)	0.0363 (0.0060)
PDR	European	1.1144	1.0462 (0.0065)	0.0533 (0.0269)

Supplemental Table 8. Significant Genetically Predicted Gene Expression Results for the Diabetic Retinopathy Multi Ancestry Analysis. Two sided p value from the linear regression of SNPs on model and the gene expression.

<u>Tissue</u>	<u>Gene</u>	<u>z score</u>	<u>Effect Size</u>	<u>p</u>	<u>SNPs Used</u>	<u>SNPs in Model</u>
Adipose Visceral Omentum	<i>SMIM9</i>	-12.611	-3.437	1.83E-36	2	2
Artery Aorta	<i>FLNA</i>	-11.439	-8.587	2.67E-30	2	4
Lung	<i>GAB3</i>	8.640	0.929	5.62E-18	5	5
Artery Tibial	<i>RENBP</i>	-8.627	-11.982	6.28E-18	3	6
Muscle Skeletal	<i>RENBP</i>	-7.895	-0.561	2.90E-15	5	7
EBV-transformed Lymphocytes	<i>G6PD</i>	-7.292	-0.388	3.05E-13	8	8
Heart Atrial Appendage	<i>RENBP</i>	-6.933	-0.769	4.13E-12	10	11
Esophagus Muscularis	<i>BRCC3</i>	6.677	1.048	2.43E-11	2	5
Esophagus Muscularis	<i>MTCP1</i>	5.778	0.893	7.58E-09	11	13
Brain Frontal Cortex	<i>RENBP</i>	-5.024	-0.257	5.07E-07	24	34
Skin Not Sun Exposed Suprapubic	<i>RENBP</i>	-4.962	-0.325	6.97E-07	9	9
Colon Transverse	<i>BRCC3</i>	4.894	1.418	9.88E-07	1	3

Supplemental Table 9. Significant Genetically Predicted Gene Expression Results for the Diabetic Retinopathy NH-African Ancestry Analysis. Two sided p value from the linear regression of SNPs on model and the gene expression.

<u>Tissue</u>	<u>Gene</u>	<u>z score</u>	<u>Effect Size</u>	<u>p</u>	<u>SNPs Used</u>	<u>SNPs in Model</u>
Artery Aorta	<i>FLNA</i>	-13.92	-12.77	5.01E-44	1	4
Adipose Visceral Omentum	<i>SMIM9</i>	-12.61	-3.44	1.83E-36	2	2
Artery Tibial	<i>RENBP</i>	-8.18	-12.04	2.76E-16	3	6
Lung	<i>GAB3</i>	7.51	0.51	5.83E-14	5	5
Muscle Skeletal	<i>RENBP</i>	-7.48	-0.56	7.37E-14	5	7
EBV-transformed Lymphocytes	<i>G6PD</i>	-7.11	-0.38	1.19E-12	8	8
Heart Atrial Appendage	<i>RENBP</i>	-6.36	-0.49	1.98E-10	10	11
Esophagus Muscularis	<i>BRCC3</i>	6.22	1.10	4.97E-10	2	5
Artery Tibial	<i>FLNA</i>	-5.73	-1.53	1.02E-08	4	7
Nerve Tibial	<i>RENBP</i>	-5.51	0.04	3.68E-08	33	41
Brain Frontal Cortex	<i>RENBP</i>	-5.12	0.09	2.98E-07	23	34
Muscle Skeletal	<i>EMD</i>	4.92	1.11	8.72E-07	22	30
Brain Cerebellum	<i>PLXNB3</i>	-4.81	-0.07	1.55E-06	69	95

Supplemental Table 10. Significant Genetically Predicted Gene Expression Results for the Proliferative Diabetic Retinopathy Multi Ancestry Analysis. Two sided p value from the linear regression of SNPs on model and the gene expression.

<u>Tissue</u>	<u>Gene</u>	<u>z score</u>	<u>Effect Size</u>	<u>p</u>	<u>SNPs Used</u>	<u>SNPs in Model</u>
Skin Not Sun Exposed Suprapubic	<i>IKBKGP1</i>	7.795	98.354	6.43E-15	2	13
Nerve Tibial	<i>VBP1</i>	6.123	3.978	9.18E-10	2	9
EBV-transformed Lymphocytes	<i>G6PD</i>	-5.950	-3.799	2.68E-09	3	8
Lung	<i>GAB3</i>	5.534	2.038	3.13E-08	3	5
Artery Aorta	<i>FLNA</i>	-5.176	-9.005	2.27E-07	1	4
Muscle Skeletal	<i>RENBP</i>	-4.975	-1.084	6.53E-07	2	7
Spleen	<i>TMEM187</i>	-4.847	-1.528	1.25E-06	6	31

Supplemental Table 11. Significant Genetically Predicted Gene Expression Results for the Proliferative Diabetic Retinopathy NH-African Ancestry Analysis. Two sided p value from the linear regression of SNPs on model and the gene expression.

Tissue	Gene	z score	Effect Size	p	SNPs Used	SNPs in Model
Skin Not Sun Exposed Suprapubic	<i>IKBKGP1</i>	7.795	98.354	6.43E-15	2	13
Uterus	<i>FAM50A</i>	-6.911	-2.320	4.81E-12	4	43
Spleen	<i>TAZ</i>	6.803	5.862	1.03E-11	4	32
Skin Sun Exposed Lower Leg	<i>TAZ</i>	6.789	7.661	1.13E-11	1	17
Cells Cultured Fibroblasts	<i>LAGE3</i>	-6.604	-7.127	4.01E-11	5	34
EBV-transformed Lymphocytes	<i>G6PD</i>	-6.383	-4.267	1.74E-10	1	8
Tibial Nerve	<i>VBP1</i>	6.179	3.943	6.43E-10	2	9
Cells Cultured Fibroblasts	<i>ATP6AP1</i>	5.465	3.349	4.64E-08	1	18
Lung	<i>GAB3</i>	5.410	2.064	6.31E-08	2	5
Brain Putamen Basal Ganglia	<i>RENBP</i>	-5.375	-2.734	7.65E-08	11	40
Artery Aorta	<i>FLNA</i>	-5.176	-9.005	2.27E-07	1	4
Uterus	<i>SSR4</i>	5.021	2.511	5.13E-07	5	69
Colon Transverse	<i>L1CAM</i>	4.978	1.649	6.43E-07	3	16
Muscle Skeletal	<i>RENBP</i>	-4.975	-1.084	6.53E-07	2	7

Supplemental Table 12. Sensitivity Analyses of rs1050828 in Men and Women of NH-African Ancestry in the MVP. SNP, rsID; EA, effect allele; EAF, effect allele frequency; OR (95% CI), odds ratio and 95% confidence interval; p, two-sided p value from a logistic regression of SNP - DR associations.

Sex	Cases	Controls	SNP	EA	EAF	OR (95% CI)	p
Male	13,371	19,911	rs1050828	T	0.093	1.46 (1.40 – 1.52)	7.52 x 10 ⁻⁶⁷
Female	984	2467			0.097	1.54 (1.27 – 1.88)	1.38 x 10 ⁻⁰⁵

Supplemental Table 13. Mean HbA1c and Random Plasma Glucose by Diabetic Retinopathy Status and G6PDd Risk Allele in Men of NH-African Ancestry Post Diabetes Diagnosis. Differences estimated with one-way ANOVA.

Sample	G6PDd Allele	n	HbA1c %	p	Glucose mg/dL	p
No Diabetic Retinopathy	C	18488	7.29 ± 1.14	–	145 ± 42	–
	T	1737	6.72 ± 1.04		169 ± 47	1.59 x 10 ⁻⁸⁵
Diabetic Retinopathy	C	12045	8.22 ± 1.35	–	171 ± 45	–
	T	1414	7.27 ± 1.06		185 ± 43	1.61 x 10 ⁻²⁸
No Diabetic Retinopathy	C	18488	7.29 ± 1.14	0.46	145 ± 42	4.93 x 10 ⁻¹⁸⁶
Diabetic Retinopathy	T	1414	7.27 ± 1.06		185 ± 43	

Supplemental Table 14. Mean HbA1c and Random Plasma Glucose by G6PDdef Risk Allele in Men of NH-African Ancestry a Year Prior to Diabetes Diagnosis, a Year Prior to Insulin Prescription, and Post Diabetes Diagnosis. Differences estimated with two-sided T-test.

Sample	rs1050828	365 Days Prior to Diabetes Diagnosis				
		<u>n</u>	<u>HbA1c %</u>	<u>p</u>	<u>Glucose mg/dL</u>	<u>p</u>
Men of African Ancestry	C	11455	7.06 ± 1.41	–	135 ± 50	–
	T	1011	6.70 ± 1.58	6.05 x 10 ⁻¹²	165 ± 63	1.12 x 10 ⁻⁴⁶
365 Days Prior to Insulin Prescription						
		<u>n</u>	<u>HbA1c %</u>	<u>p</u>	<u>Glucose mg/dL</u>	<u>p</u>
Men of African Ancestry	C	11503	9.48 ± 2.16	–	223 ± 83	–
	T	1306	8.35 ± 2.00	2.50 x 10 ⁻⁷⁴	242 ± 84	2.81 x 10 ⁻¹⁴
Post Diabetes Diagnosis						
		<u>n</u>	<u>HbA1c %</u>	<u>p</u>	<u>Glucose mg/dL</u>	<u>p</u>
Men of African Ancestry	C	30533	7.65 ± 1.31	–	155 ± 45	–
	T	3151	6.96 ± 1.08	9.02 x 10 ⁻²¹⁹	176 ± 45	7.79 x 10 ⁻¹²¹

Supplemental Table 15. Mediation Results for the G6PDd Risk Allele and Plasma Glucose on Diabetic Retinopathy in Men of NH-African Ancestry in the MVP. Two-sided.

Output	Estimate	SE	OR	LCI	UCI	p
ACME (control)	0.0234	0.0024	1.0237	1.0212	1.0261	<2e-16
ACME (treated)	0.0234	0.0023	1.0237	1.0213	1.0261	<2e-16
ADE (control)	0.0003	0.0080	1.0003	0.9924	1.0083	0.95
ADE (treated)	0.0003	0.0081	1.0003	0.9922	1.0084	0.95
Total Effect	0.0237	0.0083	1.0239	1.0155	1.0325	<2e-16
Prop. Mediated (control)	0.9922	0.2759	2.6972	2.0468	3.5543	<2e-16
Prop. Mediated (treated)	0.9923	0.2726	2.6975	2.0538	3.5429	<2e-16
ACME (average)	0.0234	0.0024	1.0237	1.0212	1.0261	<2e-16
ADE (average)	0.0003	0.0080	1.0003	0.9923	1.0083	0.95
Prop. Mediated (average)	0.9923	0.2743	-	-	-	<2e-16

Supplemental Table 16. Mediation Results for the G6PDdef Risk Allele and Plasma Glucose on Diabetic Retinopathy in Women of NH-African Ancestry in the MVP. Two-sided

Output	Estimate	SE	OR	LCI	UCI	p
ACME (control)	0.0387	0.0125	1.0395	1.0265	1.0525	<2e-16
ACME (treated)	0.0395	0.0125	1.0403	1.0274	1.0534	<2e-16
ADE (control)	0.0123	0.0332	1.0124	0.9793	1.0466	0.574
ADE (treated)	0.0131	0.0354	1.0132	0.9779	1.0497	0.574
Total Effect	0.0518	0.0381	1.0532	1.0138	1.0941	0.002
Prop. Mediated (control)	0.7463	0.3380	2.1092	1.5043	2.9574	0.002
Prop. Mediated (treated)	0.7624	0.3213	2.1434	1.5544	2.9556	0.002
ACME (average)	0.0391	0.0125	1.0399	1.0270	1.0530	<2e-16
ADE (average)	0.0127	0.0343	1.0128	0.9786	1.0481	0.574
Prop. Mediated (average)	0.7544	0.3314	-	-	-	0.002

Supplemental Table 17. Mean HbA1c and Fasting Plasma Glucose by G6PDdef Risk Allele in Men of NH-African Ancestry at enrollment in the ACCORD clinical trial. Differences estimated with two-sided T-test.

At Clinical Trial Enrollment						
Sample	rs1050828	n	HbA1c %	p	Glucose mg/dL	p
Men of African Ancestry	C	611	8.58 ± 1.14	–	166 ± 61	–
	T	40	8.05 ± 1.24	0.012	190 ± 60	0.015

Supplemental Table 18. Results of the Cox Proportional Hazards Model for the Effect of the G6PDdef Risk Allele on Diabetic Retinopathy in Individuals of NH-African ancestry in ACCORD. The p values are calculated from the Wald

Outcome	Predictor	HR (95% CI)	n Events with rs1050828_T	p
Photocoagulation, vitrectomy, renal failure, ESRD, or SCr>3.3		1.61 (1.41 – 1.82)	38	2.07 x 10 ⁻⁰⁴
Photocoagulation or vitrectomy		1.78 (1.56 – 2.04)	34	1.95 x 10 ⁻⁰⁵
3-line change in visual acuity		1.09 (0.99 – 1.20)	64	0.37
MNSI score >2.0		1.05 (0.95 – 1.17)	53	0.63
Vibratory sensation loss	rs1050828 - T	1.37 (1.22 – 1.53)	39	5.45 x 10 ⁻³
Ankle jerk loss		1.11 (1.01 – 1.23)	58	0.29
Pressure sensation loss		1.06 (0.90 – 1.24)	21	0.74
SCr doubling or >20 mL per min decrease in eGFR		1.07 (0.99 – 1.15)	108	0.40
Any of Nephropathy Outcomes 1-3		1.19 (1.09 – 1.30)	77	0.054

Supplemental Table 19. Effect of Medication Use on the Association Between G6PDdef Risk Allele and Diabetes Complications in individuals of Non-Hispanic African Ancestry in ACCORD with a Cox Proportional Hazards Model. The p values are calculated from the Wald. statistic

Outcome	Adjustment	HR	Lower	Upper	p
Diabetic Retinopathy	None	1.79	1.56	2.05	2.00E-05
	All Meds	1.82	1.58	2.09	2.56E-05
	Insulin	1.77	1.54	2.04	3.44E-05
	Metformin	1.76	1.53	2.02	4.29E-05
	TZD	1.78	1.55	2.04	2.99E-05
	Sulfonylurea	1.74	1.52	2.00	6.31E-05
	Treatment Arm	1.81	1.58	2.08	1.95E-05
Diabetic Neuropathy	None	1.36	1.21	1.52	8.30E-03
	All Meds	1.39	1.24	1.56	4.43E-03
	Insulin	1.38	1.23	1.55	4.21E-03
	Metformin	1.39	1.24	1.55	3.69E-03
	TZD	1.38	1.23	1.54	4.56E-03
	Sulfonylurea	1.37	1.22	1.53	5.90E-03
	Treatment Arm	1.40	1.25	1.57	3.38E-03
Composite	None	1.61	1.41	1.83	2.40E-04
	All Meds	1.62	1.42	1.85	2.50E-04
	Insulin	1.61	1.41	1.83	2.47E-04
	Metformin	1.58	1.39	1.80	3.97E-04
	TZD	1.61	1.41	1.83	2.45E-04
	Sulfonylurea	1.58	1.38	1.79	4.81E-04
	Treatment Arm	1.64	1.44	1.87	1.47E-04

Supplemental Table 20. Crude Excess Risk of the G6PDd Allele on Diabetic Nephropathy and Diabetic Retinopathy in Men of NH-African Ancestry

Incident Complication	rs1050828 Carrier with Complication	rs1050828 Carrier without Complication	Non-rs1050828 Carrier with Complication	Non-rs1050828 Carrier without Complication	Crude Excess Risk
Diabetic Neuropathy	17	20	124	421	232 per 1,000 individuals
Diabetic Retinopathy	8	32	49	553	119 per 1,000 individuals

Supplemental Table 21.A. Risk Difference, NNT, and Variations on NNS of Diabetic Retinopathy for G6PDdef Risk Allele in Individuals with NH-African Ancestry and Subsequent Estimates. Two-sided.

		Genotype Frequency	Crude (RD (95%CI))	p	Adjusted (RD (95%CI))	p
Homozygous Def Women	RD (95% CI)		0.3084 (0.0038, 0.6130)		0.2084 (0, 0.3877)	
	NNT (95% CI)	1.81%	3.2 (2.4, 262.0)	0.047	4.8 (2.2, UBNE)	0.11
	NNS_D (95% CI)		179.0 (90.0, 14,463.7)		264.9 (119.3, UBNE)	
Heterozygous Def Women	RD (95% CI)		0.0778 (0.0038, 0.1481)		0.0844 (0.0141, 0.1547)	
	NNT (95% CI)	23.30%	12.9 (6.8, 133.8)	0.030	11.8 (6.5, 71.0)	0.019
	NNS_D (95% CI)		55.2 (29.0, 574.3)		50.9 (27.7, 305.0)	
Women Overall**	RD (95% CI)		-		-	
	NNT (95% CI)	-	12.2 (6.7, 75.7)	-	11.4 (6.4, 50.4)	-
	NNS_D (95% CI)		48.7 (26.5, 301.7)		45.5 (25.6, 200.7)	
	NNS_AFR (95% CI)		383.8 (208.8, 2,375.4)		357.9 (201.8, 1,580.6)	
	RD (95% CI)		0.1187 (0, 0.2446)		0.1334 (0.0027, 0.2641)	
	NNT (95% CI)		8.4 (4.1, UBNE)		7.5 (3.8, 372.1)	
Men Overall	NNS_D(95% CI)	13.46%	62.6 (30.4, UBNE)	0.065	55.7 (28.1, 2,764.4)	0.045
	NNS_AFR (95% CI)		466.9 (226.7, UBNE)		415.6 (209.9, 20,629.9)	
	RD (95% CI)		-		-	
Men and Women Overall***	NNT (95% CI)	-	11.1 (6.1, 65.8)	-	10.3 (5.7, 49.1)	-
	NNS_D (95% CI)		57.4 (31.3, 340.5)		53.2 (29.7, 254.1)	
	NNS_AFR (95% CI)		439.7 (240.1, 2,609.8)		407.4 (227.5, 1,947.5)	

Supplemental Table 21.B. Risk Difference, NNT, and Variations on NNS of Diabetic Retinopathy for G6PDdef Risk Allele in Individuals with NH-African Ancestry and Subsequent Estimates: Using Combined Estimate for Hemi/Homozygous. two-sided.

		Genotype Frequency	Crude (RD (95%CI))	p	Adjusted (RD (95%CI))	p
Homozygous Def Women	RD (95% CI)		0.1538 (0.0344, 0.2733)		0.1658 (0.0445, 0.2871)	
	NNT (95% CI)	1.81%	6.5 (3.7, 29.1)	0.012	6.0 (3.5, 22.5)	0.074
	NNS_D (95% CI)		358.8 (202.0, 1,606.6)		332.9 (192.2, 1,241.1)	
Heterozygous Def Women	RD (95% CI)		0.0778 (0.0038, 0.1481)		0.0844 (0.0141, 0.1547)	
	NNT (95% CI)	23.30%	12.9 (6.8, 133.8)	0.030	11.8 (6.5, 71.0)	0.019
	NNS_D (95% CI)		55.2 (29.0, 574.3)		50.9 (27.7, 305.0)	
Women Overall**	RD (95% CI)		-		-	
	NNT (95% CI)	-	10.3 (6.3, 27.2)	-	9.5 (6.0, 22.7)	-
	NNS_D (95% CI)		40.9 (25.2, 108.4)		38.0 (24.0, 90.5)	
	NNS_AFR (95% CI)		322.2 (198.6, 853.4)		299.0 (189.2, 712.3)	
	RD (95% CI)		0.1538 (0.0344, 0.2733)		0.1658 (0.0445, 0.2871)	
Men Overall	NNT (95% CI)	13.46%	6.5 (3.7, 29.1)	0.012	6.0 (3.5, 22.5)	0.074
	NNS_D(95% CI)		48.3 (27.2, 216.2)		44.8 (25.9, 167.0)	
	NNS_AFR (95% CI)		360.4 (202.9, 1,613.7)		334.4 (193.1, 1,246.6)	
Men and Women Overall***	RD (95% CI)		-		-	
	NNT (95% CI)	-	9.2 (5.9, 20.7)	-	8.5 (5.6, 17.8)	-
	NNS_D (95% CI)		47.5 (30.5, 107.1)		44.2 (29.1, 91.9)	
	NNS_AFR (95% CI)		0.1538 (0.0344, 0.2733)		338.6 (222.8, 704.6)	

**Represents meta-analyzed RD estimates from homozygous and heterozygous deficient analyses for women

***Represents meta-analyzed RD estimates from homozygous and heterozygous deficient analyses for women and hemizygous men

#Represents genotype frequency estimates from the ACCORD Clinical Trial presented for homozygous deficient in women, heterozygous deficient in women and hemizygous deficient in men

NNT = Number needed to treat: Number of African ancestry individuals with diabetes and the G6PD variant that require adequate hyperglycemia management to prevent one neuropathy case

NNS_D = Number needed to screen: Number of African ancestry individuals with diabetes that need to be screened to identify individuals with G6PD variant and hyperglycemia managed adequately to prevent one neuropathy case

NNS_AFR = Number needed to screen: Number of African ancestry individuals that need to be screened to identify diabetics, and those with G6PD variant, and whose hyperglycemia needs to be managed adequately to prevent one neuropathy case

UBNE = Upper bound not estimable

Supplemental Table 22.A. Risk Difference, NNT, and Variations on NNS of Diabetic Neuropathy for G6PDdef Risk Allele in Individuals with NH-African Ancestry and Subsequent Estimates. Two-sided.

		Genotype Frequency	Crude (RD (95%CI))	<i>p</i>	Adjusted (RD (95%CI))	<i>p</i>
Homozygous Def Women	RD (95% CI)		0.0495 (0, 0.3232)		0.0049 (0, 0.2161)	
	NNT (95% CI)	1.81%	20.2 (3.1, UBNE)	0.72	205.8 (4.4, UBNE)	0.95
	NNS_D (95% CI)		1,114.5 (170.8, UBNE)		11,357.9 (241.2, UBNE)	
Heterozygous Def Women	RD (95% CI)		0.0059 (0, 0.0842)		0.0168 (0, 0.0952)	
	NNT (95% CI)	23.30%	170.1 (11.9, UBNE)	0.88	59.6 (10.5, UBNE)	0.68
	NNS_D (95% CI)		730.0 (51.0, UBNE)		255.8 (45.1, UBNE)	
Women Overall**	RD (95% CI)		-		-	
	NNT (95% CI)	-	62.5 (11.0, UBNE)	-	36.5 (9.9, UBNE)	-
	NNS_D (95% CI)		248.8 (43.6, UBNE)		145.2 (39.3, UBNE)	
Men Overall	NNS_AFR (95% CI)		1,959.3 (343.5, UBNE)		1,143.3 (309.1, UBNE)	
	RD (95% CI)		0.2324 (0.0680, 0.3967)		0.2454 (0.0840, 0.5068)	
	NNT (95% CI)	13.46%	4.3 (2.5, 14.7)	0.0056	4.1 (2.5, 11.9)	0.0029
Men and Women Overall***	NNS_D(95% CI)		32.0 (18.7, 109.3)		30.3 (18.3, 88.5)	
	NNS_AFR (95% CI)		238.6 (139.8, 815.8)		225.9 (136.3, 660.1)	
	RD (95% CI)		-		-	
Men and Women Overall***	NNT (95% CI)	-	18.7 (6.5, UBNE)	-	15.3 (5.9, UBNE)	-
	NNS_D (95% CI)		96.6 (33.6, UBNE)		79.2 (30.6, UBNE)	
	NNS_AFR (95% CI)		740.8 (257.3, UBNE)		607.1 (234.8, UBNE)	

Supplemental Table 22.B. Risk Difference, NNT, and Variations on NNS of Diabetic Neuropathy for G6PDdef Risk Allele in Individuals with NH-African Ancestry and Subsequent Estimates: Using Combined Estimate for Hemi/Homozygous. Two-sided.

		Genotype Frequency	Crude (RD (95%CI))	<i>p</i>	Adjusted (RD (95%CI))	<i>p</i>
Homozygous Def Women	RD (95% CI)*		0.2119 (0.0675, 0.3562)		0.1905 (0.0522, 0.3287)	
	NNT (95% CI)	1.81%	4.7 (3.5, 7.3)	0.0040	5.3 (3.0, 19.2)	0.0069
	NNS_D (95% CI)		260.5 (192.4, 403.2)		289.8 (167.9, 1,057.2)	
Heterozygous Def Women	RD (95% CI)		0.0059 (0, 0.0842)		0.0168 (0, 0.0952)	
	NNT (95% CI)	23.30%	170.1 (11.9, UBNE)	0.88	59.6 (10.5, UBNE)	0.68
	NNS_D (95% CI)		730.0 (51.0, UBNE)		255.8 (45.1, UBNE)	
Women Overall**	RD (95% CI)		-		-	
	NNT (95% CI)	-	8.8 (6.0, 16.9)	-	16.9 (7.9, UBNE)	-
	NNS_D (95% CI)		35.1 (23.8, 67.3)		67.4 (31.3, UBNE)	
Men Overall	NNS_AFR (95% CI)		276.6 (187.2, 529.8)		530.8 (246.4, UBNE)	
	RD (95% CI)*		0.2119 (0.0675, 0.3562)		0.1905 (0.0522, 0.3287)	
	NNT (95% CI)	13.46%	4.7 (3.5, 7.3)	0.0040	5.3 (3.0, 19.2)	0.0029
Men and Women Overall***	NNS_D(95% CI)		35.1 (25.9, 54.3)		39.0 (22.6, 142.3)	
	NNS_AFR (95% CI)		261.7 (193.3, 405.0)		291.1 (168.7, 1,061.9)	
	RD (95% CI)		-		-	
Men and Women Overall***	NNT (95% CI)	-	6.8 (5.0, 10.8)	-	11.8 (6.5, 60.3)	-
	NNS_D (95% CI)		35.2 (25.7, 55.6)		61.0 (33.8, 311.9)	
	NNS_AFR (95% CI)		269.5 (197.0, 426.5)		467.5 (259.1, 2,390.8)	

*To circumvent estimates with small sample sizes, combined hemizygous for men and homozygous for women estimates were used here.

**Represents meta-analyzed RD estimates from homozygous and heterozygous deficient analyses for women

***Represents meta-analyzed RD estimates from homozygous and heterozygous deficient analyses for women and hemizygous men

#Represents genotype frequency estimates from the ACCORD Clinical Trial presented for homozygous deficient in women, heterozygous deficient in women and hemizygous deficient in men

NNT = Number needed to treat: Number of African ancestry individuals with diabetes and the G6PD variant that require adequate hyperglycemia management to prevent one neuropathy case

NNS_D = Number needed to screen: Number of African ancestry individuals with diabetes that need to be screened to identify individuals with G6PD variant and hyperglycemia managed adequately to prevent one neuropathy case

NNS_AFR = Number needed to screen: Number of African ancestry individuals that need to be screened to identify diabetics, and those with G6PD variant, and whose hyperglycemia needs to be managed adequately to prevent one neuropathy case

Supplemental Table 23. African-Ancestry Phenome-Wide Association Study for the G6PDd Risk Allele in individuals with diabetes adjusted for age, sex, and the top 10 principal components. All p values are computed from associations between PheCodes and G6PDdef status as dependent variables in logistic regression models

PheCode	Phenotype	Phenotype Group	OR	LCI	UCI	p	N Cases	N Controls
282.9	Other hereditary hemolytic anemias	hematopoietic	4.61	4.32	4.92	3.90E-121	274	33008
282	Hereditary hemolytic anemias	hematopoietic	1.66	1.60	1.72	8.61E-47	1334	33065
285	Other anemias	hematopoietic	1.24	1.22	1.27	2.11E-30	15726	18673
281.9	Deficiency anemias	hematopoietic	1.49	1.42	1.55	5.69E-20	955	32327
285.2	Anemia of chronic disease	hematopoietic	1.20	1.17	1.22	7.42E-15	5581	28818
285.21	Anemia in chronic kidney disease	hematopoietic	1.21	1.17	1.24	2.48E-12	3757	30642
271.9	Other disorders of carbohydrate transport and metabolism	endocrine/metabolic	1.79	1.63	1.96	3.92E-10	159	33123
585.1	Acute renal failure	genitourinary	1.12	1.10	1.14	2.14E-09	11171	23228
585.34	Chronic Kidney Disease, Stage IV	genitourinary	1.18	1.15	1.22	9.27E-09	3067	31332
250.7	Diabetic retinopathy	endocrine/metabolic	1.12	1.10	1.14	1.36E-08	14220	20179
250.23	Type 2 diabetes with ophthalmic manifestations	endocrine/metabolic	1.11	1.09	1.14	2.51E-08	14065	20334
281	Other deficiency anemia	hematopoietic	1.19	1.15	1.23	3.08E-08	2640	31759
401.22	Hypertensive chronic kidney disease	circulatory system	1.11	1.09	1.14	6.39E-08	9584	24815
585	Renal failure	genitourinary	1.10	1.08	1.12	2.60E-07	16703	17696
401.2	Hypertensive heart and/or renal disease	circulatory system	1.10	1.08	1.12	2.75E-07	14182	20217
573.5	Jaundice (not of newborn)	digestive	1.41	1.32	1.51	4.40E-07	396	32886
276	Disorders of fluid, electrolyte, and acid-base balance	endocrine/metabolic	1.10	1.07	1.12	1.14E-06	15009	19390
585.33	Chronic Kidney Disease, Stage III	genitourinary	1.11	1.08	1.13	1.40E-06	8312	26087
428.4	Heart failure with preserved EF [Diastolic heart failure]	circulatory system	1.13	1.10	1.16	1.75E-06	4484	29915
271.3	Intestinal disaccharidase deficiencies and disaccharide malabsorption	endocrine/metabolic	0.80	0.76	0.84	2.20E-06	1958	31324
574	Cholelithiasis and cholecystitis	digestive	1.16	1.13	1.20	2.65E-06	2625	31774
428	Congestive heart failure; non-hypertensive	circulatory system	1.10	1.08	1.12	3.01E-06	9537	24862
585.3	Chronic renal failure [CKD]	genitourinary	1.09	1.07	1.11	3.13E-06	12192	22207
276.1	Electrolyte imbalance	endocrine/metabolic	1.09	1.07	1.11	4.59E-06	11902	22497
420	Carditis	circulatory system	1.18	1.14	1.23	6.31E-06	1787	32612
585.32	End stage renal disease	genitourinary	1.15	1.12	1.19	8.01E-06	2697	31702
588	Disorders resulting from impaired renal function	genitourinary	1.14	1.11	1.18	1.25E-05	2916	31483
38	Septicemia	infectious diseases	1.12	1.09	1.15	1.82E-05	4368	30031
365.1	Open-angle glaucoma	sense organs	1.08	1.06	1.11	2.13E-05	13962	20437
270.32	Paraproteinemia	endocrine/metabolic	1.23	1.17	1.29	2.37E-05	987	32295

Supplemental Table 24. African-Ancestry Phenome-Wide Association Study for the G6PDd Risk Allele in individuals without diabetes adjusted for age, sex, and the top 10 principal components. All p values are computed from associations between PheCodes and G6PDdef status as dependent variables in logistic regression models.

PheCode	Phenotype	Phenotype Group	OR	LCI	UCI	p	N Cases	N Controls
282.9	Other hereditary hemolytic anemias	hematopoietic	5.33	5.06	5.62	3.73E-222	693	56747
282	Hereditary hemolytic anemias	hematopoietic	1.90	1.85	1.95	2.52E-147	2021	55419
271.3	Intestinal disaccharidase deficiencies and disaccharide malabsorption	endocrine/metabolic	0.43	0.41	0.45	3.77E-83	4339	48674
271	Disorders of carbohydrate transport and metabolism	endocrine/metabolic	0.51	0.49	0.53	1.59E-73	4451	48562
250.4	Abnormal glucose	endocrine/metabolic	0.72	0.71	0.74	8.86E-66	10092	42921
250.41	Impaired fasting glucose	endocrine/metabolic	0.71	0.70	0.73	4.33E-43	5901	47112
277.6	Other deficiencies of circulating enzymes	endocrine/metabolic	4.09	3.68	4.54	1.22E-40	112	52901
285	Other anemias	hematopoietic	1.20	1.18	1.21	1.84E-40	15825	41615
250.42	Other abnormal glucose	endocrine/metabolic	0.75	0.73	0.77	3.50E-32	5646	47367
281.9	Deficiency anemias	hematopoietic	1.47	1.42	1.52	6.28E-30	1194	51819
281	Other deficiency anemia	hematopoietic	1.24	1.22	1.27	4.24E-22	3390	54050
271.9	Other disorders of carbohydrate transport and metabolism	endocrine/metabolic	2.31	2.11	2.52	1.32E-20	126	52887
277.4	Disorders of bilirubin excretion	endocrine/metabolic	1.48	1.42	1.55	1.24E-19	714	52299
289	Other diseases of blood and blood-forming organs	hematopoietic	1.24	1.19	1.28	3.31E-10	1448	55992
573.5	Jaundice (not of newborn)	digestive	1.33	1.27	1.40	1.03E-08	606	56834
285.2	Anemia of chronic disease	hematopoietic	1.13	1.11	1.16	9.14E-08	3612	53828
281.13	Folate-deficiency anemia	hematopoietic	1.33	1.25	1.41	8.23E-07	433	52580
278.1	Obesity	endocrine/metabolic	1.06	1.05	1.07	4.21E-06	19678	37762
281.1	Megaloblastic anemia	hematopoietic	1.13	1.10	1.16	1.19E-05	2301	55139
961.1	Poisoning/allergy of sulfonamides	injuries & poisonings	1.48	1.35	1.62	1.85E-05	156	52857
574	Cholelithiasis and cholecystitis	digestive	1.14	1.10	1.17	2.28E-05	2075	55365
327.3	Sleep apnea	neurological	1.06	1.04	1.07	2.66E-05	18597	38843

Supplemental Table 25. ICD Codes included in the identification of Diabetic Retinopathy in the UK Biobank

Retinopathy ICD9		Retinopathy ICD10				
362	E08.3	E08.37X9	E09.37X2	E10.37	E11.3599	E13.3592
362.01	E08.31	E08.39	E09.37X3	E10.37X1	E11.36	E13.3593
362.02	E08.311	E09.3	E09.37X9	E10.37X2	E11.37	E13.3599
362.03	E08.319	E09.31	E09.39	E10.37X3	E11.37X1	E13.36
362.04	E08.32	E09.311	E10.3	E10.37X9	E11.37X2	E13.37
362.05	E08.321	E09.319	E10.31	E10.39	E11.37X3	E13.37X1
362.06	E08.3211	E09.32	E10.311	E11.3	E11.37X9	E13.37X2
362.07	E08.3212	E09.321	E10.319	E11.31	E11.39	E13.37X3
	E08.3213	E09.3211	E10.32	E11.311	E13.3	E13.37X9
	E08.3219	E09.3212	E10.321	E11.319	E13.31	E13.39
	E08.329	E09.3213	E10.3211	E11.32	E13.311	
	E08.3291	E09.3219	E10.3212	E11.321	E13.319	
	E08.3292	E09.329	E10.3213	E11.3211	E13.32	
	E08.3293	E09.3291	E10.3219	E11.3212	E13.321	
	E08.3299	E09.3292	E10.329	E11.3213	E13.3211	
	E08.33	E09.3293	E10.3291	E11.3219	E13.3212	
	E08.331	E09.3299	E10.3292	E11.329	E13.3213	
	E08.3311	E09.33	E10.3293	E11.3291	E13.3219	
	E08.3312	E09.331	E10.3299	E11.3292	E13.329	
	E08.3313	E09.3311	E10.33	E11.3293	E13.3291	
	E08.3319	E09.3312	E10.331	E11.3299	E13.3292	
	E08.339	E09.3313	E10.3311	E11.33	E13.3293	
	E08.3391	E09.3319	E10.3312	E11.331	E13.3299	
	E08.3392	E09.339	E10.3313	E11.3311	E13.33	
	E08.3393	E09.3391	E10.3319	E11.3312	E13.331	
	E08.3399	E09.3392	E10.339	E11.3313	E13.3311	
	E08.34	E09.3393	E10.3391	E11.3319	E13.3312	
	E08.341	E09.3399	E10.3392	E11.339	E13.3313	
	E08.3411	E09.34	E10.3393	E11.3391	E13.3319	
	E08.3412	E09.341	E10.3399	E11.3392	E13.339	
	E08.3413	E09.3411	E10.34	E11.3393	E13.3391	
	E08.3419	E09.3412	E10.341	E11.3399	E13.3392	
	E08.349	E09.3413	E10.3411	E11.34	E13.3393	
	E08.3491	E09.3419	E10.3412	E11.341	E13.3399	
	E08.3492	E09.349	E10.3413	E11.3411	E13.34	
	E08.3493	E09.3491	E10.3419	E11.3412	E13.341	
	E08.3499	E09.3492	E10.349	E11.3413	E13.3411	
	E08.35	E09.3493	E10.3491	E11.3419	E13.3412	
	E08.351	E09.3499	E10.3492	E11.349	E13.3413	
	E08.3511	E09.35	E10.3493	E11.3491	E13.3419	
	E08.3512	E09.351	E10.3499	E11.3492	E13.349	
	E08.3513	E09.3511	E10.35	E11.3493	E13.3491	
	E08.3519	E09.3512	E10.351	E11.3499	E13.3492	

E08.352	E09.3513	E10.3511	E11.35	E13.3493
E08.3521	E09.3519	E10.3512	E11.351	E13.3499
E08.3522	E09.352	E10.3513	E11.3511	E13.35
E08.3523	E09.3521	E10.3519	E11.3512	E13.351
E08.3529	E09.3522	E10.352	E11.3513	E13.3511
E08.353	E09.3523	E10.3521	E11.3519	E13.3512
E08.3531	E09.3529	E10.3522	E11.352	E13.3513
E08.3532	E09.353	E10.3523	E11.3521	E13.3519
E08.3533	E09.3531	E10.3529	E11.3522	E13.352
E08.3539	E09.3532	E10.353	E11.3523	E13.3521
E08.354	E09.3533	E10.3531	E11.3529	E13.3522
E08.3541	E09.3539	E10.3532	E11.353	E13.3523
E08.3542	E09.354	E10.3533	E11.3531	E13.3529
E08.3543	E09.3541	E10.3539	E11.3532	E13.353
E08.3549	E09.3542	E10.354	E11.3533	E13.3531
E08.355	E09.3543	E10.3541	E11.3539	E13.3532
E08.3551	E09.3549	E10.3542	E11.354	E13.3533
E08.3552	E09.355	E10.3543	E11.3541	E13.3539
E08.3553	E09.3551	E10.3549	E11.3542	E13.354
E08.3559	E09.3552	E10.355	E11.3543	E13.3541
E08.359	E09.3553	E10.3551	E11.3549	E13.3542
E08.3591	E09.3559	E10.3552	E11.355	E13.3543
E08.3592	E09.359	E10.3553	E11.3551	E13.3549
E08.3593	E09.3591	E10.3559	E11.3552	E13.355
E08.3599	E09.3592	E10.359	E11.3553	E13.3551
E08.36	E09.3593	E10.3591	E11.3559	E13.3552
E08.37	E09.3599	E10.3592	E11.359	E13.3553
E08.37X1	E09.36	E10.3593	E11.3591	E13.3559
E08.37X2	E09.37	E10.3599	E11.3592	E13.359
E08.37X3	E09.37X1	E10.36	E11.3593	E13.3591