Supporting Information

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SI Methods

Informed Consent. All participants gave written informed consent, and the protocols were reviewed and approved by local institutional review boards.

Study Design. The participants in the original genome-wide association study were mainly collected at the University of Michigan in Ann Arbor (collection coordinated by A.S.), at the University of Pennsylvania in Philadelphia (coordinated by D.S.), and at the Mayo Clinic in Rochester, MN (coordinated by A.E.). Cases were classified according to age-related macular degeneration (AMD) diagnosis in the worse eye (neovascularization was considered to be the most severe outcome, large drusen were the least severe outcome). Controls were examined by an ophthalmologist and exhibited no signs of AMD in either eye (they had no large or intermediate drusen).

Genotyping. Genotyping used Illumina Human370 Bead Chips and the Illumina Infinium II assay protocol (1). Allele cluster definitions for each SNP were determined using Illumina BeadStudio Genotyping Module version 3.2.32 and the combined intensity data from 99% of the samples; the resulting cluster definitions were then used on all samples. Genotypes were not called if the quality threshold (gencall score) was <0.25. Genotypes were not released from the Center for Inherited Disease Research (CIDR) for SNPs that failed technical filters for call rate <85%, >1 HapMap replicate error, and >4% (autosomal) difference in call rate between sexes. Genotypes were released from CIDR for 344,942 (99.46%) of the attempted SNPs. Blind duplicate reproducibility was 99.992%.

Genotype Imputation. To expand the genome coverage, we performed a genome-wide imputation using haplotypes from the HapMap CEU samples as templates (release 22). Imputation was performed using MACH (www.sph.umich.edu/csg/abecasis/Mach/). For downstream analyses, we filtered out poorly imputed SNPs and focused on markers with estimated r^2 between imputed and true genotypes >0.3.

Statistical Analyses. To investigate the association between each genotyped or imputed SNP and AMD, we first carried out a logistic regression for each SNP assuming the additive model and adjusting for the top two principal components of ancestry (PCA). At $P < 10^{-6}$, we identified a total of seven independently associated SNPs in previously reported loci (*CFH*, *ARMS2*, *C3*, *C2*/*CFB*, and *CFI*). These SNPs were included as covariates in logistic regression analyses designed to identify additional loci associated with AMD.

Analysis for Follow-Up Study. To combine the statistics across different groups for replication, we first selected an arbitrary reference allele for each marker and then calculated a z statistic summarizing the evidence for association in each study (summarizing both the P value, in its magnitude, and the direction of effect, in its sign). We then calculated an overall z statistic as a weighted average of the individual statistics and calculated the corresponding P value. Weights were proportional to the square root of effective sample size for each study and were selected such that the sum of squared weights = 1.0.

Association Testing. Association tests compared allele frequencies between cases and controls for each sample. For samples including only unrelated individuals, the data were also analyzed using simple logistic regression models with age and sex as covariates to verify robustness of results. For the discovery samples, the first two PCAs were used as covariates in all reported analyses, and genotypes for the markers listed in Table 2 (main text) were used as covariates in analyses designed to discover previously uncharacterized loci. For follow-up samples, genotypes at *CFH* and *ARMS2* were included as covariates where available. For samples including related individuals, the data were analyzed with the test of Thornton and McPeek (2).

Risk Prediction Approach. To evaluate the cumulative contribution of the alleles identified here to disease risk, we fitted a simple logistic regression model to the data. The effect of each genotype was modeled on a log-additive scale, with no interaction terms between genotypes. Effectively, the model calculates a weighted count of risk alleles at each locus (with each allele weighted by the corresponding locus specific log of the odds ratio). This weighted count corresponds to a fitted probability of disease, which can be used to sort genotypes from high to low predicted risk and to define deciles of fitted risk. We first counted the proportion of affected individuals in each risk decile. In a subsequent analysis, we assigned different weights to cases and controls, designed to reflect the fact that cases are enriched in our sample. Cases were assigned weight f_{case}/p_{case} and controls were assigned weight $f_{control}/p_{control}$, where $p_{\text{case}} = 0.65$ and $p_{\text{control}} = 0.35$ are the fractions of cases and controls in our sample and $f_{case} = 0.20$ and $f_{control} = 0.80$ are hypothetical fractions of cases and controls in an elderly population at age ≈75 years. Taking these weights into account, we again divided the sample into deciles, this time ensuring that the summed weights in each decile were identical.

1. Gunderson KL, et al. (2006) Whole-genome genotyping. *Methods Enzymol* 410: 359–376.

2. Thornton T, McPeek MS (2007) Case-control association testing with related individuals: a more powerful quasi-likelihood score test. *Am J Hum Genet* 81:321–337.

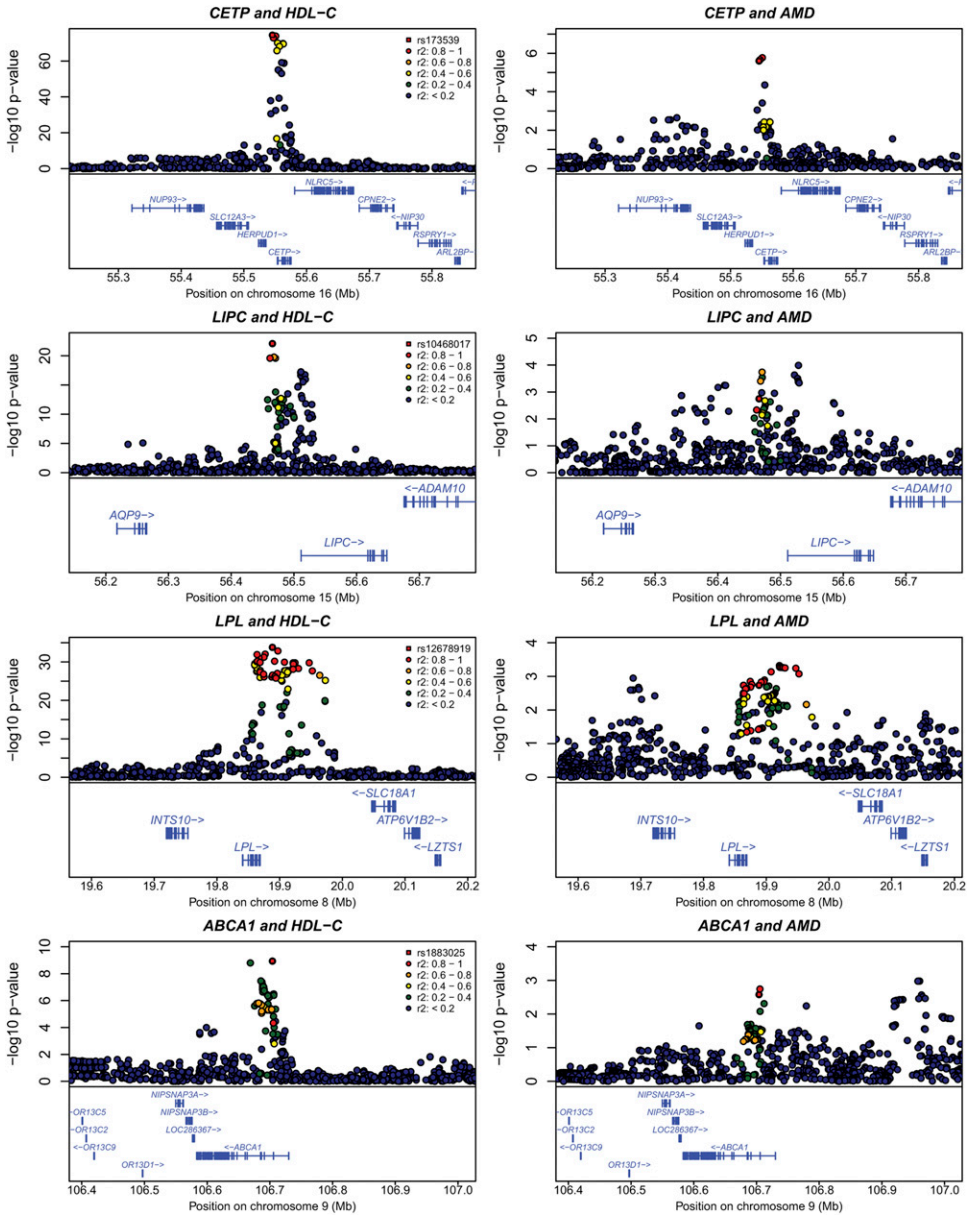

Fig. S1. Regional plot of association signals in high-density lipoprotein cholesterol (HDL-c) and AMD. Detailed plots comparing HDL-c association signals (from the discovery sample of Kathiresan et al. [Kathiresan S, et al. (2009) Common variants at 30 loci contribute to polygenic dyslipidemia. *Nat Genet* 41:56—65; *Left*]) and AMD association signals (from the discovery sample in the scan reported here; *Right*). The same marker and linkage disequilibrium proxies are highlighted in each row.

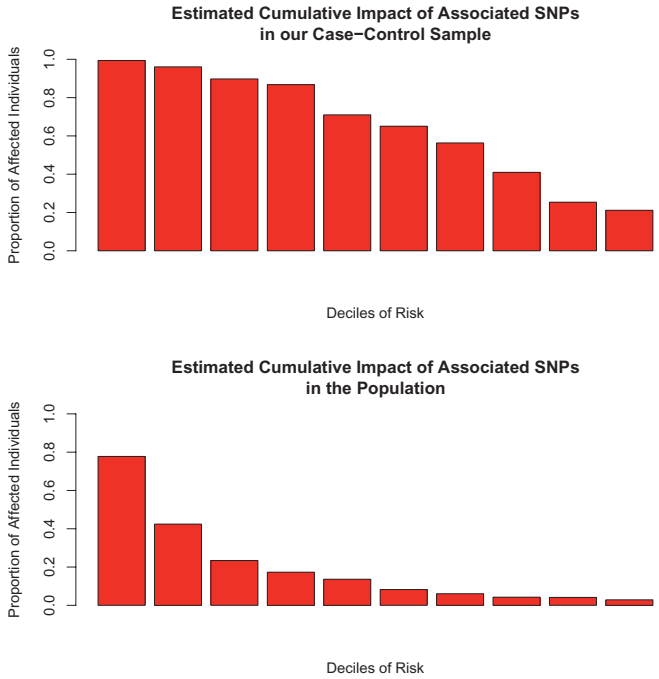

Fig. S2. Multilocus genotypes and disease risk. *Top:* Summary of the proportion of affected individuals in each risk decile, with the highest risk decile on the left, when our sample is segregated according to the risk of disease predicted by a simple logistic regression model. *Bottom:* Equivalent predictions at the population level, after weighting cases and controls to take into account that our sample is enriched for cases (see *SI Methods* for details).

Table S1. Summary description of discovery samples used in the genome-wide association and replication studies

	Cases					Controls			
Sample	*n*	Male (%)	Age (y) (Average)	Large drusen(%)	Geographic atrophy(%)	Neovascular (%)	*n*	Male (%)	Age (y) (average)	Total
Discovery samples										
Michigan	786	36.9	79.8	14.2	21.6	64.2	516	41.5	76.6	1,302
Mayo Clinic	535	36.1	77.3	46.5	13.6	39.8	433	46.7	70.2	968
AREDS	440	41.0	80.8	None genotyped	26.8	73.2	0	0	0	440
Pennsylvania	396	40.4	75.7	42.7	26.3	31.0	201	45.3	76	597
Total	2,157	38.2	78.6	24.5	21.6	53.9	1,150	44.1	74.1	3,307
Parallel discovery samples										
Tufts/MGH*	821	46.0	80.3	None genotyped	27.5	72.5	1,709	46.0	76.0	2,530
Replication samples										
Pittsburgh†	1,308	36.7	69.9	9.7†	18.9	70.0	229	49.8	76.7	1,537
Miami/Duke/	1,157	35.1	75.7	28.3	13.6	58.2	514	40.5	68.4	1,671
Vanderbilt										
Tufts/MGH II	868	40.0	79.7	None genotyped	28.3	71.7	789	40.0	73.0	1,657
Johns Hopkins†	665	32.8	75.5	21.8†	12.4	57.2	131	31.3	74.7	796
Penn-NJ	556	39.8	79.8	19.1	6.8	65.5	347	47.0	75.6	903
Oregon	515	34.0	79.8	None genotyped	27.2	72.8	263	45.0	74.0	778
Massachusetts E. E. I.	391	40.4	76.0	10.5	1.3	73.6	194	44.6	75.4	585
Spain (IDIS-Sgo)	353	46.2	76.7	None genotyped	16.1	83.9	282	44.7	75.1	635
Case Western Reserve	1,258	43.5	78.5	32.6	9.2	40.5	1,540	50.7	72.5	2,798
Total	7,071	41.1	76.2	14.9	14.0	65.8	4,289	45.5	73.0	11,360
Non-European samples										
Japan	678	69.0	74.8	None genotyped	0.0	100.0	336	42.0	74.2	1,014
Grand total†	10,727	40.9	77.0	15.7	16.6	64.0	7,484	45.3	73.9	18,211

*The Tufts/MGH samples used here exclude 158 AREDS samples that overlap with our discovery sample.
†Proportions of cases with large drusen, geographic atrophy, and neovascular disease do not add up to 100.0% because 8.6% of cases from Johns Hopkins and 0.4% of cases from Pittsburgh had intermediate drusen.

Table S2. Association results of some published candidate SNPs in our scan

Gene	SNP	Risk allele/ other	*P* value in original report	Original report	*P* value in discovery sample	*P* value in discovery sample, after adjusting for known loci	Direction of effect, vs. original report
TLR3	rs3775291	C/T	1.2×10^{-7}	1	0.526	0.885	Opposite
TLR4	rs4986790	G/A	0.001	2	0.552	0.091	Same
SERPING1	rs2511989	G/A	7.5×10^{-8}	3	0.944	0.923	Same
ERCC6	rs3793784	G/C	0.020	4	0.961	0.480	Same
LRP6	rs7294695	C/G	0.020	5	0.543	0.867	Same
CX3CR1	rs3732378	A/G	0.002	6	0.150	0.100	Same
IL8	rs4073	T/A	0.037	7	0.578	0.301	Same
VEGF	rs2010963	C/G	0.020	5	0.302	0.320	Same
VLDLR	rs2290465	C/G	0.010	5	0.782	0.402	Same

Previously associated SNPs near *APOE* and *ABCA4* are not listed because they were not genotyped in our sample and could not be imputed confidently using either 1,000 Genomes or HapMap reference haplotypes.

1. Yang Z, et al. (2008) Toll-like receptor 3 and geographic atrophy in age-related macular degeneration. *N Engl J Med* 359:1456–1463.
2. Zareparsi S, et al. (2005) Toll-like receptor 4 variant D299G is associated with susceptibility to age-related macular degeneration. *Hum Mol Genet* 14:1449–1455.
3. Ennis S, et al. (2008) Association between the SERPING1 gene and age-related macular degeneration: a two-stage case-control study. *Lancet* 372:1828–1834.
4. Tuo J, et al. (2006) Synergic effect of polymorphisms in ERCC6 5′ flanking region and complement factor H on age-related macular degeneration predisposition. *Proc Natl Acad Sci USA* 103:9256–9261.
5. Haines JL, et al. (2006) Functional candidate genes in age-related macular degeneration: significant association with VEGF, VLDLR, and LRP6. *Invest Ophthalmol Vis Sci* 47:329–335.
6. Tuo J, et al. (2004) The involvement of sequence variation and expression of CX3CR1 in the pathogenesis of age-related macular degeneration. *FASEB J* 18:1297–1299.
7. Goverdhan SV, et al. (2008) Interleukin-8 promoter polymorphism -251A/T is a risk factor for age-related macular degeneration. *Br J Ophthalmol* 92:537–540.

Table S3. Complete results for all SNPs where replication attempted

SNP	Risk/ nonrisk	GWAS	Tufts/MGH GWAS	Tufts/MGH replication	JHU	Penn-NJ	Oregon	Spain IDIS	MEEI	Case Western	Pitt	Miami DukeVanderbilt	Japan	Combined
rs9621532	A/C	3.9×10^{-5}	0.008	0.175	0.005	0.001	0.018	0.249	0.060	0.150	0.006	0.037	0.093	1.1×10^{-11}
rs493258	C/T	2.1×10^{-3}	0.0003	0.062	0.045	0.229	0.118	0.456	0.441	0.095	0.052	—	0.101	1.3×10^{-7}
rs3764261	A/C	1.7×10^{-6}	0.070	—	0.866	0.153	0.114	0.126	0.166	—	0.530	0.007	0.004	7.4×10^{-7}
rs2958154	C/T	3.8×10^{-5}	0.475	—	—	—	—	—	0.453	—	0.950	0.039	—	2.0×10^{-6}
rs11878133	T/C	3.5×10^{-4}	0.002	—	—	—	—	—	0.136	—	0.531	0.091	—	4.4×10^{-6}
rs2142541	T/G	6.5×10^{-5}	0.035	—	—	—	—	—	0.265	—	0.459	0.044	—	1.1×10^{-5}
rs17628762	A/C	8.6×10^{-3}	0.0002	—	—	—	—	—	0.080	—	0.001	0.932	—	2.4×10^{-5}
rs6022766	A/C	1.5×10^{-2}	0.0005	—	—	—	—	—	—	—	0.439	0.073	—	3.3×10^{-5}
rs9973159	C/T	2.0×10^{-3}	0.010	0.485	—	—	0.071	—	—	0.095	0.453	0.071	—	4.4×10^{-5}
rs2127740	A/G	1.6×10^{-3}	0.493	—	—	—	—	—	0.100	—	—	0.361	—	5.2×10^{-5}
rs6484926	A/G	6.5×10^{-5}	0.012	0.053	0.495	—	0.875	—	—	0.060	0.385	0.520	—	6.3×10^{-5}
rs6982567	T/C	9.5×10^{-7}	—	0.060	0.162	—	0.242	—	0.375	0.100	0.047	0.845	—	8.9×10^{-5}
rs10103849	A/G	5.2×10^{-6}	0.003	—	0.265	—	0.649	—	—	0.425	0.621	0.560	—	1.7×10^{-4}
rs 8052081	G/C	3.8×10^{-5}	0.024	—	—	—	—	—	—	—	0.417	0.636	—	2.0×10^{-4}
rs655464	G/A	1.9×10^{-3}	0.004	—	—	—	—	—	—	—	0.631	0.322	—	2.7×10^{-4}
rs13142235	A/G	6.9×10^{-5}	0.045	—	—	—	—	—	—	—	—	0.675	—	4.1×10^{-4}
rs1884807	G/A	8.3×10^{-4}	0.002	—	—	—	0.711	—	—	—	0.113	0.923	—	5.2×10^{-4}
rs1883025	C/T	2.6×1^{-3}	—	—	—	—	0.020	0.119	0.798	0.135	0.109	0.429	—	5.7×10^{-4}
rs11854497	G/A	2.0×10^{-6}	—	—	—	—	—	—	—	—	0.483	0.759	—	6.1×10^{-4}
rs7737931	C/G	8.6×10^{-5}	0.055	—	—	—	—	—	—	—	0.382	0.638	—	6.5×10^{-4}
rs12914520	T/C	1.3×10^{-3}	0.002	—	0.050	—	0.84	—	—	—	0.466	0.714	—	7.6×10^{-4}
rs7704053	A/G	5.7×10^{-2}	0.0001	—	—	—	—	—	—	—	0.631	0.353	—	7.7×10^{-4}
rs17121872	A/G	1.3×10^{-4}	0.003	—	—	—	—	—	—	—	0.908	0.825	—	1.0×10^{-3}
rs16848791	G/T	1.4×10^{-4}	0.006	0.343	0.139	—	0.319	—	0.841	0.305	0.834	0.549	—	1.3×10^{-3}
rs10468017	C/T	1.8×10^{-3}	—	—	—	0.170	0.105	0.671	0.365	—	0.050	0.484	—	1.5×10^{-3}
rs12678919	G/A	1.8×10^{-3}	—	—	—	—	0.392	0.416	—	—	0.243	0.193	0.334	3.2×10^{-3}
rs12001032	T/C	8.5×10^{-4}	0.023	0.751	—	—	0.302	—	—	—	0.112	0.779	—	5.4×10^{-3}
rs2892715	G/A	8.5×10^{-6}	0.711	—	—	—	—	—	0.872	—	0.642	0.401	—	2.0×10^{-2}
rs6445063	C/T	1.4×10^{-5}	0.814	—	—	—	—	—	—	—	0.446	0.667	—	2.8×10^{-2}
rs17296412	A/C	4.0×10^{-5}	0.153	0.892	0.252	—	0.808	—	—	0.985	0.159	0.715	—	2.6×10^{-1}

All *P* values in follow-up samples are one sided, so that a *P* value of <0.5 indicates that the direction of association is consistent with the discovery sample. Note that for our top SNP, rs9621532, direction of association is consistent across all samples examined. For our second strongest SNP, rs493258, direction of association is also consistent across all samples. Finally, for rs3764261, direction of association is only inconsistent in the JHU and Pitt follow-up samples.

Table S4. Sample-by-sample results for newly reported loci: rs9621532 (A/C) near TIMP3

	Cases				Controls					
Sample	A/A	A/C	C/C	P(A)	A/A	A/C	C/C	P(A)	OR	*P*
Discovery	2005	149	3	0.964	1022	125	3	0.943	1.81 (1.42, 2.29)	3.9×10^{-5}
Tufts/MGH	732	62	4	0.957	1466	163	3	0.947	1.31 (0.98, 1.74)	0.016
Tufts/MGH II	777	69	4	0.955	703	75	1	0.951	1.09 (0.85, 1.51)	0.350
Johns Hopkins	626	37	1	0.971	113	16	0	0.938	2.21 (1.22, 4.03)	0.008
Penn-NJ	510	46	0	0.959	295	52	0	0.925	1.90 (1.26, 2.86)	0.002
Oregon	452	24	0	0.975	229	23	0	0.954	1.88 (1.05, 3.37)	0.036
Spain(IDIS-Sgo)	330	17	0	0.976	259	17	0	0.969	1.27 (0.64, 2.50)	0.498
Massachusetts E.E.I.*	345	39	0	0.949	163	26	1	0.926	1.49 (0.90, 2.46)	0.119
Case Western Reserve	1124	95	8	0.955	1370	147	3	0.950	1.12 (0.87, 1.44)	0.300
Pittsburgh*	169	10	0	0.972	130	10	1	0.957	1.55 (0.66, 3.63)	0.011
Miami/Duke/Vanderbilt*	629	69	4	0.945	218	30	1	0.936	1.18 (0.77, 1.81)	0.074
Japan	617	37	1	0.970	303	27	0	0.959	1.38 (0.84, 2.28)	0.195
Test of heterogeneity: Q = 11.47, df = 9, *P* value = 0.2448										

*Note that for datasets that include related individuals (Pittsburgh, Miami/Due/Vanderbilt, and Massachusetts. E.E. I.), this samples counts include only unrelated individuals. Thus, the results differ from those in Table 3 in the main paper, where all available samples were analyzed using the method of Thornton and McPeek. The tabulated *P* values are calculated from the complete family data set. *P* values are two sided.

Table S5. Sample-by-sample results for newly reported loci: rs493258 (C/T) near LIPC

	Cases				Controls					
Sample	C/C	C/T	T/T	P(C)	C/C	C/T	T/T	P(C)	OR	*P*
Discovery	691	1053	413	0.564	323	569	258	0.528	1.21 (1.10, 1.34)	0.002
Tufts/MGH	260	391	147	0.579	470	782	380	0.524	1.25 (1.11, 1.41)	0.001
Tufts/MGH II	254	428	172	0.548	213	387	182	0.520	1.12 (0.98, 1.29)	0.124
Johns Hopkins	203	315	119	0.566	35	58	33	0.508	1.26 (0.96, 1.66)	0.090
Penn-NJ	193	273	90	0.593	110	179	58	0.575	1.08 (0.89, 1.31)	0.458
Oregon	167	228	104	0.563	78	111	63	0.530	1.14 (0.92, 1.42)	0.235
Spain(IDIS-Sgo)	104	164	79	0.536	82	128	64	0.533	1.01 (0.81, 1.27)	0.911
Massachusetts E.E.I.*	128	159	88	0.553	52	88	35	0.549	1.02 (0.79, 1.31)	0.822
Case Western Reserve	366	595	217	0.563	404	726	300	0.536	1.12 (1.00, 1.24)	0.190
Pittsburgh*	66	70	39	0.577	52	64	35	0.556	1.09 (0.80, 1.49)	0.104
Miami/Duke/Vanderbilt*	222	337	131	0.566	65	149	31	0.569	0.99 (0.80, 1.21)	—
Japan	35	200	408	0.210	10	102	217	0.185	1.17 (0.94, 1.46)	0.202
Test of heterogeneity: Q = 6.96, df = 9, *P* = 0.6412										

*Note that for datasets that include related individuals (Pittsburgh, Miami/Due/Vanderbilt, and Massachusetts. E.E. I.), this samples counts include only unrelated individuals. Thus, the results differ from those in Table 3 in the main paper, where all available samples were analyzed using the method of Thornton and McPeek. The tabulated *P* values are calculated from the complete family data set. *P* values are two sided.

Table S6. Sample-by-sample results for newly reported loci: rs3764261 (A/C) near CETP

	Cases				Controls					
Sample	A/A	A/C	C/C	P(A)	A/A	A/C	C/C	P(A)	OR	*P*
Discovery	296	979	882	0.364	118	486	546	0.314	1.36 (1.26, 1.46)	1.7×10^{-6}
Tufts/MGH	104	377	340	0.356	216	784	709	0.329	1.13 (1.00, 1.28)	0.140
Tufts/MGH II	—	—	—	—	—	—	—	—	—	—
Johns Hopkins	87	293	261	0.364	24	50	48	0.402	0.85 (0.70, 1.04)	0.268
Penn-NJ	58	251	247	0.330	31	151	165	0.307	1.11 (0.96, 1.29)	0.306
Oregon	60	252	197	0.365	26	117	110	0.334	1.15 (0.98, 1.34)	0.227
Spain(IDIS-Sgo)	33	145	170	0.303	22	107	147	0.274	1.15 (0.97, 1.37)	0.252
Massachusetts E.E.I.*	45	178	163	0.347	17	87	86	0.318	1.14 (0.95, 1.37)	0.332
Case Western Reserve	—	—	—	—	—	—	—	—	—	—
Pittsburgh*	24	77	69	0.368	18	55	70	0.318	1.25 (0.99, 1.58)	0.940
Miami/Duke/Vanderbilt*	—	—	—	—	—	—	—	—	—	—
Japan	31	228	395	0.222	17	80	236	0.171	1.39 (1.17, 1.65)	0.008
Test of heterogeneity: Q = 4.18, df = 6, *P* = 0.6524										

*Note that for datasets that include related individuals (Pittsburgh, Miami/Due/Vanderbilt, and Massachusetts. E.E. I.), this samples counts include only unrelated individuals. Thus, the results differ from those in Table 3 in the main paper, where all available samples were analyzed using the method of Thornton and McPeek. The tabulated *P* values are calculated from the complete family data set. *P* values are two sided.

Table S7. Sample-by-sample results for newly reported loci: rs12678919 (G/A) near LPL

	Cases				Controls					
Sample	G/G	G/A	A/A	P(G)	G/G	G/A	A/A	P(G)	OR	*P*
Discovery	23	448	1686	0.115	9	206	939	0.097	1.38 (1.17, 1.63)	0.002
Tufts/MGH	—	—	—	—	—	—	—	—	—	—
Tufts/MGH II	—	—	—	—	—	—	—	—	—	—
Johns Hopkins	—	—	—	—	—	—	—	—	—	—
Penn-NJ	—	—	—	—	—	—	—	—	—	—
Oregon	6	85	416	0.096	2	42	208	0.091	1.06 (0.73, 1.53)	0.783
Spain(IDIS-Sgo)	2	81	162	0.173	5	63	149	0.168	1.04 (0.74, 1.46)	0.832
Massachusetts. E.E.I.*	—	—	—	—	—	—	—	—	—	—
Case Western Reserve	—	—	—	—	—	—	—	—	—	—
Pittsburgh*	1	32	141	0.098	1	21	127	0.077	1.30 (0.75, 2.27)	0.486
Miami/Duke/Vanderbilt*	5	139	555	0.107	3	40	203	0.093	1.17 (0.83, 1.66)	0.385
Japan	10	141	496	0.124	6	64	253	0.118	1.06 (0.80, 1.42)	0.668
Test of heterogeneity: Q = 0.62, df = 3, *P* = 0.9826										

*Note that for datasets that include related individuals (Pittsburgh, Miami/Due/Vanderbilt, and Massachusetts. E.E. I.), this samples counts include only unrelated individuals. Thus, the results differ from those in Table 3 in the main paper, where all available samples were analyzed using the method of Thornton and McPeek. The tabulated *P* values are calculated from the complete family data set. *P* values are two sided.

Table S8. Sample-by-sample results for newly reported loci: rs1883025 (G/A) near ABCA1

	Cases				Controls					
Sample	G/G	G/A	A/A	P(G)	G/G	G/A	A/A	P(G)	OR	*P*
Discovery	1171	845	141	0.739	571	480	99	0.705	1.25 (1.12, 1.40)	0.003
Tufts/MGH	—	—	—	—	—	—	—	—	—	—
Tufts/MGH II	—	—	—	—	—	—	—	—	—	—
Johns Hopkins	—	—	—	—	—	—	—	—	—	—
Penn-NJ	—	—	—	—	—	—	—	—	—	—
Oregon	299	180	27	0.769	126	111	15	0.720	1.29 (1.01, 1.65)	0.039
Spain(IDIS-Sgo)	174	155	17	0.727	143	97	35	0.696	1.16 (0.91, 1.49)	0.238
Massachusetts. E.E. I.*	205	138	42	0.712	98	79	10	0.735	0.89 (0.67, 1.17)	0.405
Case Western Reserve	713	418	67	0.770	821	563	77	0.755	1.09 (0.96, 1.23)	0.270
Pittsburgh*	104	66	7	0.774	89	45	12	0.764	1.06 (0.73, 1.53)	0.318
Miami/Duke/Vanderbilt*	378	275	47	0.736	130	98	20	0.722	1.08 (0.86, 1.36)	0.858
Japan	—	—	—	—	—	—	—	—	—	—
Test of heterogeneity: Q = 4.25, df = 5, *P* = 0.5137										

*Note that for datasets that include related individuals (Pittsburgh, Miami/Due/Vanderbilt and Massachusetts. E.E. I.), this samples counts include only unrelated individuals. Thus, the results differ from those in Table 3 in the main paper where all available samples were analyzed using the method of Thornton and McPeek. The tabulated *P* values are calculated from the complete family data set. P values are two sided.

Table S9. Best genotyped proxy SNPs for reported loci

SNP	Chromosome	Position	Gene	*P* value at imputed SNP	Best genotyped proxy	Allele 1/ allele2	Cases 1/1 1/2 2/2	Controls 1/1 1/2 2/2	Rsq	*P* value at genotyped SNP*
rs10737680	1	194,946,078	*CFH*	1.6×10^{-76}	rs1329428	A/G	86/685/1384	214/571/365	1.00	5.2×10^{-76}
rs3793917	10	124,209,265	*ARMS2/HTRA1*	4.1×10^{-60}	rs6585827	G/A	377/993/782	335/557/256	0.32	7.5×10^{-22}
rs429608	6	32,038,441	*C2/CFB*	2.5×10^{-21}	rs429608	A/G	18/311/1827	27/311/812	1.00	2.5×10^{-21}
rs2230199	19	6,669,387	*C3*	1.0×10^{-10}	rs2250656	G/A	139/775/1243	107/491/552	0.08	1.3×10^{-7}
rs2285714	4	110,858,259	*CFI*	3.4×10^{-7}	rs2285714	T/C	462/1076/617	187/534/429	1.00	3.4×10^{-7}
rs1329424	1	194,912,799	*CFH*	6.4×10^{-16}	rs2019724	G/A	271/998/886	432/546/172	0.79	1.3×10^{-14}
rs9380272	6	32,013,989	*C2/CFB*	2.3×10^{-8}	rs9332702	G/C	0/67/2089	0/27/1123	0.50	1.1×10^{-7}
rs9621532	22	31,414,511	*SYN3/TIMP3*	3.9×10^{-5}	rs135150	C/T	45/519/1592	32/330/787	0.14	0.001
rs493258	15	56,475,172	*LIPC*	2.1×10^{-3}	rs1532085	A/G	255/949/951	179/509/462	0.64	0.002
rs3764261	16	55,550,825	*CETP*	1.4×10^{-6}	rs3764261	T/G	296/979/882	118/485/546	1.00	1.4×10^{-6}

*The second cluster is conditional on the five SNPs in the first cluster. The third cluster is conditional on the seven SNPs above. Marginally, the SNPs in second cluster are not significant.

Table S10. Association results in discovery sample for different analysis models

		Analysis covariates			
SNP	Notable nearby genes	None	PCA	PCA and index SNPs at previous loci	PCA, previous loci, age, and sex
rs10737680	*CFH*	2.5×10^{-78}	1.6×10^{-76}	—	—
rs3793917	*ARMS2*	1.7×10^{-60}	4.1×10^{-60}	—	—
rs429608	*C2/CFB*	4.7×10^{-21}	2.5×10^{-21}	—	—
rs2230199	*C3*	3.6×10^{-11}	1.0×10^{-10}	—	—
rs2285714	*CFI*	8.0×10^{-8}	3.4×10^{-7}	—	—
rs9621532	*TIMP3*	5.9×10^{-5}	2.6×10^{-4}	4.5×10^{-5}	7.1×10^{-4}
rs493258	*LIPC*	5.1×10^{-3}	6.9×10^{-3}	3.6×10^{-3}	1.1×10^{-2}
rs3764261	*CETP*	5.8×10^{-5}	1.2×10^{-4}	4.6×10^{-6}	9.5×10^{-6}
rs12678919	*LPL*	1.7×10^{-2}	2.0×10^{-2}	4.0×10^{-3}	2.9×10^{-3}
rs1883025	*ABCA1*	3.4×10^{-3}	6.4×10^{-3}	5.2×10^{-3}	4.9×10^{-3}

Table S11. Evaluation of association of loci with $P < 5 \times 10^{-8}$ overall in specific AMD subtypes

Parameter	rs10737680 (*CFH*) Alleles (A/C)	rs3793917 (*ARMS2*) Alleles (G/C)	rs429608 (*C2/CFB*) Alleles (G/A)	rs2230199 (*C3*) Alleles (C/G)	rs2285714 (*CFI*) Alleles (T/C)	rs9621532 (*TIMP3*) Alleles (T/C)
Large drusen (529) vs. control (1,150)	2.69 (2.27, 3.20)	2.36 (1.94, 2.87)	2.03 (1.59, 2.59)	1.66 (1.32, 2.08)	1.26 (1.08,1.45)	1.47 (1.03, 2.12)
	2.2×10^{-29}	4.4×10^{-26}	1.8×10^{-8}	1.2×10^{-5}	2.3×10^{-3}	0.03
GA (465) vs. control (1,150)	3.85 (3.15, 4.71)*	3.68 (3.07, 4.42)	2.46 (1.95, 3.10)*	2.00 (1.62, 2.46)*	1.38 (1.21,1.57)*	1.31 (0.91, 1.88)
	1.0×10^{-39}	1.7×10^{-44}	2.0×10^{-14}	6.3×10^{-11}	1.4×10^{-6}	0.14
Neovascular (1,163) vs. Control (1,150)	3.15 (2.73, 3.63)	4.28 (3.63, 5.04)*	2.16 (1.79,2.61)	1.67 (1.38, 2.00)	1.34 (1.19,1.50)	1.91 (1.42, 1.91)*
	1.4×10^{-57}	1.1×10^{-66}	1.3×10^{-15}	7.9×10^{-8}	1.3×10^{-6}	1.9×10^{-5}
GA (465) vs. Large Drusen (529)	1.38 (1.11, 1.73)	1.26 (1.02, 1.55)	1.12 (0.81, 1.55)	1.22 (0.93, 1.60)	1.09 (0.91,1.30)	1.12 (0.72, 1.73)
	4.3×10^{-3}	0.032	0.48	0.15	0.36	0.62
Neovascular (1,163) vs. Large Drusen (529)	1.13 (0.95, 1.35)	1.79 (1.50, 2.13)	1.07 (0.83, 1.39)	0.99 (0.80, 1.24)	1.06 (0.92,1.23)	1.30 (0.88, 1.92)
	0.16	4.3×10^{-11}	0.59	0.95	0.43	0.19
Neovascular (888) vs. GA (465)	0.76 (0.61, 0.93)	1.36 (1.13, 1.63)	0.90 (0.67, 1.20)	0.78 (0.62, 1.00)	0.95 (0.81,1.12)	1.39 (0.93, 1.39)
	0.009	0.0009	0.47	0.046	0.54	0.11

Values are odds ratio (95% confidence interval), with *P* value below.
*Entry corresponding to the largest odds ratio in that column.

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