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Trabajo Original

Obesidad y síndrome metabólico

Body mass index and risk of inflammatory breast disease: a Mendelian randomization study

Índice de masa corporal y riesgo de mastitis: un estudio de aleatorización mendeliana

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Abstract

Introduction: in previous studies, obesity was identified as a risk factor for inflammatory breast disease, but its causality is uncertain. In the present study, we performed a two-sample Mendelian randomization (TSMR) analysis to investigate the causal relationship between obesity and inflammatory breast disease.

Methods: we use body mass index (BMI) as a measure of obesity. Data for single nucleotide polymorphisms (SNPs) associated with BMI were obtained from UK Biobank. Data for single nucleotide polymorphisms (SNPs) associated with mastitis were obtained from FinnGen Biobank. We used several MR analysis methods, such as inverse-variance weighting (IVW), MR-Egger, weighted median, simple mode and weighted mode to make our results more convincing. We also performed MR-PRESSO test, MR-Egger test, heterogeneity test, pleiotropy test and leave-one-out analysis to make our analysis results more robust and credible. We used odds ratio (OR) to evaluate the causal relationship between BMI and mastitis.

Results: based on the IVW random effects model, we found that a one-standard deviation (SD) increase in BMI increased the risk of mastitis by 62.1 % (OR = 1.621, 95 % CI: 1.262-2.083, p = 1.59E-4), which is almost consistent with the results of several other methods.

Conclusions: in European individuals, an increase in the number of BMI increases the risk of inflammatory breast disease. People with high BMI need to control their weight to reduce the incidence of inflammatory breast disease.

Keywords:

Mendelian randomization. GWAS. Body mass index. Mastitis.

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Conflict of interest: the authors declare no conflict of interest.

Artificial intelligence: the authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

Data availability statement: the data supporting the results of this study are available in the IEU GWAS database (https://gwas.mrcieu.ac.uk), the UK Biobank and the FinnGen consortium.

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Statement of ethic: this article does not contain any studies conducted by any of the authors on human or animal subjects.

Author contributions: Changlong Wei conceived and initiated the project and completed the data collection, analysis, and writing of the manuscript. Xiaofang Wang assisted Changlong Wei with the data analysis and writing of the manuscript. Jinsheng Zeng made constructive suggestions after reviewing the paper, and Xiaofang Wang and Gongyin Zhang made complementary suggestions to the paper. Jinsheng Zeng, Xiaofang Wang and Gongyin Zhang supervised this project. All authors read and approved the final manuscript.

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Resumen

Introducción: en estudios previos, la obesidad se identificó como un factor de riesgo para la enfermedad inflamatoria de mama, pero su causalidad es incierta. En el presente estudio, se realizó un análisis de aleatorización mendeliana de dos muestras (TSMR) para investigar la relación causal entre la obesidad y la enfermedad inflamatoria de mama.

Métodos: se empleó el índice de masa corporal (IMC) como medida de obesidad. Los datos de los polimorfismos de nucleótido único (SNP) asociados con el IMC se obtuvieron del Biobank de Reino Unido y los datos de los polimorfismos de nucleótido único (SNP) asociados con la mastitis se obtuvieron de FinnGen Biobank. Se utilizaron varios métodos de análisis de RM, como la ponderación inversa de la varianza (IVW), RM-Egger, mediana ponderada, modo simple y modo ponderado para que nuestros resultados fueran más convincentes. También se realizaron la prueba MR-PRESSO, la prueba MR-Egger, la prueba de heterogeneidad, el test de pleiotropía y la validación dejando uno fuera (en inglés, *leave-one-out*) para que los resultados de nuestro análisis fueran más sólidos y creíbles. Se utilizó la *odds ratio* (OR) para evaluar la relación causal entre el IMC y la mastitis.

Resultados: basándonos en el modelo de efectos aleatorios IVW, se halló que un aumento de una desviación estándar (DE) en el IMC aumentaba el riesgo de mastitis en un 62,1 % (OR = 1,621, IC 95 %: 1,262-2,083, p = 1,59E-4), que es casi consistente con los resultados de otros diversos métodos.

Conclusiones: en los individuos europeos, un aumento del número de IMC aumenta el riesgo de enfermedad inflamatoria mamaria. Las personas con un IMC elevado deben controlar su peso para reducir la incidencia de enfermedad inflamatoria de la mama.

Palabras clave:

Aleatorización mendeliana. GWAS. Índice de masa corporal. Mastitis.

INTRODUCTION

The global obesity epidemic continues to grow and now affects more than two billion people, or 30 % of the world's population (1). Obesity is ranked as the fifth leading cause of death worldwide and is associated with the development of many diseases (2). Body mass index (BMI) is commonly used to define overweight and obesity (3). It has been shown that obesity is associated with a higher risk of breast cancer, while relatively little research has been done on the relationship between obesity and inflammatory breast disease (4).

Inflammatory breast diseases are common benign breast diseases and are classified as lactational mastitis and non-lactational mastitis. Non-lactating mastitis is less common and includes idiopathic granulomatous mastitis, periductal mastitis, and tuberculous mastitis (5). Many previous observational studies have shown a strong association between obesity and mastitis (6,7). From the perspective of evidence-based medicine, the causal relationship between obesity and inflammatory breast disease is unclear. There are few clinical studies on obesity and mastitis and only a few observational studies, which are not convincing enough due to their shortcomings and many confounding factors.

Mendelian randomization (MR) studies have gotten a lot of attention since the recent addition of genome-wide association studies (GWAS) databases. Mendelian randomization (MR), conceptually similar to randomized controlled trials (RCTs), is based on the principle of random assignment of genetic variants at meiosis, which reduces the impact of confounding encountered in observational epidemiology (8-10). MR studies have been widely employed to determine the causal relationship between an exposure and an outcome.

In this study, we investigated the genetic causal relationship between BMI and inflammatory breast disease using MR analysis.

The overview of the research design is shown in figure 1.

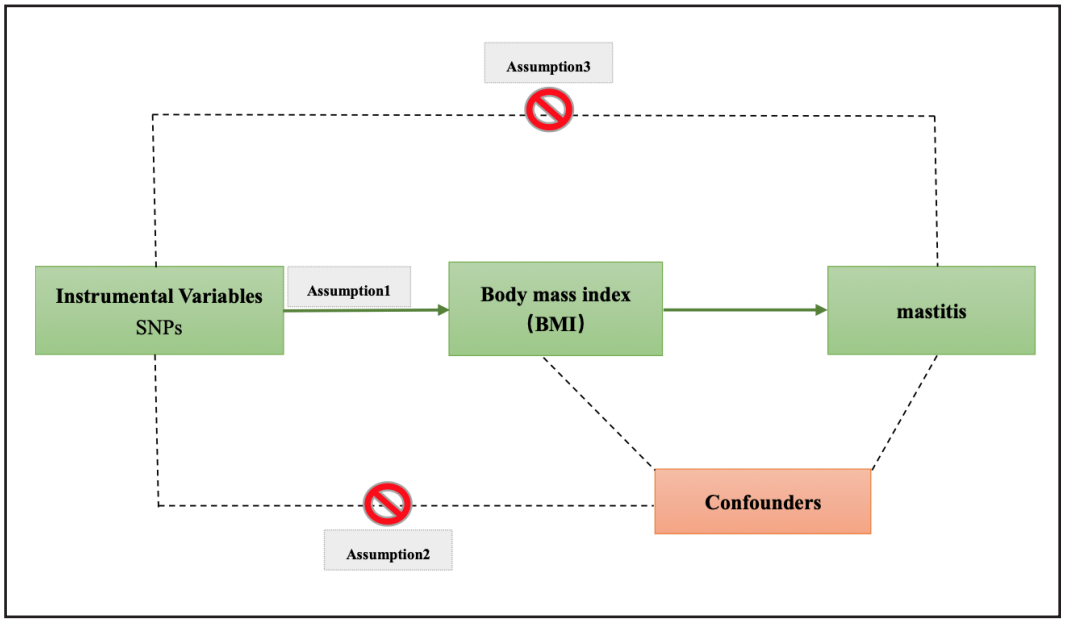

Figure 1.

The study assumptions of the two-sample Mendelian randomization analysis between body mass index (BMI) and mastitis. The assumptions included: a) single nucleotide polymorphisms (SNPs) selected as instrumental variables (IVs) should be closely related with exposure; b) selected SNPs must be independent of confounders; and c) IVs are associated to outcome only via exposure rather than through a direct association.

MATERIALS AND METHODS

DATA SOURCE

Data on BMI were obtained from the GWAS European Population Summary database supported by the UK Biobank (https://gwas.mrcieu.ac.uk/datasets/ukb-b-19953/). This database contains 461,460 European participants. Data on outcome variables for inflammatory breast disease were obtained from the FinnGen Biobank (https://r8.finngen.fi), which contains 1,435 cases of inflammatory breast disease and 176,011 controls of European ancestry (11).

INSTRUMENT SELECTION CRITERIA

We extracted genetic instrumental variables (IVs) using the following criteria: a) p value (genome-wide significance threshold < 5e-8) (12); and b) in order to avoid the potential bias caused by strong linkage disequilibrium (LD) (13), a linkage disequilibrium correlation coefficient r^2 ($r^2 < 0.001$), and a number of bases between two SNPs (kb > 10,000) were set. Next, we combined the exposed and outcome data and removed the palindromic SNPs, leaving the remaining SNPs as the final instrumental variables used for analysis. We then used the F-statistic ($F = beta^2/se^2$) to assess the statistical power of the remaining SNPs and calculated the F-values of all SNPs and removed those with low statistical power (F-statistic < 10) (14). If the F value for the instrument exposure correlation was significantly greater than 10, the likelihood of weak instrumental variable bias was low (15).

STATISTICAL APPROACHES AND SENSITIVITY ANALYSES

Data analysis in this study was performed using R (version 4.2.2) through TwoSampleMR (0.5.6) package and the MR-Pleiotropy Residual Sum and Outlier method (MR-PRESSO) (1.0) (16). First, to assess the level of significance of the causal relationship between BMI and mastitis, we used a two-sample MR analysis. In order to assess whether BMI has a causal effect on mastitis, we mostly used the inverse-variance weighted (IVW) method and the MR-Egger method, along with weighted median, simple mode, and weighted mode approaches (17-19). The IVW method is a crucial method for realizing unbiased estimates since it guarantees the necessary statistical power to establish a link between an exposure factor and an outcome. MR-Egger regression is similar to IVW, except that it includes an intercept term for the average pleiotropic effect. The intercept in the MR-Egger regression can be used to test the IV hypothesis (20). Evaluation of potential heterogeneity and horizontal pleiotropy requires sensitivity analysis. Cochran's Q test was performed to assess the heterogeneity of effect sizes for selected genetic IVs. The MR-PRESSO analysis was also applied to exclude outliers and moderate horizontal pleiotropy (21). The intercept derived from MR-Egger regression was employed to evaluate vertical pleiotropy (22). We also performed a "leave-one-out" sensitivity test as part of our sensitivity analysis to check for significant variations in our models both before and after eliminating each IV (17,23). The flow chart regarding the Mendelian randomization analysis of this study is shown in figure 2.

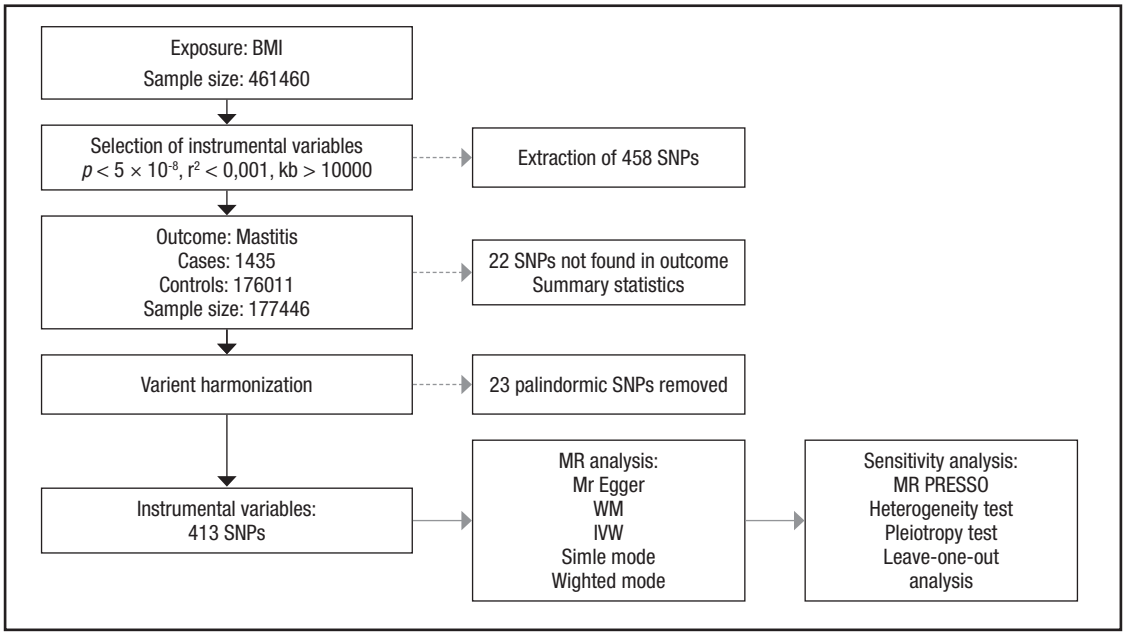

Figure 2.

Flowchart of Mendelian randomization analysis of the effect of BMI on mastitis (BMI: body mass index; SNP: single nucleotide polymorphisms; MR: Mendelian randomization; IVW: inverse-variance weighted; MR-PRESSO: MR-Pleiotropy Residual Sum and Outlier method).

RESULTS

GENETICS VARIANTS SELECTION

We strictly followed the selection criteria for the genetic instrumental variables. The details of the SNPs finally selected for MR analysis are shown in Supplementary Table I.

THE CAUSAL RELATIONSHIP BETWEEN BMI AND MASTITIS

We evaluated the causal relationship of BMI on mastitis. The results are summarized in figure 3.

Causal relationships assessed by IVW random effects models indicated that each standard deviation (SD) increased genetically determined BMI increased the risk of mastitis by 62.1 % (n = 413 SNPs, OR = 1.621, 95 % CI: 1.262-2.083, p = 1.59E-4),and this causality was further verified by MR Egger (OR = 1.541, 95 % CI: 0.789-3.007; p = 0.206), weighted median (OR = 1.359, 95 % CI: 0.885-2.086; p = 0.161), simple mode (OR = 1.857,95 % CI: 0.567-6.079; p = 0.307) and weighted mode (OR = 1.142, 95 % CI: 0.552-2.362; p = 0.720) methods. Figure 4 shows a scatter plot of the relationship between BMI and mastitis. Figure 5 shows a forest plot of the causal effect of single nucleotide polymorphisms (SNPs) associated with BMI on mastitis.

The p-value obtained by Cochran's Q test was 0.017 < 0.05, so we used the random effects model as the gold standard. According to MR-PRESSO test, no outliers were found, which was consistent with the leave-one-out analysis (Fig. 6) and funnel plot (Fig. 7). Horizontal pleiotropy was absence in MR-Egger intercept analysis (p = 0.873).

Table I. Details of the GWAS included in the Mendelian randomization

Trait	Consortium	Population	Sample size	Number of SNPs
Body mass index	UK Biobank/MRC-IEU	European	461,460	9,851,867
Inflammatory disorders of breast	FinnGen	European	177,446	20,158,120

SNPs: single nucleotide polymorphisms.

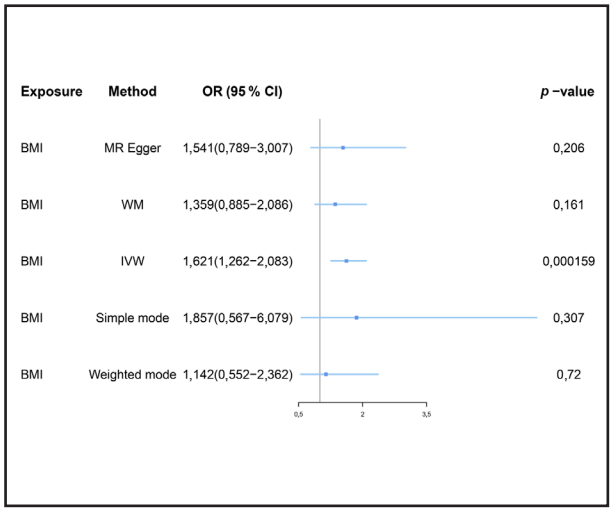

Figure 3.

Forest plot of MR analysis results (BMI: body mass index; MR: Mendelian randomization; IVW: inverse-variance weighted; MR-PRESSO: MR-Pleiotropy Residual Sum and Outlier method).

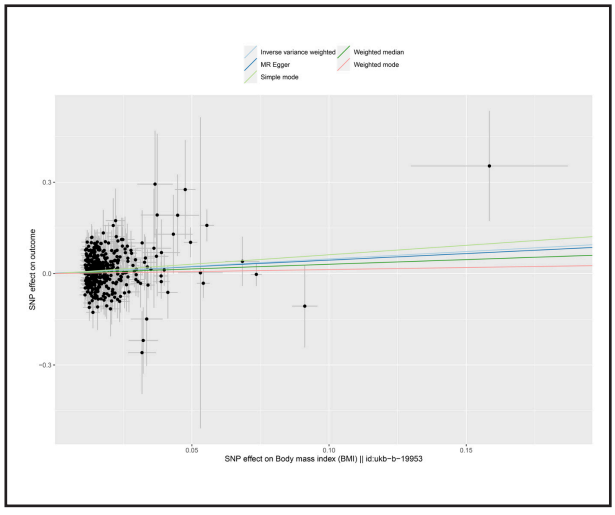

Figure 4.

Scatter plot of MR analysis of the effect of BMI on mastitis (BMI: body mass index; SNP: single nucleotide polymorphisms; MR: Mendelian randomization).

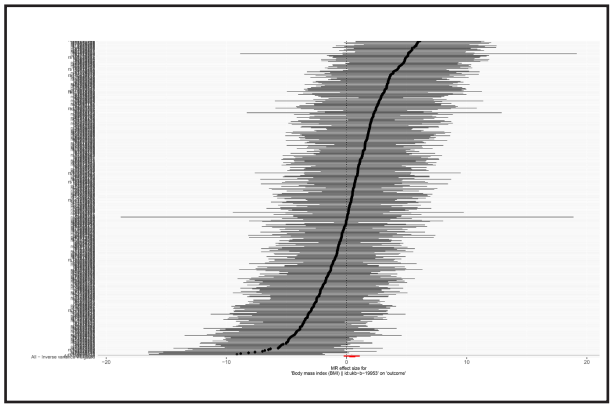

Figure 5.

Forest plots of the causal effects of BMI-associated SNPs on mastitis (BMI: body mass index; SNP: single nucleotide polymorphisms; MR: Mendelian randomization).

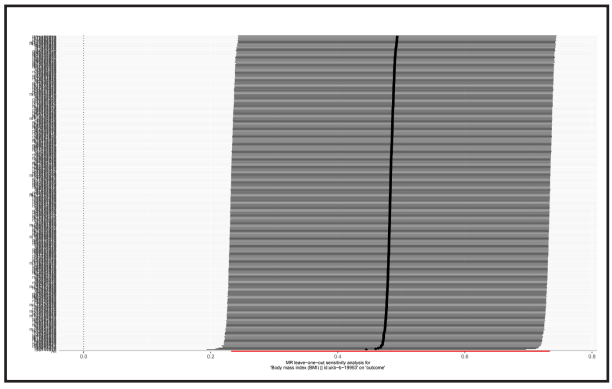

Figure 6.

"Leave-one-out" sensitivity analysis results in the two-sample MR analysis (BMI: body mass index; MR: Mendelian randomization).

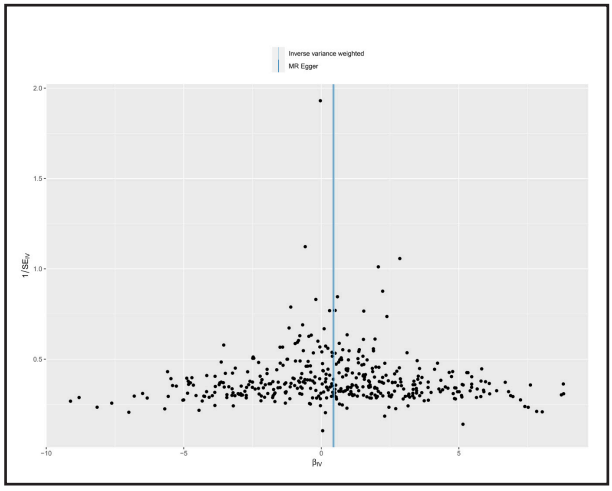

Figure 7.

Funnel plot of the causality of BMI to mastitis (BMI: body mass index; MR: Mendelian randomization).

DISCUSSION

In the present study, we applied MR methods to determine the causal relationship between BMI and mastitis, and we found that for every one standard deviation (SD) increase in BMI, the risk of mastitis increased by 62.1 %.

We selected BMI as the exposed genetic phenotype and found a genetic causal relationship between BMI and mastitis. BMI is often used as a measure of obesity, and the relationship between obesity and mastitis can be reflected laterally through this study (24). Many retrospective studies have been conducted to evaluate potential risk factors for mastitis, however, many of them suffer from recollection and selection bias (25). It has been shown that obesity is a low-grade chronic inflammatory condition with changes in associated factors that can directly affect local estrogen receptor expression and the development of inflammation (26,27). Multiple studies have found that obese individuals are more likely to develop various types of infections than normal weight individuals (28,29). In a previous Mendelian randomization study, high BMI was found to be associated with an increased risk of any infection (30), and infections may contribute to the development of some mastitis. Granulomatous lobular mastitis (GLM) is a benign chronic inflammatory breast disease of unknown etiology, and because GLM is a rare disease, prospective studies are difficult to perform. In a retrospective analysis, obesity or overweight was found to be associated with GLM recurrence (7). Periductal mastitis (PDM) is a long-term inflammatory disease, but little is known about the etiology of PDM. In a retrospective study, overweight/obesity was shown to be an independent risk factor for PDM (6). Non-bacterial mastitis (NBM) is a solid disease of the breast that accounts for 4-5 % of all benign breast diseases (31). In some studies, obesity has been suggested to be possibly related to NBM (32).

There were several advantages for the current two-sample MR studies. First, because alleles follow the principle of random distribution when forming gametes during meiosis, the causal relationship between genotype and disease in MR studies will not be distorted by confounding factors, which is the main limitation of traditional observation studies (33,34). Second, it is much easier to assess the causal relationship between BMI and mastitis risk using the public GWAS database than using prospective cohort studies or randomized controlled trials. This study also required less time and cost than a general epidemiological study.

However, we acknowledge some limitations to our study. First, there might be an ethnic bias in our study due to all the selected GWAS database populations being of European ancestry. Second, there was some heterogeneity in our results in the heterogeneity test, which may have compromised the accuracy of our results, although the results of our other analytical methods were robust. Third, our study did not differentiate between the different types of mastitis, and the relationship between BMI values and each type of mastitis needs further study. Fourth, this study needs to be further validated by other types of studies (observational studies, cohort studies, etc.).

CONCLUSIONS

According to our study, there is a genetic causal relationship between an increased number of BMI and an increased risk of inflammatory breast disease. Patients with high BMI need to control their weight to reduce the incidence of mastitis, and clinicians may also need to be concerned about the potential risk of inflammatory breast disease in some patients with high BMI.

Supplementary Table I. Basic information about the SNPs used in this study

SNP	EA	OA	Beta	eaf	SE	pval	F
rs1000096	T	C	-0.01334	0.401094	0.00203101	5.10035E-11	43.13039
rs10063055	T	C	0.013678	0.253365	0.00226991	1.7E-09	36.30749
rs10099330	G	A	0.012425	0.45285	0.00198907	4.20001E-10	39.0186
rs10144067	T	C	0.018574	0.591294	0.00202937	5.60015E-20	83.76637
rs10160769	C	G	-0.01559	0.21751	0.00242199	1.2E-10	41.41291
rs10169594	C	T	0.012188	0.363139	0.00205506	2.99999E-09	35.17064
rs10172070	T	C	0.016139	0.146466	0.00278352	6.69993E-09	33.61827
rs10182416	G	A	0.013038	0.512223	0.00197134	3.69999E-11	43.74068
rs10423928	A	T	-0.03401	0.194358	0.00249869	3.40017E-42	185.3021
rs10505836	C	A	0.018485	0.860012	0.00287086	1.2E-10	41.45907
rs10510025	T	C	0.017564	0.247013	0.00229886	2.19989E-14	58.37631
rs1064213	A	G	0.01493	0.478377	0.00197196	3.69999E-14	57.32304
rs10742752	C	T	0.011798	0.612239	0.00202961	6.1E-09	33.78969
rs10756714	G	A	-0.02079	0.444196	0.00199408	1.9002E-25	108.6588
rs10756792	T	C	-0.01906	0.742901	0.00227201	4.90004E-17	70.36283
rs10760277	T	C	0.013873	0.385049	0.00203825	1E-11	46.32879
rs10780248	A	G	-0.01212	0.559454	0.00199415	1.2E-09	36.95889
rs1078141	T	C	0.014224	0.383867	0.00205862	4.90004E-12	47.74028
rs10809621	G	C	-0.01253	0.350143	0.00207043	1.40001E-09	36.62821
rs10824211	T	C	0.020769	0.139491	0.00286631	4.30031E-13	52.50208
rs10927006	C	T	-0.01682	0.143704	0.00281467	2.30001E-09	35.69191
rs10965698	T	C	-0.01127	0.369897	0.002052	3.89996E-08	30.18624
rs10989067	A	G	0.016951	0.31593	0.00212349	1.39991E-15	63.72513
rs11001963	T	C	0.011679	0.581338	0.00201921	7.29995E-09	33.45631
rs11009685	T	C	-0.01308	0.244096	0.00230766	1.40001E-08	32.14383
rs11012732	G	A	0.021643	0.331683	0.00210126	7.10068E-25	106.0853
rs11079849	T	C	-0.02009	0.328531	0.00211163	1.80011E-21	90.5428
rs11099020	T	C	-0.0142	0.640609	0.00206202	5.60015E-12	47.44859
rs11115160	A	G	-0.01308	0.237797	0.00233641	2.19999E-08	31.32599
rs11122450	G	T	-0.01163	0.611739	0.00202425	9.09997E-09	33.01799
rs11134679	G	A	0.018246	0.684753	0.00213286	1.20005E-17	73.18227
rs11150745	G	A	-0.02116	0.317711	0.00212961	2.90001E-23	98.73618
rs111598585	T	C	-0.01422	0.208671	0.00243798	5.39995E-09	34.0419
rs11165643	T	C	0.019332	0.590103	0.00200337	4.90004E-22	93.11652
rs111689389	C	G	-0.01367	0.282614	0.00219522	4.70002E-10	38.781
rs11218510	A	G	-0.01446	0.40047	0.00202121	8.4004E-13	51.19291
rs1126930	C	G	0.03227	0.035271	0.00535892	1.7E-09	36.26018

(Continues on next page)

Supplementary Table I (cont.). Basic information about the SNPs used in this study

SNP	EA	OA	Beta	eaf	SE	pval	F
rs113079574	T	C	-0.01559	0.19279	0.00251598	5.80003E-10	38.39331
rs113603865	T	C	0.018601	0.21205	0.00242689	1.80011E-14	58.7471
rs113624107	A	G	0.015046	0.22586	0.00236876	2.1E-10	40.34649
rs115056380	A	G	-0.02564	0.048344	0.0046006	0.000000025	31.06888
rs11525873	C	T	-0.02398	0.097701	0.00333603	6.59933E-13	51.66181
rs11607476	C	A	0.015712	0.486574	0.00199179	3.10027E-15	62.22657
rs11610621	A	T	0.016487	0.148174	0.00278318	3.09999E-09	35.09097
rs116374395	A	G	0.031882	0.035444	0.00536236	2.80001E-09	35.3485
rs11641179	G	A	-0.01255	0.257141	0.00227364	3.40001E-08	30.44907
rs11642090	C	T	0.011418	0.373536	0.00205925	2.90001E-08	30.74626
rs11656076	A	G	-0.01543	0.224774	0.00237054	7.59976E-11	42.3597
rs1167311	A	G	-0.01926	0.681309	0.00213109	1.59993E-19	81.7203
rs11675464	G	A	0.011975	0.562988	0.00198558	1.6E-09	36.37337
rs11691869	A	C	-0.01932	0.362038	0.00205562	5.60015E-21	88.29574
rs11699828	A	G	-0.03354	0.035832	0.00582677	8.60003E-09	33.13729
rs11709402	G	A	0.022819	0.278732	0.00220796	4.90004E-25	106.8116
rs117118217	C	G	0.044819	0.017711	0.00788004	1.29999E-08	32.34892
rs117342986	T	C	0.036579	0.026415	0.00646781	0.000000016	31.98591
rs11757278	C	T	-0.01463	0.303879	0.00214834	9.8992E-12	46.35521
rs11778219	G	A	0.015796	0.163123	0.0026874	4.20001E-09	34.54853
rs118136827	T	G	-0.01326	0.281086	0.0022019	1.7E-09	36.2555
rs11842871	T	G	-0.01504	0.259959	0.0022601	2.80027E-11	44.29865
rs11919665	T	A	-0.01279	0.679775	0.00211292	1.40001E-09	36.61529
rs12001437	C	T	0.012184	0.367678	0.00205069	2.80001E-09	35.29809
rs12072739	G	A	0.015701	0.224478	0.00236691	3.29989E-11	44.00278
rs12088284	T	C	0.013932	0.300838	0.00214854	8.9002E-11	42.04568
rs12089815	A	G	-0.01231	0.54861	0.00198606	5.69994E-10	38.43081
rs12140153	T	G	-0.03308	0.094252	0.0034589	1.20005E-21	91.43736
rs12149660	A	G	-0.02273	0.114956	0.00311586	2.99985E-13	53.23389
rs12259464	A	G	0.01309	0.48447	0.00198686	4.49987E-11	43.40218
rs12273545	T	C	0.024839	0.056505	0.00428551	6.80002E-09	33.59493
rs1229984	C	T	0.037357	0.972775	0.00599385	4.60002E-10	38.84474
rs12364470	G	T	0.019271	0.164556	0.0026658	4.90004E-13	52.25536
rs12440603	T	C	0.013929	0.433693	0.0020011	3.40017E-12	48.44747
rs12459368	G	A	-0.01701	0.268203	0.00223235	2.49977E-14	58.08893
rs12462975	A	G	0.019582	0.329692	0.00212071	2.60016E-20	85.26296
rs12541408	C	T	-0.01433	0.31742	0.00212723	1.59993E-11	45.3552
rs1266874	G	A	0.014097	0.349619	0.0020712	1E-11	46.32172
rs12681792	A	C	0.014869	0.1926	0.00251693	3.50002E-09	34.90107
rs12692596	T	C	0.013087	0.37185	0.00203738	1.29999E-10	41.26192
rs12696039	G	A	-0.01528	0.149405	0.0027705	3.50002E-08	30.41878
rs1286058	A	T	0.014913	0.703747	0.00216922	6.20012E-12	47.26063
rs12881629	G	A	0.022075	0.08265	0.00358929	7.69999E-10	37.82478

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Supplementary Table I (cont.). Basic information about the SNPs used in this study

SNP	EA	OA	Beta	eaf	SE	pval	F
rs12889639	A	G	0.015534	0.651265	0.00207775	7.70016E-14	55.89303
rs12921986	G	A	0.020333	0.077984	0.0036983	3.79997E-08	30.22636
rs12937411	T	C	-0.01719	0.408167	0.00201383	1.39991E-17	72.83742
rs1296328	C	A	-0.01886	0.559032	0.001999	3.90032E-21	89.03277
rs12974458	T	C	0.015247	0.543175	0.00199717	2.29985E-14	58.27952
rs13012070	A	G	-0.01365	0.228388	0.00234795	6.1E-09	33.79823
rs13033310	A	G	0.012611	0.25276	0.0022826	3.29997E-08	30.52386
rs13097918	A	T	0.014556	0.212315	0.0024161	1.7E-09	36.29612
rs13107325	T	C	0.04758	0.07492	0.00375479	8.49963E-37	160.5742
rs13176429	C	T	0.014156	0.687609	0.00213122	3.10027E-11	44.11577
rs1320251	T	C	-0.01803	0.454791	0.00199407	1.50003E-19	81.77335
rs13218383	G	C	-0.0144	0.335132	0.00209236	5.79963E-12	47.38086
rs1322842	G	A	-0.01313	0.609274	0.00203539	1.09999E-10	41.60842
rs13248187	C	T	0.015764	0.268557	0.00224155	1.99986E-12	49.45794
rs1327259	G	A	-0.01485	0.387722	0.00203363	2.80027E-13	53.3453
rs1330199	T	G	-0.01175	0.483137	0.00198642	3.29997E-09	34.99452
rs13420048	A	C	-0.01548	0.365037	0.00205272	4.60045E-14	56.88239
rs13427822	G	A	-0.01815	0.271198	0.00224142	5.60015E-16	65.58108
rs1346841	A	G	-0.01306	0.405041	0.0020172	9.70063E-11	41.89116
rs1360201	T	C	0.013008	0.481546	0.00197747	4.79954E-11	43.2681
rs13642	T	A	-0.01614	0.360654	0.00205695	4.30031E-15	61.54042
rs140159717	T	C	-0.02469	0.082292	0.00370967	2.80027E-11	44.29027
rs1438945	A	T	-0.01338	0.715119	0.00219791	1.09999E-09	37.07219
rs1441264	A	G	0.017903	0.593681	0.00205854	3.40017E-18	75.63931
rs1451963	T	G	0.022201	0.082266	0.00360585	7.39997E-10	37.9079
rs1458156	T	C	0.014075	0.488431	0.00197951	1.20005E-12	50.55701
rs145981104	G	A	0.022711	0.063711	0.00404552	0.00000002	31.51547
rs146569428	A	G	0.013953	0.200749	0.00248571	0.00000002	31.51033
rs1471093	A	G	0.013462	0.616663	0.00203996	4.10015E-11	43.54812
rs147568678	C	T	-0.01333	0.23807	0.00233034	1.09999E-08	32.73389
rs1477290	C	T	0.033777	0.136947	0.00289815	2.19989E-31	135.8331
rs147730268	T	G	-0.03508	0.087243	0.00358357	1.29987E-22	95.82634
rs1503526	C	T	0.015431	0.480077	0.00197681	5.90065E-15	60.93222
rs156201	C	G	0.01319	0.753455	0.00228932	8.30004E-09	33.1948
rs156914	A	G	0.011155	0.491786	0.00197308	0.000000016	31.96431
rs1582931	A	G	-0.01334	0.473242	0.0019956	2.29985E-11	44.69803
rs159037	C	T	0.012371	0.253903	0.00226776	4.90004E-08	29.76073
rs1609010	G	A	0.020977	0.565728	0.0019963	7.89951E-26	110.42
rs1657930	A	G	-0.01468	0.802936	0.00248602	3.50002E-09	34.8878
rs16916303	G	A	-0.01924	0.119736	0.00307931	4.20001E-10	39.02684
rs17056301	C	T	0.013583	0.256425	0.0022697	2.19999E-09	35.81466
rs17132130	C	G	-0.01784	0.221467	0.00238564	7.50067E-14	55.93292

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Supplementary Table I (cont.). Basic information about the SNPs used in this study

SNP	EA	OA	Beta	eaf	SE	pval	F
rs17218879	G	C	0.012655	0.33868	0.00209842	1.6E-09	36.3691
rs17289010	G	A	-0.01347	0.32787	0.00210438	1.6E-10	40.94825
rs17399739	G	A	0.027071	0.068893	0.00391006	4.40048E-12	47.93485
rs17446299	G	C	0.015324	0.165544	0.00266515	8.9E-09	33.0577
rs17544384	C	T	0.014093	0.210864	0.00241434	5.30005E-09	34.07346
rs17668356	G	C	-0.02305	0.146029	0.00279318	1.50003E-16	68.12492
rs17770336	T	C	0.024293	0.322437	0.00211161	1.29987E-30	132.3544
rs1778830	A	G	0.014078	0.362165	0.00205596	7.50067E-12	46.88369
rs1788808	G	A	-0.0204	0.49478	0.00198255	7.70016E-25	105.9211
rs1793636	C	G	-0.01333	0.309144	0.0021408	4.70002E-10	38.79612
rs1834144	A	C	-0.01401	0.373192	0.00205213	8.60003E-12	46.61664
rs1861410	T	C	-0.02126	0.555423	0.00198918	1.20005E-26	114.1844
rs1884897	G	A	0.020001	0.627378	0.00205634	2.29985E-22	94.60489
rs1919243	C	T	0.011676	0.487406	0.00200175	5.49997E-09	34.0221
rs2035936	T	G	0.037086	0.055892	0.00435778	1.69981E-17	72.42632
rs2051559	C	T	0.020408	0.13254	0.00291963	2.80027E-12	48.85812
rs2075466	C	G	0.01329	0.267182	0.00223627	2.80001E-09	35.32003
rs2102278	G	A	0.011858	0.322486	0.0021139	0.00000002	31.4685
rs2133561	T	A	-0.0141	0.611084	0.00204744	5.79963E-12	47.40575
rs213518	C	T	0.015789	0.145608	0.00280491	1.79999E-08	31.6879
rs2153740	G	A	-0.01126	0.479914	0.00199313	0.000000016	31.88801
rs215634	G	A	-0.01552	0.611879	0.00203492	2.39994E-14	58.18586
rs2172131	C	T	-0.01494	0.578723	0.00200386	8.99912E-14	55.57274
rs2192158	G	A	-0.01501	0.553308	0.00198302	3.69999E-14	57.30901
rs2216931	A	C	0.016911	0.661966	0.00208587	5.19996E-16	65.72929
rs2234458	T	C	-0.02038	0.639519	0.00205579	3.59998E-23	98.31631
rs2248551	A	G	0.014652	0.164522	0.00266497	3.79997E-08	30.22922
rs2271189	A	G	-0.01631	0.40272	0.00201869	6.4998E-16	65.26707
rs2289379	T	C	-0.01528	0.395648	0.00202952	5.19996E-14	56.65798
rs2307111	C	T	-0.028	0.395025	0.00202203	1.29987E-43	191.81
rs2342892	G	T	-0.0127	0.516212	0.00197715	1.29999E-10	41.24171
rs2381404	C	T	0.013966	0.243837	0.00229974	1.29999E-09	36.88175
rs2383377	A	G	0.016129	0.130687	0.00293564	3.89996E-08	30.18514
rs2398861	G	A	0.017993	0.259169	0.00226733	2.09991E-15	62.97778
rs2425816	A	G	0.012228	0.415111	0.00201106	1.2E-09	36.97339
rs2433733	A	G	-0.01718	0.677659	0.00210907	3.80014E-16	66.35744
rs2439823	G	A	0.0192	0.545612	0.00199108	5.30029E-22	92.98566
rs2482356	C	T	-0.01135	0.429018	0.00199506	1.29999E-08	32.37159
rs2512892	C	T	0.012947	0.566085	0.00199819	9.20026E-11	41.98086
rs252761	T	G	-0.0115	0.587966	0.00201769	0.000000012	32.51129
rs2568958	A	G	0.022293	0.603656	0.00201204	1.59993E-28	122.7598
rs2569993	C	T	0.01267	0.320327	0.00212202	2.39999E-09	35.64957

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Supplementary Table I (cont.). Basic information about the SNPs used in this study

SNP	EA	OA	Beta	eaf	SE	pval	F
rs2606228	C	A	-0.01388	0.646368	0.00208379	2.70023E-11	44.36237
rs2616143	A	G	-0.01387	0.319862	0.00212547	6.70039E-11	42.60699
rs2678204	G	T	0.024161	0.340162	0.00208158	3.80014E-31	134.7236
rs2725371	G	A	-0.01603	0.696115	0.00215845	1.10002E-13	55.15546
rs2791643	T	C	-0.01338	0.761794	0.00231332	7.19996E-09	33.47195
rs28350	G	A	-0.01803	0.820684	0.00258234	2.90001E-12	48.7678
rs28366156	C	T	-0.02648	0.130595	0.00292978	1.59993E-19	81.70549
rs2837996	C	T	0.012665	0.651408	0.00207859	1.09999E-09	37.12378
rs28404639	T	C	-0.01171	0.366041	0.00205533	0.000000012	32.47624
rs28489620	A	G	-0.01537	0.290349	0.00220025	2.80027E-12	48.82168
rs2861685	C	T	-0.01713	0.411984	0.00199763	1E-17	73.51108
rs28670671	C	T	-0.01246	0.286024	0.00226426	3.69999E-08	30.3004
rs2870111	T	C	-0.01572	0.412066	0.00201912	7.10068E-15	60.57732
rs2875762	C	G	0.015339	0.242953	0.0023121	3.29989E-11	44.01299
rs2899644	T	C	0.014966	0.229995	0.0023609	2.30001E-10	40.18375
rs2920503	T	C	-0.01403	0.285413	0.00219666	1.7E-10	40.79745
rs2922757	T	A	0.012247	0.597368	0.00201926	1.29999E-09	36.78235
rs2962334	T	G	0.043255	0.020065	0.00703547	7.79992E-10	37.79988
rs317656	A	T	-0.01448	0.724452	0.00221303	6.09958E-11	42.78983
rs3213943	A	C	-0.01794	0.131525	0.00288163	4.79999E-10	38.76122
rs32421	T	A	0.013232	0.224315	0.00237757	2.59998E-08	30.97074
rs329118	T	C	-0.01657	0.419409	0.0020038	1.29987E-16	68.40919
rs329651	T	G	0.015722	0.803977	0.00250202	3.29997E-10	39.48417
rs34045288	T	C	0.023478	0.334435	0.00209371	3.50026E-29	125.7488
rs34153025	C	T	-0.03892	0.022158	0.00678155	9.59997E-09	32.92899
rs34234296	A	G	-0.01495	0.392437	0.00204032	2.39994E-13	53.66752
rs34481751	A	C	-0.0185	0.165329	0.00270404	7.8001E-12	46.82237
rs34517439	A	C	0.038848	0.121787	0.00304983	3.59998E-37	162.2505
rs34696181	C	T	0.011435	0.476084	0.00198283	8.10009E-09	33.25549
rs34811474	A	G	-0.02853	0.230756	0.00234269	4.10015E-34	148.3039
rs349071	A	G	-0.01331	0.500388	0.00198231	1.9002E-11	45.05728
rs35154326	G	A	-0.01304	0.274044	0.00223442	5.30005E-09	34.07261
rs35364449	T	C	0.021707	0.109739	0.00318335	9.20026E-12	46.4972
rs35697587	A	G	-0.01647	0.508121	0.00198067	9.20026E-17	69.12603
rs35697691	G	C	0.023031	0.089346	0.00352223	6.20012E-11	42.75346
rs35809007	A	G	-0.0171	0.363205	0.00205627	9.09913E-17	69.16361
rs35957544	T	G	-0.01964	0.574316	0.00200438	1.10002E-22	96.03977
rs36007635	A	G	-0.02105	0.137698	0.00286788	2.19989E-13	53.84879
rs36061954	T	C	0.012845	0.398747	0.00201928	2E-10	40.46144
rs3764625	G	T	-0.01177	0.587594	0.00201523	5.19996E-09	34.11984
rs3784710	C	T	-0.02971	0.226602	0.00236042	2.49977E-36	158.3909
rs3803286	G	A	-0.01864	0.666815	0.00209828	6.4003E-19	78.93037
rs3807566	T	G	-0.01207	0.43832	0.00199583	1.5E-09	36.58994

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Supplementary Table I (cont.). Basic information about the SNPs used in this study

SNP	EA	OA	Beta	eaf	SE	pval	F
rs3814883	T	C	0.024011	0.482402	0.00198424	1E-33	146.427
rs3845344	T	C	0.016361	0.391115	0.00201927	5.40008E-16	65.64862
rs3851998	G	C	-0.01361	0.743064	0.00226874	0.000000002	35.97176
rs3866805	A	C	0.011784	0.355683	0.00206546	0.000000012	32.54731
rs3897102	T	C	0.012084	0.411157	0.00202716	2.5E-09	35.53293
rs3901286	A	C	-0.02256	0.15244	0.00275602	2.70023E-16	66.97805
rs3935190	A	G	-0.01449	0.536784	0.00199701	4.00037E-13	52.62117
rs394608	C	T	0.018635	0.537697	0.00199484	9.49948E-21	87.26833
rs40071	C	T	-0.02617	0.179536	0.00258163	3.80014E-24	102.7322
rs4017425	T	C	-0.01258	0.470208	0.00198035	2.1E-10	40.36405
rs4055791	T	C	-0.01781	0.416804	0.00200801	7.39946E-19	78.65173
rs406388	G	C	0.015973	0.177266	0.00260181	8.30004E-10	37.68963
rs41279738	G	T	0.068426	0.025988	0.0062225	4.00037E-28	120.9251
rs4148155	G	A	-0.02297	0.113268	0.00310659	1.39991E-13	54.66159
rs4261944	G	T	0.013855	0.364935	0.00205652	1.59993E-11	45.39061
rs4267103	C	T	0.015392	0.186347	0.00254312	1.40001E-09	36.62974
rs4284600	C	T	0.011967	0.467122	0.00199506	0.000000002	35.9816
rs429343	G	A	-0.01738	0.576573	0.00199729	3.29989E-18	75.71681
rs429358	C	T	-0.02667	0.154166	0.00274373	2.39994E-22	94.50139
rs4307239	G	A	0.012141	0.458941	0.00198816	0.000000001	37.29303
rs4444317	G	A	-0.01616	0.216141	0.00242104	2.49977E-11	44.55539
rs4456769	T	C	0.014611	0.333444	0.00210138	3.59998E-12	48.34556
rs4477562	T	C	0.029612	0.128644	0.00298011	2.90001E-23	98.73361
rs4482463	A	C	-0.03132	0.923002	0.00370692	2.99985E-17	71.37527
rs45486197	A	G	0.025766	0.065685	0.00403737	1.7E-10	40.72836
rs4605363	C	A	0.016364	0.341595	0.00207733	3.29989E-15	62.05222
rs4648450	A	C	-0.01484	0.466824	0.00198775	8.4004E-14	55.71456
rs4658403	T	C	-0.01889	0.833659	0.00264997	1E-12	50.80147
rs4672338	T	C	0.013565	0.336228	0.00208669	8.00018E-11	42.25695
rs4722398	T	C	0.018699	0.136137	0.00287545	7.89951E-11	42.29013
rs4764949	G	A	-0.01839	0.325892	0.00211197	3.10027E-18	75.84052
rs4790292	A	C	-0.02545	0.153693	0.00275603	2.60016E-20	85.27828
rs4820410	G	A	-0.01775	0.345317	0.00208527	1.69981E-17	72.42053
rs4832298	T	C	-0.01597	0.686142	0.00212268	5.40008E-14	56.56774
rs4858940	C	T	0.022928	0.885569	0.00309976	1.39991E-13	54.71167
rs4876611	G	A	0.019755	0.720243	0.00220502	3.29989E-19	80.2647
rs4929923	C	T	0.018942	0.645204	0.00206436	4.49987E-20	84.19749
rs5011579	G	C	0.014027	0.715152	0.00219322	1.6E-10	40.90278
rs512121	C	T	-0.01594	0.192054	0.00252176	2.59998E-10	39.93426
rs529200	G	A	0.016897	0.527829	0.0019785	1.29987E-17	72.93255
rs539515	C	A	0.049529	0.204942	0.0024426	1.99986E-91	411.165
rs55707359	G	T	0.053129	0.015432	0.00812381	6.20012E-11	42.77077
rs55714539	C	A	0.017572	0.343587	0.00210043	6.00067E-17	69.98759

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Supplementary Table I (cont.). Basic information about the SNPs used in this study

SNP	EA	OA	Beta	eaf	SE	pval	F
rs55726687	A	G	0.02483	0.209709	0.00242628	1.39991E-24	104.7301
rs55769038	A	G	0.016096	0.590384	0.00201096	1.20005E-15	64.06701
rs558887	G	A	-0.013	0.307507	0.00214881	1.5E-09	36.58729
rs559231	T	G	0.013491	0.393053	0.00203562	3.40017E-11	43.92134
rs55966114	T	C	0.014589	0.192958	0.00251342	6.49995E-09	33.68923
rs56038322	A	G	0.013928	0.31062	0.00214833	8.99912E-11	42.02915
rs56094641	G	A	0.073497	0.404564	0.00201412	1E-200	1331.573
rs56133507	G	T	0.013762	0.196875	0.00247385	2.69998E-08	30.94774
rs56143236	T	C	0.012667	0.256388	0.00226533	2.30001E-08	31.2654
rs56161855	T	A	0.022458	0.132847	0.00291784	1.39991E-14	59.23793
rs56203622	C	T	0.017977	0.145529	0.00280183	1.40001E-10	41.1667
rs56352336	C	T	-0.01633	0.154894	0.00275021	2.90001E-09	35.24367
rs56399737	T	C	-0.01613	0.449124	0.00199646	6.4003E-16	65.29533
rs56858768	A	G	0.015919	0.296861	0.00217378	2.39994E-13	53.62774
rs56893062	G	T	0.012514	0.303342	0.00215383	6.19998E-09	33.75798
rs56930105	T	C	0.015756	0.139295	0.00286187	3.69999E-08	30.30928
rs57636386	C	T	-0.04126	0.08383	0.00358326	1.10002E-30	132.5571
rs57989773	C	T	0.013349	0.244995	0.00236315	0.000000016	31.90817
rs58862095	T	C	-0.02299	0.419266	0.00200786	2.39994E-30	131.0763
rs59068084	T	G	0.011055	0.410232	0.00201048	3.79997E-08	30.23665
rs59227842	G	A	0.022968	0.31149	0.00215313	1.50003E-26	113.7855
rs6023655	G	A	-0.01473	0.765741	0.00234997	3.59998E-10	39.31444
rs60764613	T	G	0.02099	0.144883	0.00282688	1.10002E-13	55.13281
rs61740466	A	G	-0.01352	0.237203	0.00231885	5.60003E-09	33.97082
rs61813324	T	C	0.029026	0.135728	0.00292038	2.80027E-23	98.78538
rs61828641	A	G	0.022459	0.10925	0.00315913	1.20005E-12	50.53898
rs61871615	T	C	-0.02672	0.091551	0.00359269	1E-13	55.29682
rs61903695	G	A	0.016624	0.254964	0.00227115	2.49977E-13	53.5739
rs61992671	G	A	-0.01619	0.49195	0.00206924	5.10035E-15	61.2359
rs62020775	A	T	-0.01657	0.14168	0.0028635	7.19996E-09	33.47088
rs62107261	C	T	-0.09116	0.048327	0.00460882	4.60045E-87	391.1921
rs62176243	T	A	-0.01497	0.244987	0.00228878	6.09958E-11	42.77891
rs62190049	C	G	-0.01118	0.390446	0.00203614	0.00000004	30.1476
rs62241847	G	A	-0.01243	0.314443	0.00212897	5.30005E-09	34.06784
rs62246311	A	G	0.020754	0.102364	0.00325487	1.79999E-10	40.6567
rs62379271	G	T	0.011724	0.578511	0.00200557	0.000000005	34.17069
rs62407562	A	T	0.014439	0.268584	0.00222463	8.49963E-11	42.12857
rs6265	T	C	-0.03992	0.188472	0.00252719	3.29989E-56	249.5012
rs6430068	A	G	0.018607	0.108559	0.0031882	5.30005E-09	34.05987
rs6444950	A	G	0.015853	0.237474	0.00232007	8.30042E-12	46.68672
rs6545714	A	G	-0.02052	0.601448	0.00201573	2.39994E-24	103.6503
rs6560906	C	T	-0.0122	0.691874	0.00214136	0.000000012	32.44874
rs6561937	A	T	-0.01593	0.753587	0.00230346	4.60045E-12	47.8507

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Supplementary Table I (cont.). Basic information about the SNPs used in this study

SNP	EA	OA	Beta	eaf	SE	pval	F
rs6567160	C	T	0.054172	0.232714	0.00234213	2.3014E-118	534.9739
rs6575340	A	G	0.020733	0.636038	0.00206189	8.69961E-24	101.1127
rs66679256	T	C	0.014886	0.445826	0.00198759	6.89922E-14	56.09521
rs6669341	G	A	-0.01703	0.582679	0.0019986	1.59993E-17	72.59575
rs6682438	C	T	0.013159	0.673081	0.00210047	3.69999E-10	39.24519
rs6707827	G	A	0.011944	0.703627	0.00217332	3.89996E-08	30.20163
rs6710091	G	C	-0.01168	0.348174	0.00206707	0.000000016	31.9474
rs6713781	C	G	-0.01357	0.401882	0.00202799	2.19989E-11	44.79798
rs6725931	T	C	0.019105	0.847658	0.00274403	3.29989E-12	48.47281
rs6744646	G	A	0.055468	0.828299	0.00261213	4.4999E-100	450.9223
rs6752979	A	G	0.012524	0.31688	0.00211721	3.29997E-09	34.98836
rs67609008	C	T	0.017086	0.283614	0.0022021	8.60003E-15	60.20353
rs6769617	T	A	-0.01358	0.66386	0.00208902	8.10028E-11	42.2299
rs6774894	A	T	0.013309	0.358148	0.00205674	9.70063E-11	41.87155
rs6777784	T	G	0.011613	0.61678	0.00202753	0.00000001	32.80325
rs6831088	A	G	-0.01152	0.640139	0.0020591	2.19999E-08	31.31237
rs6843852	T	C	0.01309	0.507861	0.00197607	3.50026E-11	43.8788
rs6909685	T	C	-0.01461	0.326809	0.00211352	4.70002E-12	47.79766
rs6922607	G	A	0.014885	0.189847	0.00251479	3.2E-09	35.03342
rs6938973	C	T	0.018222	0.601456	0.00201872	1.80011E-19	81.4806
rs6950388	A	G	0.015522	0.795086	0.00244806	2.30001E-10	40.20181
rs698147	G	A	-0.01285	0.543596	0.00198514	9.60064E-11	41.90879
rs7024334	G	T	-0.01382	0.77914	0.00238338	6.69993E-09	33.61127
rs7027304	T	C	0.014549	0.652661	0.00208703	3.10027E-12	48.59827
rs7034554	G	A	-0.01298	0.373825	0.00204252	2.1E-10	40.40087
rs7038943	C	T	-0.01402	0.33879	0.00208641	1.80011E-11	45.15534
rs704061	C	T	0.014637	0.45505	0.00198552	1.69981E-13	54.34747
rs705158	A	T	0.015595	0.244747	0.00230446	1.29987E-11	45.79769
rs7070670	T	C	-0.01233	0.327923	0.00211928	5.99998E-09	33.83501
rs7081254	C	T	-0.01425	0.205739	0.00245216	6.19998E-09	33.77767
rs7124681	A	C	0.025698	0.408353	0.0020063	1.50003E-37	164.0578
rs7132908	A	G	0.02979	0.384458	0.00203363	1.39991E-48	214.5897
rs71495038	A	G	0.0278	0.076936	0.00370969	6.70039E-14	56.15754
rs7201895	A	G	-0.01498	0.354291	0.00207999	6.00067E-13	51.85504
rs7206608	G	C	0.013512	0.32162	0.00211797	1.79999E-10	40.7017
rs7218014	C	T	0.018952	0.197305	0.00249216	2.90001E-14	57.83312
rs7232171	T	G	0.01234	0.58263	0.00200821	8E-10	37.76072
rs723672	T	C	0.011127	0.43151	0.00200698	2.99999E-08	30.73927
rs7250833	T	C	0.013504	0.288866	0.002188	6.69993E-10	38.09225
rs7259070	C	T	0.021869	0.596062	0.00203628	6.59933E-27	115.3408
rs72634826	A	G	-0.02128	0.259858	0.00228001	1E-20	87.08579
rs72649373	C	T	0.017806	0.143188	0.00287805	6.1E-10	38.2777
rs72892910	T	G	0.03878	0.172232	0.00262053	1.50003E-49	218.9943

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Supplementary Table I (cont.). Basic information about the SNPs used in this study

SNP	EA	OA	Beta	eaf	SE	pval	F
rs72976986	A	G	-0.02323	0.190123	0.00254712	7.59976E-20	83.14551
rs73052033	C	T	-0.03039	0.18493	0.00254634	7.70016E-33	142.4661
rs7306534	A	G	-0.01128	0.621712	0.00205437	4.09996E-08	30.12358
rs73124396	C	T	-0.01545	0.205144	0.0024548	3.09999E-10	39.59746
rs73142879	T	C	-0.02669	0.192297	0.00252257	3.59998E-26	111.9767
rs73193736	G	A	-0.01772	0.243934	0.00232002	2.19989E-14	58.31394
rs73213484	T	A	-0.02258	0.141236	0.0028364	1.69981E-15	63.35518
rs7331420	A	G	-0.01437	0.285276	0.00220081	6.59933E-11	42.63444
rs7357754	G	A	0.014115	0.500139	0.00198362	1.10002E-12	50.63143
rs73601548	T	C	0.017735	0.114527	0.00311639	1.29999E-08	32.38757
rs73985439	C	A	0.013662	0.307299	0.00214059	1.7E-10	40.73204
rs7442885	G	C	-0.02282	0.214049	0.00241251	3.19963E-21	89.4442
rs745249	T	C	0.017612	0.281945	0.00219724	1.10002E-15	64.24695
rs74750282	C	T	-0.01964	0.086623	0.00352561	0.000000025	31.02665
rs7516554	T	C	0.012007	0.399941	0.00201565	2.59998E-09	35.48214
rs7519259	A	G	0.014003	0.52836	0.00198381	1.69981E-12	49.82297
rs7539903	A	T	-0.01317	0.615562	0.0020273	8.30042E-11	42.19647
rs754635	G	C	0.021993	0.886582	0.0031093	1.50003E-12	50.02924
rs75499503	T	C	-0.01803	0.220101	0.00241845	8.9002E-14	55.59895
rs7571496	G	A	-0.01589	0.260545	0.00225454	1.80011E-12	49.68432
rs76183894	C	T	-0.02196	0.080747	0.00364437	1.7E-09	36.30417
rs7619139	A	T	0.013454	0.588616	0.00201061	2.19989E-11	44.7742
rs76702514	G	C	-0.01649	0.210623	0.00243278	1.20005E-11	45.92355
rs7683836	A	G	-0.01225	0.557215	0.00199427	8.19993E-10	37.71242
rs7707394	A	G	-0.01925	0.35732	0.00205858	8.60003E-21	87.46317
rs7708584	G	A	-0.01593	0.572344	0.0019949	1.39991E-15	63.78283
rs7761673	A	T	-0.01359	0.21988	0.0023901	1.29999E-08	32.33722
rs7762794	G	A	0.014908	0.285408	0.00218606	9.09913E-12	46.50473
rs7774	A	C	0.014988	0.310467	0.00215169	3.29989E-12	48.5208
rs7776021	A	G	0.01237	0.287599	0.00218251	1.40001E-08	32.12432
rs7802342	G	T	0.012275	0.288566	0.00218145	1.79999E-08	31.662
rs7805441	T	C	0.013375	0.502261	0.00198884	1.80011E-11	45.22394
rs78086698	C	T	0.031836	0.039838	0.0050761	3.59998E-10	39.33403
rs784257	C	T	0.017932	0.812541	0.00254968	1.99986E-12	49.46089
rs78605811	C	A	-0.03274	0.05405	0.00444673	1.80011E-13	54.19962
rs7893571	T	G	0.014055	0.665897	0.00210152	2.29985E-11	44.73147
rs7924036	T	G	-0.01428	0.503265	0.0019778	5.10035E-13	52.15676
rs7925100	A	G	0.014725	0.396117	0.0020221	3.29989E-13	53.02801
rs7928320	G	C	0.024338	0.056563	0.00428501	1.29999E-08	32.26092
rs7944782	G	T	0.015761	0.509784	0.00198748	2.19989E-15	62.88397
rs7947143	A	G	-0.01828	0.163483	0.00267522	8.30042E-12	46.68183
rs79780963	T	C	0.02368	0.077428	0.00369591	1.5E-10	41.05175
rs7996639	A	G	0.014556	0.449354	0.00200245	3.59998E-13	52.83902

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Supplementary Table I (cont.). Basic information about the SNPs used in this study

SNP	EA	OA	Beta	eaf	SE	pval	F
rs80135274	T	A	0.021339	0.070324	0.00388113	3.79997E-08	30.22955
rs8015400	A	C	0.021342	0.677097	0.00211709	6.70039E-24	101.6248
rs8020365	A	T	0.025107	0.220464	0.00239517	1E-25	109.8778
rs8024137	T	A	0.015633	0.848207	0.00276778	0.000000016	31.90186
rs8025516	G	T	-0.01466	0.645928	0.00207578	1.69981E-12	49.849
rs8076669	C	T	0.014068	0.561561	0.00199601	1.80011E-12	49.67587
rs8089514	A	T	0.012988	0.36868	0.00207588	3.89996E-10	39.14534
rs815163	C	T	-0.01649	0.563148	0.00198582	1E-16	68.91252
rs852042	G	A	-0.01312	0.758575	0.00231309	1.40001E-08	32.17577
rs862320	T	C	-0.02317	0.40965	0.00201345	1.20005E-30	132.4285
rs879620	T	C	0.024114	0.613237	0.00203595	2.29985E-32	140.2781
rs909001	G	C	0.01606	0.17211	0.00261353	8E-10	37.75895
rs909892	A	G	-0.01841	0.134817	0.00291255	2.59998E-10	39.95622
rs923994	G	A	-0.01458	0.783195	0.00240219	1.29999E-09	36.81866
rs9267671	A	G	0.026149	0.060733	0.00413587	2.59998E-10	39.97389
rs9294260	A	G	0.014782	0.476559	0.00198818	1E-13	55.27834
rs9349235	T	C	0.011181	0.410635	0.00200924	2.59998E-08	30.96634
rs935166	A	G	-0.01611	0.506805	0.00197292	3.19963E-16	66.64826
rs9463175	T	C	-0.0115	0.338958	0.00210115	4.39997E-08	29.95584
rs9478496	C	T	0.018184	0.164225	0.00267493	1.10002E-11	46.20989
rs9515446	G	A	0.015105	0.447709	0.00199052	3.19963E-14	57.58563
rs9522180	T	C	-0.01411	0.553392	0.00199325	1.50003E-12	50.10715
rs9571687	A	C	-0.01354	0.329363	0.0021094	1.40001E-10	41.19481
rs9638713	G	A	-0.03617	0.97477	0.00635399	0.000000012	32.41067
rs9673839	G	A	0.013034	0.490967	0.00198783	5.50047E-11	42.99094
rs9674487	G	C	0.158445	0.001338	0.0286171	3.09999E-08	30.65532
rs9830592	A	C	0.015485	0.582421	0.00200164	1E-14	59.84734
rs9835772	T	A	0.016629	0.243646	0.00229878	4.70002E-13	52.32777
rs9839081	A	G	-0.0117	0.325232	0.00214045	4.60002E-08	29.8838
rs9843653	C	T	0.029451	0.511652	0.00197538	2.90001E-50	222.2777
rs9876664	T	G	-0.01805	0.375389	0.00204174	9.60064E-19	78.13537
rs9888533	T	C	0.012004	0.538079	0.0020182	2.69998E-09	35.37603
rs9926784	C	T	-0.02382	0.184576	0.00254677	8.60003E-21	87.46436
rs9951619	G	T	0.014423	0.767369	0.00235777	9.49992E-10	37.42091

SNPs: single nucleotide polymorphisms; EA: effect allele; OA: other allele; SE: standard error.

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