

**Supplementary Information for: Fine-scale mapping of the *CYP19A1* locus and Mendelian randomisation support a causal role for estradiol in endometrial cancer risk.**

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## SUPPLEMENTARY NOTE

### A. Detailed Description of the Endometrial Cancer Case and Control Sample Sets

A summary of the studies included in the iCOGS fine-mapping dataset and the genome-wide association study (GWAS) datasets is shown in **Supplementary Table 1a**, with additional details provided below. All studies were predominantly of women of European ancestry. All studies have the relevant IRB approval in each country in accordance with the principles embodied in the Declaration of Helsinki, and informed consent was obtained from all participants. A total of 6,608 cases and 37,925 controls were included in the meta-analysis.

#### *Fine-mapping (iCOGS) Case Sample Sets:*

The iCOGS fine-mapping data set included cases from 9 studies detailed below, as well as additional European ancestry cases from ANECS and SEARCH (non-overlapping with the GWAS datasets).

#### **BECS**

The Bavarian Endometrial Cancer Cases and Controls Study (BECS) is a single-center case-control study, conducted between 2002 and 2008, with the aim of investigating genetic and epidemiological risk factors for endometrial cancer. Cases were either incident cases referred to the University Hospital Erlangen by surrounding practitioners (66% of the case sample set), or prevalent cases that were outpatients in follow-up care approached within 6.2 ( $\pm 4.6$  SD) years after treatment for primary endometrial cancer in the same hospital (34% of the case sample set). Epidemiological information was collected by a structured questionnaire completed during an interview and clinical data for the cases was obtained from clinical health records.

#### **CAHRES**

Details of the population selection process have been published previously for the Cancer Hormone Replacement Epidemiology Study (CAHRES)<sup>1</sup>. Formerly known as the Singapore and Sweden Breast/Endometrial Cancer Study (SASBAC), this population based case-control study was conducted among Swedish women aged 50-74 years, who were residing in Sweden between January 1<sup>st</sup> 1994 and December 31<sup>st</sup> 1995. Endometrial cancer cases were identified through the nation-wide cancer registries in Sweden. All participants provided detailed questionnaire information. For endometrial cancer, histological specimens were reviewed and re-classified by the study pathologist. All participants reported Caucasian ethnicity.

#### **HJECS**

The Hannover-Jena Endometrial Cancer Study (HJECS), a hospital-based case-control study, included 250 German women, aged 31-89 years, who were recruited either at the Friedrich Schiller University of Jena or at Hannover Medical School after having been diagnosed with histologically confirmed primary incident endometrial carcinoma between 2004 and 2010. Epidemiological data were obtained from questionnaires, and information on tumor stage and histology was obtained from pathology and clinical reports. Over 98% were of German descent. Interviews were conducted at either the Friedrich Schiller University of Jena or at Hannover Medical School, and peripheral blood was collected for the extraction of DNA from white blood cells.

#### **LES**

The Leuven Endometrial Study (LES) is a hospital based case-control study. Eligible cases, identified by active surveillance of electronic patient files at the Leuven University Hospital, were white women aged 27-80 years diagnosed with endometrial cancer. Clinical data for endometrial cancer patients were recorded during interview at the time of diagnosis, and from pathology reports. All medical records were reviewed by trained abstractors and pathology reports compatible with primary, invasive, epithelial endometrial adenocarcinoma of all stages (I–IV) and all grades were consulted. Participation rates exceeded 95% for cases.

#### **MECS**

The Mayo Endometrial Cancer Study (MECS) is a hospital based prospective biobank collection. The majority

of patients seen at Mayo Clinic Rochester with primary endometrial cancer diagnosed at age 18 and older are enrolled. The collection was started in 2006 and contains blood and fresh frozen tissue. DNA was isolated from white blood cells using Qiagen isolation kits. DNA concentration was measured with picogreen. Clinical data were abstracted from electronic medical records.

### **MoMaTEC**

Molecular Markers in Treatment of Endometrial Cancer (MoMaTEC) cases were recruited from an unselected patient population primarily treated for endometrial carcinoma at Haukeland University Hospital, Bergen during 2001-2009. This is the referral hospital for Hordaland county; the area is demographically well defined, with about 450,000 inhabitants, representing approximately 10% of the Norwegian population and with a similar incidence rate and prognosis as the total Norwegian population of endometrial cancers<sup>2,4</sup>. Clinical Information for cases regarding age, FIGO stage, histologic subtype, grade and prognosis was extracted from medical records. DNA was extracted from peripheral blood samples.

### **NECS**

The Newcastle Endometrial Cancer Study (NECS) includes histologically confirmed endometrial cancer cases consecutively recruited from 1992 up to 2005 at the Hunter Centre for Gynaecological Cancer, John Hunter Hospital, Newcastle, New South Wales, Australia<sup>5</sup>. The final analysis included 194 endometrial cancer patients. Data on reproductive and environmental risk factors including ethnicity, was collected using self-reported questionnaires. Information regarding recurrence, stage, grade and histology of endometrial cancer was collected from medical records. Patients presenting at this hospital-based site were captured by ANECS recruitment from 2005 onwards.

### **NSECG**

National Study of the Genetics of Endometrial Cancer (NSECG) cases were identified from collaborating clinicians throughout the UK from 2008 to present, taking care not to recruit from centres involved in SEARCH. Inclusion criteria were adenocarcinomas of the uterus presenting at 70 years of age or younger. Almost all cases were incident and sampled within 6 months of diagnosis. Peripheral blood was collected from each participant and DNA extracted using standard methods. Tumor histology was confirmed from routine hospital reports and further details of histopathology and other tumor pathology characteristic was abstracted from these clinical pathology reports. A sample of 797 cases that were non-overlapping with the NSECG GWAS were genotyped using the iCOGS chip, as indicated in **Supplementary Table 1a**.

### **RENDOCAS**

The Registry of Endometrial Cancer in Sweden (RENDOCAS) is a hospital based case-control study. Patients (n=262) who underwent surgery for endometrial cancer at Karolinska University hospital Solna, Sweden between 2008 and 2011 were included in the study. For each patient, the following was collected: blood and tumor samples; detailed family history and formulation of a pedigree where all suspected cancer cases were verified in medical records/pathology report if possible; questionnaire covering relevant environmental factors underlying endometrial cancer.

### **Control sample sets**

As indicated in **Supplementary Table 1a**, endometrial cancer case sample sets were matched by country to combined control sample sets from the same country that had been genotyped using the iCOGS chip. Data was largely from control sample sets that participated in the Breast Cancer Association Consortium iCOGS experiment<sup>6</sup>, with iCOGS data also accessed for controls from the Mayo Clinic via the Ovarian Cancer Association Consortium (MAY)<sup>7</sup>. In addition, iCOGS genotyping was performed for 183 Norwegian female controls, recruited in Bergen via the blood bank specifically for use in the MoMaTEC case-control genotyping studies.

### ***GWAS Case and Control Sample Sets:***

#### **AN ECS**

The Australian National Endometrial Cancer Study (AN ECS) is an Australian population-based case-control family study of cancer of the uterine corpus<sup>8</sup>. Women aged 18-79, newly diagnosed with histologically confirmed primary cancer of the endometrium between July 2005 and December 2007 were identified through major hospitals nationally, and also from state-based cancer registries. Excluding women who could not be contacted (mostly due to death, illness or failure to contact), case participation rate was 63%. Participants completed a detailed questionnaire providing clinical and epidemiological information, including ethnicity of all four grandparents. Information on tumor pathology characteristics was abstracted in standardized format from clinical pathology reports for all patients.

#### **SEARCH**

The Studies of Epidemiology and Risk factors in Cancer Heredity (SEARCH) is an ongoing population-based study with cases ascertained through the Eastern Cancer Registration and Information Centre (<http://www.ecric.org.uk>). All women diagnosed with endometrial cancer between the ages of 18-69 years (average age of diagnosis 58 years) from August 2001 to September 2007 were eligible for inclusion. Approximately 54% of eligible patients have enrolled in the study. Women taking part in the study were asked to provide a 20ml blood sample for DNA analysis, and to complete a comprehensive epidemiological questionnaire. Controls were also drawn from SEARCH (<http://ccge.medschl.cam.ac.uk/search/>), but had no prior history of cancer at the time of recruitment. They were female, also between the ages of 18-69 at the time of recruitment and matched to cases in geographical profile. Approximately 35% of eligible controls enrolled in the study. All participants reported Caucasian ethnicity. Information on tumor pathology characteristics was provided by the Eastern Cancer Registration and Information Centre and was derived from clinical pathology reports for all patients.

Genome-wide genotyping of the AN ECS and SEARCH cases was performed using an Illumina Infinium 610K array and called using the Illuminus algorithm. Genotypes were available for 1317 cases with endometrial cancer. Samples were excluded as follows: probable Turner's syndrome or male sex based on genotypes for markers on the X and Y chromosomes (n=4); call rate <95% (n=15); heterozygosity outside 5 standard deviations from the mean (n=7); probable sibling pairs identified as close relatives by identity-by-state probabilities >0.85 (n=3); >15% non-European ancestry estimated from identity-by-state scores (n=1), leaving a total of 1287 cases (606 from AN ECS and 681 from SEARCH). The duplicate concordance was 99.998%.

#### **QIMR**

The QIMR Berghofer Medical Research Institute control sample<sup>2</sup> is a subsection of individuals recruited as part of the Brisbane Adolescent Twin Study. Twins were recruited from schools in Brisbane, Australia and surrounding areas of southeast Queensland and were examined close to their 12th birthday. Blood was obtained from all twins and most parents. Parents were asked the ancestry of all eight great-grandparents of the twins. More than 95% of great-grandparents were identified as being of northern European ancestry, mainly from Britain and Ireland. This analysis used genotype data from parents and siblings only, extracted from an existing Illumina 610K BeadChip genome-wide association scan<sup>2</sup> and recalled using the Illuminus algorithm. After standard QC steps (as for the case data) 1,846 QIMR Berghofer controls were included in the analysis.

#### **HCS**

The Hunter Community Study (HCS) is a population-based cohort study consisting of men and women aged 55-85 years of age in Newcastle, New South Wales, Australia<sup>12</sup>. Participants were randomly selected from the NSW State electoral roll (listing on the electoral roll is compulsory in Australia) and contacted between December 2004 and December 2007. Non-English speaking persons and those living in a residential aged-care facility were ineligible for participation in the study. Participants were asked to complete five self-report questionnaires as well as attend the HCS data collection centre so clinical measures could be obtained. In total, 44.5% of eligible controls agreed to participate in this study. Genotype data for this study were extracted from



an existing Illumina 610K BeadChip genome-wide association study scan and recalled using the Illuminus algorithm. After standard QC steps (as for the case data) 1,237 HCS controls were included in the analysis.

### **WTCCC**

Controls utilized for stage 1 analysis were genotyped as part of the Wellcome Trust Case Control Consortium (WTCCC2)<sup>13</sup>. These controls are drawn from two sources: 2,922 controls from the 1958 Birth Cohort (1958BC), a population-based study in the United Kingdom of individuals born in 1 week in 1958<sup>14</sup>; and 2,737 controls identified through the UK National Blood Service (NBS)<sup>13</sup>. The analyses presented here are based on 2,694 1958BC and 2,496 NBS controls for which valid genotype data were available at the time of analysis.

### **NSECG**

As detailed above, NSECG cases were identified from collaborating clinicians throughout the UK, based on diagnosis of adenocarcinoma of the uterus at 70 years of age or younger. A sample of 919 non-overlapping NSECG cases were genotyped at the Wellcome Trust Centre for Human Genetics Oxford using the Illumina 660K genome-wide array. Controls were spouses or partners of colorectal cancer cases unaffected by cancer and without a personal family history (to 2<sup>nd</sup> degree relative level) of colorectal neoplasia drawn from the UK1/CORGI colorectal cancer sample set<sup>15</sup>, genotyped previously using the Illumina 550K genome-wide array<sup>15</sup>.

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**Supplementary Table 1a: Details of cases and controls included in the endometrial cancer analyses**

<b>Study</b>	<b>Abbreviation</b>	<b>Description</b>	<b>Cases</b>
<b>Genome-wide association studies</b>			
Australian National Endometrial Cancer Study	ANECS	Australia; population based case-control study	606
Queensland Institute of Medical Research	QIMR	Australia; parents of participants in adolescent twin study	-
Hunter Community Study	HCS	Australia; population-based cohort	-
Study of Epidemiology and Risk Factors in Cancer Heredity	SEARCH	England; population based case-control study	681
Wellcome Trust Case-Control Consortium	WTCCC	UK: sample from 1958 Birth Cohort and UK Blood Donors from NBS	-
National Study of the Genetics of Endometrial Cancer	NSECG	United Kingdom; population based case-control study	919
Colorectal Tumour Gene Identification	CORGI	United Kingdom; cancer-free spouse/partner controls for colorectal cancer study	-
<b>iCOGS Sample Sets**</b>			

Australian National Endometrial Cancer Study***	AN ECS	Australia; population-based case-control study	439
Newcastle Endometrial Cancer Study***	NECS	Newcastle, Australia; hospital-based cases	182
Australian Breast Cancer Family Study	ABCFS	Melbourne/Sydney Australia; from electoral rolls	-
Australian Ovarian Cancer Study	AOCS	Australia; population-based, from electoral rolls	-
Melbourne Collaborative Cohort Study	MCCS	Melbourne, Australia; random sample from initial cohort	-
Study of Epidemiology and Risk Factors in Cancer Heredity	SEARCH	England; population based case-control study	829
National Study of the Genetics of Endometrial Cancer	NSECG	UK; population based case-control study	797
British Breast Cancer Study	BBCS	UK; friend, sister-in-law, daughter-in-law or other non-blood relative of breast cancer case	-
Sheffield Breast Cancer Study	SBCS	Sheffield, UK; women attending Sheffield Mammography Screening, with no breast cancer	-
UK Breakthrough Generations Study	UKBGS	UK; women without breast lesions selected from BGS cohort	-
Mayo Endometrial Cancer Study	MECS	Mayo Clinic, USA. Hospital based case-control study.	236



Mayo Clinic Breast Cancer Study	MCBCS	Mayo Clinic, USA. Cancer-free women presenting for general medical examination	-
Mayo Clinic Ovarian Cancer Case-Control Study	MCOCCCS	Mayo Clinic, USA. Cancer-free women presenting for general medical examination	-
Leuven Endometrial Cancer Study	LES	Leuven, Belgium; hospital based case-control study	327
Leuven Multidisciplinary Breast Centre	LMBC	Leuven, Belgium; blood donors.	-
Bavarian Endometrial Cancer Study/Hannover-Jena Endometrial Cancer Study	BECS/HJECS	Germany; hospital-based/population-based case-control study	139
Bavarian Breast Cancer Cases and Controls	BBCC	Bavaria, Germany; healthy women >55yrs from newspaper advertisement	-
Breast Cancer Study of the University Clinic Heidelberg	BSUCH	Mannheim, Germany; female blood donors	-
ESTHER Breast Cancer Study	ESTHER	Saarland, Germany; random sample from routine health check-up	-
German Consortium for Hereditary Breast & Ovarian Cancer	GC-HBOC	Augsburg, Germany; KORA study	-
Gene Environment Interaction and Breast Cancer in Germany	GENICA	Bonn area, Germany; random address sample	-
Mammary Carcinoma Risk Factor Investigation	MARIE	Hamburg/Rhein-Neckar-Karlsruhe, Germany;	-

		randomly drawn from population registries	
Molecular Markers in Treatment of Endometrial Cancer	MoMaTEC	Norway; population based case-control study	637
Norwegian Breast Cancer Study	NBCS	Tromso/Bergen, Norway; attendees at Norwegian Breast Cancer Screening Program	-
Cancer Hormone Replacement Epidemiology in Sweden	CAHRES	Sweden, population based case-controls study	554
Registry of Endometrial Cancer in Sweden	RENDOCAS	Stockholm, Sweden. Hospital based study	262
Karolinska Breast Cancer Study	KARBAC	Stockholm, Sweden; blood donors	-
Karolinska Mammography Project for Risk Prediction of Breast Cancer	pKARMA	Helsingborg/Stockholm, Sweden; cancer-free participants in KARMA mammographic screening program	-
<b>TOTAL</b>			<b>6,608</b>

The number of cases and controls represents the maximum number of genotypes from cases and controls of reported Caucasian ethnicity, following exclusions

\*\*For the iCOGS sample sets, studies which are grouped together in the table were analysed as a single strata.

“iCOGS array” is a Custom Illumina Infinium iSelect array

**Supplementary Table 1b: Further details of cases and controls included in the endometrial cancer analyses**

	iCOGS: cases (n=4,401)	iCOGS: controls (n=28,758)	SEARCH GWAS: cases (n=681)	SEARCH GWAS: WTCCC controls (n=5,190)	ANECs GWAS: cases (n=606)	ANECs GWAS: HCS controls (n=1,237)
Mean (sd) age in years at diagnosis (cases) or recruitment (controls)	62.9 (9.2)	55.7 (10.5)	62.0 (7.0)	44*	61.2 (9.1)	66.3 (7.5)
Number with missing age	91	1,696	0	*	3	0
Mean (sd) BMI in kg/m <sup>2</sup>	29.9 (7.3)	26.3 (4.9)	29.1 (6.6)	26.7 (5.3)**	32.1 (8.5)	28.7 (4.8)
Number with missing BMI	2,858	14,098	37	3,931	22	0
Histology: number (%)					606	
Endometrioid	3,535 (80.3%)	-	681 (100%)	-	(100%)	-
Other	757 (17.2)	-	0	-	0	-
Missing	109 (2.5%)	-	0	-	0	-

\*, \*\*Data for 1261 (females only) 1958 Birth Cohort samples genotyped by the WTCCC. BMI data were collected during the 2002-2003 Biomedical Survey.

**Supplementary Table 1c: Details of women included in the analyses of circulating hormone levels**

Study	Age (yrs)	BMI kg/m2	Estradiol pmol/L			Genotyping					
	Mean (sd)	Mean (sd)	N	Min-max	Mean (sd)	N	Min-max	Mean (sd)	Min-max	Mean(sd)	
<b>Main Analysis</b>											
EPIC Norfolk Health Check 2	67.0 (6.7)	26.7 (4.3)	1500	2.9 - 29 8.0 3.0	20.0 (22.4)	1431	0.17-4.12	0.81 (0.50)	3.63-952	30.7 (39.8)	iCOGS array
EPIC Norfolk Health Check 1*	65.3 (6.3)	26.5 (4.0)	416	22 7.0 1.0	26.3 (26.2)	0	n/a	n/a	n/a	n/a	iCOGS array
Sisters in Breast Screening (SIBS)	62.9 (5.5)	27.2 (5.2)	302	76. 0	20.3 (18.2)	302	0.14-3.43	0.84 (0.52)	1.74-168	28.1 (24.3)	iCOGS array
<b>Additional Replication Genotyping</b>			2218			1733					
Sisters in Breast Screening (SIBS)**	61.7 (5.3)	27.2 (5.2)	549	1.0 - 76. 0	20.4 (25.1)						TaqMan
<b>TOTAL</b>			2767								

\* excludes women also in Health Check 2

\*\* excludes SIBS women in iCOGS study

\*\*\* The ratio of estradiol to testosterone/1000

"iCOGS array" is a Custom Illumina Infinium iSelect array

Supplementary Table 2: Results of the endometrial cancer and estradiol:testosterone ratio analyses for the 171 SNPs in the CYP19A1 region for which P<10 <sup>-4</sup> in the endometrial cancer case-control study.																																												
Endometrial Cancer					Endometrial Cancer					Endometrial Cancer Meta					Endometrial Cancer Meta					Endometrial Cancer					Endometrial Cancer					Endometrial Cancer					Estradiol:Testosterone ratio									
Meta-analysis					Conditional on rs727475					Endometrioid Histology Case					Non-endometrioid histology ca: by histology					iCOGS					SEARCH GWAS					ANECs GWAS					NSECg GWAS									
SNP	Position (build 37)	A1/A2	OR (95% CI)	P	hetp	I2	OR (95% CI)	P	r2 with rs727475	OR (95% CI)	P	OR (95% CI)	P	Case-only P	Freq (A2)	Info	OR (95% CI)	P	Freq (A2)	Info	OR (95% CI)	P	Freq (A2)	Info	OR (95% CI)	P	Freq (A2)	Info	OR (95% CI)	P	Rsq	beta(se)	P	conditional on rs727475										
chr15:51412282:0	51412282	T/TG	1.09 (1.04,1.14)	8.78E-05	0.83	0.0%	1.01 (0.96,1.06)	8.27E-01	0.356	1.09 (1.04,1.14)	4.77E-04	1.08 (0.97,1.20)	1.55E-01	8.18E-01	0.593	0.883	1.10 (1.04,1.16)	5.01E-04	0.599	0.89	1.11 (0.98,1.26)	9.75E-02	0.589	0.888	1.08 (0.95,1.23)	2.52E-01	0.594	0.919	1.03 (0.90,1.18)	6.93E-01	0.884	-0.043 (0.025)	9.01E-02	4.46E-01										
chr15:51452275:0	51452275	AAAT/A	1.10 (1.05,1.14)	2.00E-05	0.99	0.0%	1.06 (1.02,1.11)	4.12E-03	0.141	1.10 (1.05,1.15)	1.95E-05	1.04 (0.94,1.16)	4.31E-01	3.54E-01	0.347	0.954	1.10 (1.05,1.16)	2.58E-04	0.365	0.99	1.07 (0.95,1.21)	2.43E-01	0.355	0.986	1.10 (0.97,1.25)	1.57E-01	0.354	0.939	1.09 (0.95,1.24)	2.17E-01	0.962	-0.033 (0.023)	1.41E-01	9.30E-01										
rs4774872	51454065	C/T	1.10 (1.05,1.14)	1.57E-05	0.98	0.0%	1.07 (1.02,1.11)	3.26E-03	0.128	1.10 (1.06,1.15)	1.50E-05	1.04 (0.94,1.16)	4.25E-01	3.45E-01	0.344	0.962	1.10 (1.05,1.16)	1.91E-04	0.364	0.99	1.07 (0.95,1.21)	2.44E-01	0.354	0.992	1.09 (0.96,1.24)	1.65E-01	0.353	0.996	1.09 (0.95,1.24)	2.16E-01	0.970	-0.032 (0.023)	1.55E-01	9.59E-01										
rs8035909	51454712	C/T	1.13 (1.07,1.19)	7.07E-06	0.40	0.0%	1.09 (1.04,1.15)	9.71E-04	0.074	1.14 (1.08,1.21)	7.93E-06	1.11 (0.97,1.27)	1.27E-01	6.88E-01	0.174	0.150	0.962	1.16 (1.08,1.24)	1.78E-05	0.174	0.99	1.06 (0.91,1.23)	4.58E-01	0.164	0.989	1.17 (1.00,1.38)	5.47E-02	0.168	0.994	1.01 (0.85,1.21)	8.80E-01	0.969	-0.061 (0.027)	2.57E-02	3.59E-01									
rs720316	51455815	G/T	1.13 (1.07,1.19)	8.90E-06	0.38	3.1%	1.09 (1.04,1.15)	1.16E-03	0.074	1.14 (1.07,1.21)	9.50E-06	1.11 (0.97,1.26)	1.39E-01	6.87E-01	0.151	0.153	0.962	1.16 (1.08,1.23)	2.20E-05	0.174	0.99	1.06 (0.91,1.23)	4.53E-01	0.164	0.987	1.18 (1.00,1.39)	4.99E-02	0.169	0.991	1.01 (0.85,1.20)	9.47E-01	0.968	-0.062 (0.027)	2.35E-02	3.41E-01									
rs7181680	51456110	A/G	1.10 (1.05,1.14)	1.45E-05	0.98	0.0%	1.07 (1.02,1.11)	3.07E-03	0.128	1.10 (1.06,1.15)	1.38E-05	1.04 (0.94,1.16)	4.24E-01	3.40E-01	0.344	0.962	1.10 (1.05,1.16)	1.77E-04	0.364	0.99	1.07 (0.95,1.21)	2.41E-01	0.354	0.992	1.10 (0.96,1.24)	1.63E-01	0.353	0.996	1.09 (0.95,1.24)	2.16E-01	0.970	-0.033 (0.023)	1.50E-01	9.45E-01										
rs12902455	51456500	A/G	1.10 (1.05,1.14)	1.45E-05	0.98	0.0%	1.07 (1.02,1.11)	3.07E-03	0.128	1.10 (1.06,1.15)	1.38E-05	1.04 (0.94,1.16)	4.25E-01	3.40E-01	0.344	0.962	1.10 (1.05,1.16)	1.77E-04	0.364	0.99	1.07 (0.95,1.21)	2.42E-01	0.354	0.992	1.10 (0.96,1.24)	1.63E-01	0.353	0.996	1.09 (0.95,1.24)	2.17E-01	0.969	-0.033 (0.023)	1.49E-01	9.42E-01										
rs12594156	51456518	C/T	1.10 (1.05,1.14)	1.45E-05	0.98	0.0%	1.07 (1.02,1.11)	3.07E-03	0.128	1.10 (1.06,1.15)	1.38E-05	1.04 (0.94,1.16)	4.25E-01	3.40E-01	0.344	0.962	1.10 (1.05,1.16)	1.77E-04	0.364	0.99	1.07 (0.95,1.21)	2.42E-01	0.354	0.992	1.10 (0.96,1.24)	1.63E-01	0.353	0.996	1.09 (0.95,1.24)	2.17E-01	0.969	-0.033 (0.023)	1.49E-01	9.42E-01										
rs10152435	51457263	C/T	1.10 (1.05,1.14)	1.38E-05	0.99	0.0%	1.07 (1.02,1.11)	3.01E-03	0.128	1.10 (1.06,1.15)	1.30E-05	1.04 (0.94,1.16)	4.27E-01	3.39E-01	0.344	0.962	1.10 (1.05,1.16)	1.73E-04	0.365	0.99	1.08 (0.96,1.21)	2.23E-01	0.354	0.993	1.10 (0.96,1.24)	1.62E-01	0.353	0.996	1.09 (0.95,1.24)	2.17E-01	0.969	-0.033 (0.023)	1.47E-01	9.36E-01										
rs1898738	51457302	C/T	1.10 (1.05,1.14)	1.82E-05	0.98	0.0%	1.07 (1.02,1.11)	3.35E-03	0.122	1.10 (1.05,1.15)	1.71E-05	1.04 (0.94,1.16)	4.07E-01	3.44E-01	0.348	0.955	1.10 (1.05,1.16)	2.02E-04	0.367	0.99	1.07 (0.95,1.21)	2.59E-01	0.356	0.986	1.09 (0.96,1.24)	1.68E-01	0.356	0.988	1.09 (0.95,1.24)	2.21E-01	0.958	-0.034 (0.023)	1.28E-01	8.73E-01										
rs12591759	51457366	G/A	1.10 (1.05,1.14)	1.24E-05	0.99	0.0%	1.07 (1.02,1.11)	2.79E-03	0.129	1.10 (1.06,1.16)	1.14E-05	1.04 (0.94,1.16)	4.29E-01	3.28E-01	0.345	0.960	1.10 (1.05,1.16)	1.65E-04	0.365	0.99	1.08 (0.96,1.21)	2.20E-01	0.355	0.990	1.09 (0.96,1.24)	1.67E-01	0.355	0.993	1.09 (0.95,1.25)	2.12E-01	0.967	-0.032 (0.023)	1.56E-01	9.70E-01										
rs12591785	51457423	T/C	1.10 (1.05,1.14)	1.54E-05	0.98	0.0%	1.07 (1.02,1.11)	3.27E-03	0.129	1.10 (1.06,1.15)	1.45E-05	1.04 (0.94,1.16)	4.24E-01	3.44E-01	0.344	0.961	1.10 (1.05,1.16)	1.73E-04	0.366	0.99	1.07 (0.95,1.21)	2.42E-01	0.356	0.985	1.09 (0.96,1.24)	1.73E-01	0.355	0.993	1.09 (0.95,1.24)	2.26E-01	0.966	-0.033 (0.023)	1.45E-01	9.37E-01										
rs12592286	51457606	T/C	1.10 (1.05,1.14)	1.44E-05	0.98	0.0%	1.07 (1.02,1.11)	3.07E-03	0.128	1.10 (1.06,1.15)	1.38E-05	1.04 (0.94,1.16)	4.25E-01	3.39E-01	0.344	0.962	1.10 (1.05,1.16)	1.77E-04	0.365	0.99	1.07 (0.95,1.21)	2.42E-01	0.354	0.993	1.10 (0.96,1.24)	1.63E-01	0.353	0.996	1.09 (0.95,1.24)	2.17E-01	0.969	-0.033 (0.023)	1.46E-01	9.34E-01										
rs1438920	51458054	T/C	1.10 (1.05,1.14)	1.44E-05	0.98	0.0%	1.07 (1.02,1.11)	3.07E-03	0.128	1.10 (1.06,1.15)	1.38E-05	1.04 (0.94,1.16)	4.25E-01	3.39E-01	0.344	0.962	1.10 (1.05,1.16)	1.77E-04	0.365	0.99	1.07 (0.95,1.21)	2.42E-01	0.354	0.993	1.10 (0.96,1.24)	1.62E-01	0.353	0.996	1.09 (0.95,1.24)	2.17E-01	0.969	-0.033 (0.023)	1.45E-01	9.30E-01										
rs1550339	51459096	A/G	1.13 (1.07,1.20)	6.29E-06	0.40	0.0%	1.09 (1.04,1.15)	8.07E-04	0.074	1.14 (1.08,1.21)	7.02E-06	1.11 (0.97,1.27)	1.27E-01	6.79E-01	0.150	0.955	1.16 (1.08,1.24)	1.60E-05	0.174	0.99	1.06 (0.91,1.23)	4.53E-01	0.164	0.988	1.18 (1.00,1.38)	5.39E-02	0.168	0.993	1.01 (0.85,1.21)	8.81E-01	0.969	-0.062 (0.027)	2.48E-02	3.30E-01										
rs475923	51459264	C/T	1.10 (1.05,1.14)	1.44E-05	0.98	0.0%	1.07 (1.02,1.11)	3.05E-03	0.128	1.10 (1.06,1.15)	1.37E-05	1.04 (0.94,1.16)	4.25E-01	3.39E-01	0.344	0.962	1.10 (1.05,1.16)	1.77E-04	0.365	0.99	1.07 (0.95,1.21)	2.41E-01	0.354	0.993	1.10 (0.96,1.24)	1.62E-01	0.353	0.996	1.09 (0.95,1.24)	2.17E-01	0.969	-0.033 (0.023)	1.42E-01	9.21E-01										
chr15:51459417:0	51459417	T/TTTG	1.12 (1.06,1.18)	3.61E-05	0.45	0.0%	1.09 (1.03,1.14)	1.80E-03	0.112	1.12 (1.06,1.19)	4.24E-05	1.09 (0.96,1.24)	1.81E-01	6.35E-01	0.211	0.801	1.14 (1.07,1.22)	5.78E-05	0.224	0.85	1.01 (0.87,1.18)	8.72E-01	0.213	0.847	1.15 (0.89,1.35)	8.92E-02	0.218	0.873	1.05 (0.89,1.25)	5.39E-01	0.829	-0.058 (0.027)	2.99E-02	3.55E-01										
chr15:51459418:0	51459418	T/TTG	1.13 (1.07,1.19)	1.65E-05	0.27	22.6%	1.09 (1.03,1.15)	1.64E-03	0.072	1.13 (1.07,1.20)	2.23E-05	1.11 (0.97,1.27)	1.39E-01	7.49E-01	0.165	0.881	1.15 (1.07,1.23)	4.28E-05	0.172	0.94	1.07 (0.92,1.25)	3.62E-01	0.173	0.945	1.19 (1.01,1.40)	3.60E-02	0.178	0.945	1.07 (0.82,1.16)	7.73E-01	0.900	-0.066 (0.028)	1.76E-02	6.36E-01										
chr15:51459419:0	51459419	T/TG	1.12 (1.06,1.19)	2.56E-05	0.56	0.0%	1.10 (1.04,1.16)	8.58E-04	0.063	1.13 (1.07,1.20)	3.15E-05	1.10 (0.96,1.26)	1.59E-01	7.32E-01	0.165	0.869	1.15 (1.07,1.23)	5.57E-05	0.184	0.93	1.05 (0.90,1.23)	5.04E-01	0.177	0.928	1.15 (0.97,1.35)	1.03E-01	0.176	0.948	1.03 (0.87,1.23)	7.19E-01	0.947	-0.048 (0.027)	8.22E-02	5.96E-01										
rs475925	51459501	C/T	1.10 (1.05,1.15)	6.91E-06	0.97	0.0%	1.07 (1.03,1.12)	1.48E-03	0.152	1.11 (1.06,1.16)	7.14E-06	1.05 (0.95,1.17)	3.61E-01	3.46E-01	0.348	0.922	1.11 (1.05,1.17)	1.04E-04	0.370	0.98	1.08 (0.96,1.22)	2.19E-01	0.360	0.977	1.11 (0.97,1.26)	1.19E-01	0.363	0.984	1.08 (0.95,1.24)	2.43E-01	0.986	-0.032 (0.023)	1.55E-01	9.65E-01										
rs6493483	51459583	A/T	1.10 (1.05,1.15)	1.23E-05	0.98	0.0%	1.07 (1.02,1.11)	2.51E-03	0.125	1.11 (1.06,1.16)	1.09E-05	1.04 (0.94,1.16)	4.33E-01	3.21E-01	0.342	0.947	1.11 (1.05,1.16)	1.50E-04	0.365	0.99	1.07 (0.95,1.21)	2.36E-01	0.354	0.994	1.10 (0.96,1.24)	1.63E-01	0.353	0.997	1.09 (0.95,1.24)	2.18E-01	0.969	-0.033 (0.023)	1.41E-01	9.18E-01										
rs1438922	51460148	T/C	1.10 (1.05,1.15)	1.22E-05	0.98	0.0%	1.07 (1.02,1.11)	2.51E-03	0.125	1.11 (1.06,1.16)	1.09E-05	1.04 (0.94,1.16)	4.33E-01	3.21E-01	0.342	0.947	1.11 (1.05,1.16)	1.50E-04	0.365	0.99	1.07 (0.95,1.21)	2.36E-01	0.354	0.994	1.10 (0.96,1.24)	1.63E-01	0.353	0.997	1.09 (0.95,1.24)	2.18E-01	0.969	-0.033 (0.023)	1.40E-01	9.13E-01										
rs1595584	51460404	G/A	1.13 (1.07,1.19)	6.67E-06	0.40	0.0%	1.09 (1.04,1.15)	9.17E-04	0.074	1.14 (1.08,1.21)	7.39E-06	1.11 (0.97,1.27)	1.28E-01	6.78E-01	0.150	0.955	1.16 (1.08,1.24)	1.68E-05	0.174	0.99	1.06 (0.91,1.23)	4.55E-01	0.164	0.988	1.17 (1.00,1.38)	5.43E-02	0.168	0.993	1.01 (0.85,1.21)	8.82E-01	0.966	-0.061 (0.027)	2.71E-02	3.65E-01										
rs1438923	51460414	A/G	1.10 (1.05,1.15)	1.22E-05	0.98	0.0%	1.07 (1.02,																																					

rs8024515	51532276	T/C	1.15 (1.10,1.20)	2.20E-10	0.93	0.0%	1.02 (0.91,1.14)	7.40E-01	0.930	1.16 (1.11,1.22)	3.83E-10	1.09 (0.97,1.21)	1.36E-01	2.04E-01	0.616	0.906	1.16 (1.10,1.22)	7.27E-08	0.610	0.90	1.11 (0.98,1.26)	1.14E-01	0.609	0.910	1.16 (1.02,1.33)	2.55E-02	0.619	0.918	1.17 (1.01,1.34)	3.17E-02	0.913 0.112 (0.026)	1.48E-05	5.11E-01
rs56097510	51533478	C/G	1.11 (1.06,1.15)	6.61E-07	0.41	0.0%	1.00 (0.94,1.05)	9.06E-01	0.543	1.11 (1.06,1.15)	3.66E-06	1.12 (1.01,1.24)	2.59E-02	8.57E-01	0.491	0.992	1.13 (1.08,1.19)	5.32E-07	0.522	0.99	1.06 (0.95,1.19)	2.89E-01	0.515	0.990	1.03 (0.91,1.16)	6.92E-01	0.529	0.993	1.08 (0.95,1.23)	2.59E-01	0.987 0.119 (0.027)	9.71E-06	1.47E-01
rs61018102	51533530	G/C	1.11 (1.06,1.15)	5.52E-07	0.68	0.0%	1.02 (0.97,1.07)	4.55E-01	0.478	1.11 (1.06,1.16)	2.81E-06	1.11 (1.01,1.23)	3.41E-02	9.27E-01	0.476	0.991	1.13 (1.07,1.18)	1.58E-06	0.490	0.99	1.05 (0.94,1.18)	3.86E-01	0.477	0.986	1.09 (0.96,1.23)	1.90E-01	0.494	0.986	1.07 (0.94,1.23)	2.93E-01	0.985 0.102 (0.027)	1.59E-04	3.31E-01
rs7173595	51533736	C/T	1.15 (1.10,1.20)	7.90E-11	0.88	0.0%	0.88 (0.58,1.33)	5.52E-01	0.990	1.16 (1.11,1.22)	1.57E-10	1.08 (0.97,1.20)	1.44E-01	1.39E-01	0.654	0.993	1.16 (1.10,1.23)	1.28E-08	0.657	0.99	1.11 (0.98,1.26)	9.60E-02	0.655	0.986	1.12 (0.99,1.28)	8.08E-02	0.661	0.994	1.18 (1.02,1.35)	2.19E-02	0.985 0.133 (0.026)	3.41E-07	6.73E-01
rs7175531	51534055	T/C	1.15 (1.11,1.20)	6.66E-11	0.90	0.0%	0.90 (0.58,1.39)	6.26E-01	0.989	1.16 (1.11,1.22)	1.52E-10	1.08 (0.98,1.21)	1.30E-01	1.53E-01	0.653	1.000	1.16 (1.10,1.23)	1.17E-08	0.656	0.99	1.12 (0.99,1.26)	7.61E-02	0.655	0.994	1.12 (0.98,1.28)	8.77E-02	0.659	0.995	1.17 (1.02,1.35)	2.40E-02	1.000 0.132 (0.026)	4.15E-07	1.33E-01
rs727479	51534547	C/A	1.15 (1.11,1.21)	4.81E-11	0.92	0.0%				1.16 (1.11,1.22)	1.12E-10	1.08 (0.98,1.20)	1.31E-01	1.50E-01	0.651	1.000	1.16 (1.10,1.23)	1.10E-08	0.654	1.00	1.12 (0.99,1.27)	7.33E-02	0.653	1.000	1.13 (0.99,1.29)	6.74E-02	0.658	1.000	1.17 (1.02,1.35)	2.53E-02	1.000 0.135 (0.026)	2.06E-07	-
rs4775936	51536022	C/T	1.11 (1.06,1.15)	5.29E-07	0.63	0.0%	1.02 (0.97,1.07)	4.46E-01	0.478	1.11 (1.06,1.16)	2.83E-06	1.11 (1.01,1.23)	3.13E-02	9.34E-01	0.476	0.991	1.13 (1.07,1.18)	1.23E-06	0.488	0.98	1.05 (0.93,1.18)	4.13E-01	0.476	0.978	1.08 (0.96,1.23)	2.01E-01	0.493	0.980	1.07 (0.94,1.22)	3.07E-01	0.986 0.103 (0.027)	1.40E-04	3.06E-01
rs10459592	51536141	T/G	1.12 (1.07,1.16)	1.03E-07	0.96	0.0%	1.02 (0.95,1.09)	5.96E-01	0.700	1.12 (1.07,1.17)	3.88E-07	1.07 (0.97,1.19)	1.75E-01	4.82E-01	0.573	1.000	1.12 (1.07,1.18)	4.35E-06	0.578	0.98	1.10 (0.98,1.24)	1.09E-01	0.570	0.977	1.13 (1.00,1.28)	5.29E-02	0.580	0.979	1.08 (0.95,1.24)	2.43E-01	1.000 0.091 (0.025)	2.89E-04	4.04E-01
rs10851498	51537012	T/C	1.11 (1.06,1.15)	5.63E-07	0.61	0.0%	1.02 (0.97,1.07)	4.58E-01	0.475	1.11 (1.06,1.16)	2.96E-06	1.12 (1.01,1.23)	3.09E-02	9.33E-01	0.475	0.988	1.13 (1.07,1.18)	1.18E-06	0.488	0.98	1.05 (0.93,1.18)	4.34E-01	0.475	0.977	1.08 (0.96,1.23)	1.99E-01	0.493	0.979	1.07 (0.94,1.22)	3.19E-01	0.984 0.104 (0.027)	1.38E-04	3.03E-01
rs10851499	51537127	T/C	1.12 (1.07,1.17)	8.37E-08	0.94	0.0%	1.02 (0.95,1.10)	5.59E-01	0.706	1.12 (1.07,1.17)	3.14E-07	1.07 (0.97,1.19)	1.66E-01	4.68E-01	0.572	0.991	1.12 (1.07,1.18)	3.14E-06	0.578	0.97	1.10 (0.98,1.24)	1.13E-01	0.570	0.975	1.13 (1.00,1.28)	5.32E-02	0.580	0.977	1.08 (0.94,1.24)	2.57E-01	0.989 0.093 (0.025)	2.28E-04	4.58E-01
rs2414098	51537806	G/C	1.15 (1.10,1.20)	9.08E-11	0.82	0.0%	1.09 (0.99,1.21)	9.05E-02	0.861	1.16 (1.11,1.21)	1.51E-10	1.07 (0.97,1.19)	1.75E-01	1.82E-01	0.617	0.975	1.15 (1.10,1.22)	3.98E-08	0.618	0.97	1.10 (0.97,1.24)	1.43E-01	0.610	0.970	1.19 (1.04,1.36)	8.31E-03	0.619	0.973	1.15 (1.00,1.32)	4.43E-02	1.000 0.111 (0.025)	1.24E-05	5.92E-01
rs17523270	51538280	G/T	1.11 (1.06,1.15)	5.89E-07	0.53	0.0%	1.02 (0.97,1.07)	4.69E-01	0.474	1.11 (1.06,1.16)	3.01E-06	1.12 (1.01,1.23)	2.82E-02	9.25E-01	0.474	0.979	1.13 (1.08,1.19)	8.54E-07	0.487	0.97	1.04 (0.93,1.17)	4.83E-01	0.474	0.974	1.08 (0.96,1.23)	2.01E-01	0.493	0.977	1.06 (0.93,1.21)	3.72E-01	0.978 0.104 (0.027)	1.46E-04	2.99E-01
rs17523284	51538723	G/A	1.11 (1.06,1.15)	5.65E-07	0.51	0.0%	1.02 (0.97,1.07)	4.63E-01	0.475	1.11 (1.06,1.16)	2.88E-06	1.12 (1.01,1.24)	2.69E-02	9.24E-01	0.473	0.979	1.13 (1.08,1.19)	7.22E-07	0.486	0.98	1.04 (0.93,1.17)	4.88E-01	0.473	0.974	1.08 (0.96,1.23)	2.06E-01	0.493	0.978	1.06 (0.93,1.21)	3.93E-01	0.978 0.104 (0.027)	1.39E-04	2.86E-01
rs12899068	51538810	A/G	1.12 (1.08,1.17)	6.16E-08	0.88	0.0%	1.02 (0.96,1.10)	5.04E-01	0.711	1.12 (1.07,1.17)	2.25E-07	1.08 (0.97,1.19)	1.51E-01	4.60E-01	0.570	0.980	1.13 (1.07,1.19)	1.81E-06	0.573	0.98	1.10 (0.97,1.24)	1.23E-01	0.566	0.971	1.14 (1.00,1.29)	4.65E-02	0.579	0.971	1.07 (0.94,1.22)	3.19E-01	0.976 0.097 (0.025)	1.37E-04	6.62E-01
rs12591359	51539368	A/G	1.12 (1.07,1.17)	8.84E-08	0.32	13.8%	1.00 (0.93,1.07)	9.35E-01	0.725	1.12 (1.07,1.17)	3.85E-07	1.10 (0.99,1.22)	6.76E-02	3.77E-01	0.587	1.000	1.15 (1.09,1.21)	4.14E-08	0.594	1.00	1.06 (0.94,1.19)	3.30E-01	0.592	1.000	1.05 (0.92,1.19)	4.60E-01	0.601	0.930	1.06 (0.93,1.22)	3.88E-01	1.000 -0.111 (0.025)	1.00E-05	5.69E-01
rs62020093	51539777	C/G	1.17 (1.10,1.25)	6.28E-07	0.07	58.2%	1.12 (1.05,1.19)	3.28E-04	0.052	1.17 (1.07,1.25)	4.48E-06	1.25 (1.07,1.46)	5.63E-03	7.47E-01	0.126	0.737	1.25 (1.15,1.35)	8.25E-08	0.154	0.94	1.09 (0.84,1.17)	9.30E-01	0.144	0.941	1.08 (0.91,1.29)	3.95E-01	0.156	0.945	1.13 (0.94,1.35)	1.84E-01	0.779 0.110 (0.034)	2.74E-03	5.93E-02
rs11633715	51539843	A/G	1.10 (1.06,1.15)	1.91E-06	0.38	3.1%	1.00 (0.94,1.05)	8.82E-01	0.521	1.10 (1.05,1.15)	1.09E-05	1.12 (1.02,1.24)	2.20E-02	9.41E-01	0.498	0.989	1.13 (1.08,1.19)	8.26E-07	0.515	0.99	1.05 (0.93,1.17)	4.39E-01	0.507	0.988	1.04 (0.92,1.18)	5.04E-01	0.524	0.996	1.05 (0.92,1.20)	4.80E-01	0.991 0.120 (0.027)	7.77E-06	8.81E-02
rs767199	51540387	G/A	1.10 (1.06,1.15)	2.13E-06	0.40	0.0%	1.00 (0.94,1.05)	9.00E-01	0.504	1.10 (1.05,1.15)	1.28E-05	1.12 (1.02,1.24)	2.12E-02	9.67E-01	0.498	1.000	1.13 (1.07,1.18)	1.04E-06	0.515	1.00	1.05 (0.93,1.17)	4.50E-01	0.507	1.000	1.05 (0.93,1.19)	4.48E-01	0.524	1.000	1.05 (0.92,1.19)	5.01E-01	1.000 0.116 (0.027)	1.69E-05	1.29E-01
rs35808887	51541261	C/T	1.10 (1.06,1.15)	1.97E-06	0.34	10.9%	1.00 (0.95,1.05)	9.39E-01	0.510	1.10 (1.05,1.15)	1.10E-05	1.12 (1.02,1.24)	2.21E-02	9.18E-01	0.500	0.992	1.13 (1.08,1.19)	6.81E-07	0.512	0.99	1.04 (0.93,1.17)	4.83E-01	0.505	0.987	1.05 (0.92,1.18)	4.85E-01	0.523	0.994	1.04 (0.91,1.19)	5.35E-01	0.988 0.120 (0.027)	7.10E-06	7.73E-02
rs35241865	51541301	C/T	1.10 (1.06,1.15)	1.65E-06	0.40	0.0%	1.00 (0.95,1.05)	9.56E-01	0.508	1.10 (1.06,1.15)	9.79E-06	1.12 (1.02,1.24)	2.12E-02	9.47E-01	0.499	0.994	1.13 (1.08,1.19)	8.23E-07	0.515	0.99	1.05 (0.93,1.18)	4.19E-01	0.507	0.993	1.05 (0.93,1.19)	4.57E-01	0.524	0.996	1.05 (0.92,1.19)	5.00E-01	0.993 0.120 (0.027)	8.44E-06	9.01E-02
rs10519297	51541660	G/A	1.10 (1.06,1.15)	1.64E-06	0.39	0.8%	1.00 (0.95,1.05)	9.57E-01	0.508	1.10 (1.05,1.15)	1.02E-05	1.13 (1.02,1.24)	1.93E-02	9.65E-01	0.498	0.994	1.13 (1.08,1.19)	7.72E-07	0.515	1.00	1.04 (0.93,1.17)	4.54E-01	0.507	1.000	1.05 (0.93,1.18)	4.69E-01	0.522	1.000	1.05 (0.92,1.20)	4.62E-01	0.992 0.120 (0.027)	8.19E-06	8.85E-02
rs11636686	51542066	G/A	1.10 (1.06,1.15)	1.65E-06	0.40	0.0%	1.00 (0.95,1.05)	9.57E-01	0.507	1.10 (1.06,1.15)	9.75E-06	1.12 (1.02,1.24)	2.11E-02	9.47E-01	0.499	0.994	1.13 (1.08,1.19)	8.10E-07	0.514	0.99	1.05 (0.93,1.18)	4.23E-01	0.507	0.994	1.05 (0.93,1.19)	4.63E-01	0.524	0.996	1.05 (0.92,1.20)	4.94E-01	0.992 0.120 (0.027)	7.90E-06	8.69E-02
rs11632036	51542162	T/G	1.10 (1.06,1.15)	1.64E-06	0.40	0.0%	1.00 (0.95,1.05)	9.58E-01	0.507	1.10 (1.06,1.15)	9.71E-06	1.12 (1.02,1.24)	2.11E-02	9.47E-01	0.499	0.994	1.13 (1.08,1.19)	8.09E-07	0.514	0.99	1.05 (0.93,1.18)	4.22E-01	0.507	0.994	1.05 (0.93,1.19)	4.63E-01	0.524	0.996	1.05 (0.92,1.20)	4.93E-01	0.992 0.120 (0.027)	7.85E-06	8.66E-02
rs11636667	51542193	C/T	1.10 (1.06,1.15)	1.64E-06	0.40	0.0%	1.00 (0.95,1.05)	9.59E-01	0.507	1.10 (1.06,1.15)	9.69E-06	1.12 (1.02,1.24)	2.11E-02	9.48E-01	0.499	0.994	1.13 (1.08,1.19)	8.08E-07	0.514	0.99	1.05 (0.93,1.18)	4.22E-01	0.507	0.994	1.05 (0.93,1.19)	4.63E-01	0.524	0.996	1.05 (0.92,1.20)	4.93E-01	0.992 0.120 (0.027)	7.83E-06	8.65E-02
rs12911554	51542757	C/T	1.12 (1.08,1.17)	1.85E-08	0.45	0.0%	1.01 (0.95,1.07)	8.03E-01	0.607	1.13 (1.08,1.18)	7.88E-08	1.12 (1.02,1.24)	2.10E-02	9.67E-01	0.546	1.000	1.15 (1.09,1.21)	4.13E-08	0.555	0.99	1.04 (0.93,1.17)	4.57E-01	0.548	0.989	1.08 (0.95,1.23)	2.24E-01	0.562	0.992	1.11 (0.97,1.27)	1.29E-01	1.000 0.133 (0.026)	4.10E-07	3.39E-02
rs8041967	51543234	G/A	1.10 (1.06,1.15)	1.51E-06	0.40	0.0%	1.00 (0.95,1.05)	9.81E-01	0.507	1.10 (1.06,1.15)	9.94E-06	1.13 (1.02,1.24)	1.75E-02	9.95E-01	0.499	0.991	1.13 (1.08,1.19)	7.75E-07	0.514	0.99	1.05 (0.94,1.18)	4.10E-01	0.506	0.991	1.05 (0.92,1.18)	4.71E-01	0.523	0.993	1.05 (0.92,1.20)	4.81E-01	0.989 0.120 (0.027)	8.14E-06	8.67E-02
rs12050772	51544871	T/G	1.11 (1.06,1.15)	5.76E-07	0.60	0.0%	1.03 (0.98,1.08)	3.01E-01	0.447	1.11 (1.06,1.15)	4.10E-06	1.13 (1.01,1.24)	2.73E-02	9.99E-01	0.467	0.988	1.13 (1.07,1.18)	1.34E-06	0.473	0.99	1.05 (0.94,1.18)	3.87E-01	0.460	0.984	1.10 (0.97,1.24)	3.15E-01	0.483	0.989	1.05 (0.92,1.20)	4.67E-			

**Supplementary Table 3.** *In silico* transcription factor binding motif alterations predicted by HaploReg ([http://www.broadinstitute.org/mammals/haploreg/haploreg\\_v3.php](http://www.broadinstitute.org/mammals/haploreg/haploreg_v3.php)) for the 28 candidate causal risk variants prioritized by genetic analysis.

SNP	PRE location	Variation (Ref/Alt) <sup>a</sup>	Predicted TF binding (PWM) <sup>b</sup>	Ref allele score <sup>c</sup>	Alt allele score <sup>c</sup>	Evidence of TF implicated in endometrial cancer
rs2899470	-	T/G	-	-	-	-
rs12595627	PRE-1	T/C	-	-	-	-
rs4775935	PRE-1	T/G	Bbx Mef2_known5 PLZF	12.2 1 7.9	11.9 -3.4 9.6	- - -
rs2414095	-	A/G	-	-	-	-
rs12592697	-	T/C	-	-	-	-
rs2414097	-	G/A	BAF155_disc1 GATA_known1 Maf_known1 Nrf-2_2	11.7 9.7 11.1 3.9	10.8 11.2 12.1 13.6	- Engelsen et al., 2008. - Li et al., 2014.
rs8024515	PRE-2	T/C	BDP1_disc3 Ets_disc9 GR_disc6 Klf7 MZF1::1-4_2 MZF1::1-4_3 Pou2f2_disc2 SP1_known1 Sp4 UF1H3BETA WT1 Zfp281	12.4 8.7 10.2 12.4 6.4 11 0.4 12.1 15 -9.6 1.9 11.1	12.2 10.6 10.6 11.3 12.9 12.8 11.4 14.3 14.4 2 10.8 12	- Fujimoto et al., 2002. Zachos et al., 1996. - - - - Knappskog et al., 2012. - - Hedley et al., 2014. -
rs7173595	PRE-2	C/T	CCNT2_disc2 Pax-4_4 Pax-4_5 UF1H3BETA Zfp281 Zfp740	12.6 11.7 12.2 10.3 13.1 14.5	0.6 10.7 11.4 -1.6 10.8 13.3	- - - - - -
rs7175531	PRE-2	T/C	CAC-bp GR_disc1 GR_known3 GR_known8 Hic1_3 Rad21_disc6	0.6 13 -2.1 9 4.1 10.2	12.5 12.8 9.2 -2.7 12.2 11.5	- Zachos et al., 1996. Zachos et al., 1996. Zachos et al., 1996. - Supernat et al., 2012.
rs727479	PRE-2	C/A	IRF1 Mef2_disc2 SP1_known4 TATA_disc4	11.2 -35.3 10.5 11.8	8.8 -30.4 11 9.8	Giatromanolaki et al., 2004. - Knappskog et al., 2012. -
rs2414098	-	T/C	CEBPA_1 CEBPA_2 Pax-4_5	10.3 11.2 10.3	9.6 12.1 11.7	Takai et al., 2005. Takai et al., 2005. -
rs10519299	-	C/G	GR_disc6 STAT_known13	10.5 9.8	11.4 8.9	Zachos et al., 1996. -
rs28520437	-	C/T	TATA_disc8	11	8	Zhao et al., 2013.
rs28440805	-	C/G	GR_known2 Sox11 Sox15	5.3 10.7 9.6	10.6 13.4 12.4	Zachos et al., 1996. - -



rs28518777	-	G/A	GR_disc4 Myb_1 THAP1_disc1 <b>YY1_disc1<sup>d</sup></b> <b>YY1_known5<sup>d</sup></b> <b>YY1_known6<sup>d</sup></b>	12.1 0.7 8.1 15.4 14.3 11.8	11 12.7 7.7 15.5 11.7 11.1	Zachos et al., 1996. - - Yang et al., 2013. Yang et al., 2013. Yang et al., 2013.
rs17601876	-	A/G	E2F_known5 E2F_known6 TR4_disc3 Zic2	-0.5 0.7 0.5 9	11.3 12.7 12.5 10.1	- - - Bidus et al., 2006.
rs17523527	-	C/T	VDR_4 Znf143_disc3	10.7 12.2	8.7 12.7	Bergada et al., 2014. -
rs8028111	-	C/T	SOX9 Sox17 SRY	11.7 10.5 10.5	12 11.3 12.1	Saegusa et al., 2012. - -
rs35939475	-	C/A	CAC-bp ERalpha- a_known3 Klf7 Pax_4_4 Pax_4_5 SP1_known3 SP1_known4	12.5 2.1 11 11.9 12.5 13.1 13.3	0.6 14.1 3.1 12.1 13.5 2.1 1.3	- Hou et al., 2014. - - - Knappskog et al., 2012. Knappskog et al., 2012.
rs17523541	-	G/A	FXR_3 Hoxb8 Pbx-1_4 Pdx1_1 SIX5_known2	4.5 3.9 11.2 0.5 10.4	5.1 11.3 5 12.5 4	- - - - -
rs12910259	-	G/A	ATF4 Dmbx1 Gsc <b>MAFK<sup>e</sup></b> Maf_known1 Nrf-2_2 Obox6	14.3 12.6 11.2 9.4 12.1 12 12	12.7 8.5 6.7 13.9 13.8 14.8 7.4	- - - - - Li et al., 2014. -
rs12050767	PRE-3	T/C	RORalpha1_2	-6	6	-
rs8029537	PRE-3	A/G	AP-1_disc10 CAC-bp E2F4 Ets_disc7 IRF1 Klf7 NRSF_disc5 NRSF_disc9 Nrf1_disc3 SP1_disc3 SP1_known1 SP1_known2 SP1_known4 STAT3 Sp4 TCF12_disc5 YY1_disc3 <sup>d</sup> Zic2	10.2 13 8.1 0.1 5.4 4.3 10.5 8.7 9.2 12.6 11.8 7.9 12.3 13 3.1 11 5.8 9	11.1 2.8 12.1 11.9 10.9 11.4 11.5 12.8 10.9 14.3 14.5 12.5 13.3 12.3 11.4 9.6 11 10.1	Dai et al., 2003. - - Fujimoto et al., 2002. Giatromanolaki et al., 2004. - - - - - Knappskog et al., 2012. Knappskog et al., 2012. Knappskog et al., 2012. Knappskog et al., 2012. - - - Yang et al., 2013. Bidus et al., 2006.
rs749292	PRE-3	G/A	-	-	-	-
rs7181429	PRE-3	G/A	SRF_disc2	10.4	7	Yamaguchi et al., 2009.
rs28637352	PRE-3	C/A	ERalpha-a_disc3 HNF4_disc1 RXRA_known6	10.9 14.2 11.3	8.5 10.3 9.2	Hou et al., 2014. - -
rs28490942	PRE-3	G/C	HNF4_known2 p53_3	10.7 9.4	6.7 11.1	- Markova et al., 2010.

rs11636639	-	T/G	Egr-1_disc4	3.5	-8.5	Vivacqua et al., 2012
			PPAR_2	9.5	10.7	Nickkho-Amiry et al., 2012
			Znf143_disc3	12.1	11.1	-

<sup>a</sup> Ref=reference allele, Alt=alternative allele.

<sup>b</sup> Transcription factor (TF) position weight matrix (PWM) ID from the HaploReg library.

<sup>c</sup> The reference and alternate alleles for each of the 1000 Genomes pilot SNPs and indels were concatenated with 29 bp of genomic context on each side, using the hg19 sequence obtained from the UCSC Genome Browser. PWMs were then scored for instances that passed a threshold of  $p < 4^{-7}$ . Only instances where a motif in the sequence (a) passed the threshold of a PWM in either the reference or the alternate genomic sequence, and (b) overlapped the variable nucleotide(s) (thus changing the PWM score) were considered. Then, the change in log-odds (LOD) score was calculated.

<sup>d</sup> ENCODE ChIP-seq analysis demonstrates that YY1 binds a region containing rs2851877 in K562 cells.

<sup>e</sup> ENCODE ChIP-seq analysis demonstrates that MAFK binds a region containing rs12910259 in HepG2 cells.

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**Supplementary Table 4. Candidate variants associate with CYP19A1 expression in whole blood, adipose tissue and skin.** eQTL data were explored using the GTEx browser (<http://www.gtexportal.org/>). eQTL associations with  $P \leq 1 \times 10^{-3}$  are shown in bold.

SNP ID	PRE location	A1/A2	Freq A2 in iCOGS	Endometrial cancer meta-analysis		GTEx CYP19A1 eQTL analysis		
				OR (95% CI)	P-value	Whole blood (n=168)	Subcutaneous adipose (n=111)	Sun exposed skin (n=112)
rs2899470	-	T/G	0.562	1.13 (1.09,1.18)	2.57E-09	2.00E-02	1.00E-01	2.00E-02
rs12595627	PRE-1	T/C	0.655	1.15 (1.10,1.20)	1.58E-10	2.00E-02	3.00E-02	1.00E-02
rs4775935	PRE-1	T/G	0.655	1.15 (1.10,1.20)	2.27E-10	2.00E-02	3.00E-02	1.00E-02
rs2414095	-	A/G	0.655	1.15 (1.10,1.20)	1.55E-10	5.00E-02	4.00E-02	1.00E-02
rs12592697	-	T/C	0.655	1.15 (1.10,1.20)	1.99E-10	2.00E-02	3.00E-02	1.00E-02
rs2414097	-	G/A	0.654	1.15 (1.10,1.20)	1.09E-10	5.00E-02	4.00E-02	1.00E-02
rs8024515	PRE-2	T/C	0.616	1.15 (1.10,1.20)	2.20E-10	1.00E-02	6.00E-02	4.00E-02
rs7173595	PRE-2	C/T	0.654	1.15 (1.10,1.20)	7.90E-11	5.00E-02	4.00E-02	1.00E-02
rs7175531	PRE-2	T/C	0.653	1.15 (1.11,1.20)	6.66E-11	5.00E-02	4.00E-02	1.00E-02
rs727479	PRE-2	C/A	0.651	1.15 (1.11,1.21)	4.81E-11	4.00E-02	4.00E-02	1.00E-02
rs2414098	-	T/C	0.617	1.15 (1.10,1.20)	9.08E-11	1.00E-01	3.00E-02	5.00E-03
rs10519299	-	C/G	0.445	1.13 (1.09,1.18)	2.45E-09	<b>2.00E-04</b>	4.00E-03	<b>1.00E-03</b>
rs28520437	-	C/T	0.444	1.13 (1.09,1.18)	1.36E-09	<b>3.00E-04</b>	2.00E-03	<b>1.00E-03</b>
rs28440805	-	C/G	0.445	1.13 (1.09,1.18)	1.24E-09	2.00E-03	5.00E-03	<b>9.00E-04</b>
rs28518777	-	G/A	0.443	1.13 (1.09,1.18)	2.26E-09	<b>1.00E-03</b>	6.00E-03	2.00E-02
rs17601876	-	A/G	0.479	1.14 (1.10,1.19)	1.32E-10	6.00E-03	9.00E-03	2.00E-02
rs17523527	-	C/T	0.442	1.13 (1.08,1.17)	3.65E-09	<b>1.00E-03</b>	6.00E-03	2.00E-02
rs8028111	-	C/T	0.445	1.13 (1.09,1.18)	1.91E-09	<b>3.00E-04</b>	2.00E-03	<b>1.00E-03</b>
rs35939475	-	C/A	0.445	1.13 (1.09,1.18)	1.87E-09	<b>3.00E-04</b>	2.00E-03	<b>1.00E-03</b>
rs17523541	-	G/A	0.445	1.13 (1.09,1.18)	1.83E-09	<b>3.00E-04</b>	2.00E-03	<b>1.00E-03</b>
rs12910259	-	G/A	0.444	1.13 (1.09,1.18)	1.96E-09	<b>3.00E-04</b>	<b>1.00E-03</b>	<b>6.00E-04</b>
rs12050767	PRE-3	T/C	0.444	1.13 (1.08,1.18)	2.92E-09	2.00E-03	5.00E-03	<b>9.00E-04</b>
rs8029537	PRE-3	A/G	0.444	1.13 (1.08,1.17)	3.97E-09	<b>3.00E-04</b>	4.00E-03	<b>9.00E-04</b>
rs749292	PRE-3	G/A	0.444	1.13 (1.08,1.17)	5.06E-09	<b>7.00E-04</b>	6.00E-03	<b>9.00E-04</b>
rs7181429	PRE-3	G/A	0.445	1.13 (1.09,1.18)	3.05E-09	<b>6.00E-05</b>	2.00E-03	<b>3.00E-04</b>
rs28637352	PRE-3	C/A	0.438	1.13 (1.08,1.18)	3.82E-09	<b>7.00E-04</b>	1.00E-02	<b>8.00E-04</b>
rs28490942	PRE-3	G/C	0.446	1.13 (1.09,1.18)	1.05E-09	2.00E-03	9.00E-03	<b>5.00E-04</b>
rs11636639	-	T/G	0.447	1.13 (1.08,1.17)	3.91E-09	<b>8.00E-04</b>	7.00E-03	<b>8.00E-04</b>

Footnote - Other tissue types investigated were: Artery Aorta (n=74), Artery Tibial (n=124), Esophagus Muscularis (n=91), Heart Left Ventricle (n=87), Lung (n=124), Muscle Skeletal (n=143), Nerve Tibial (n=102), Thyroid (n=122).

**Supplementary Table 5: Primer probe sequences for the rs727479 SNP genotyped using Taqman**

<b>Forward Primer</b>	<b>Reverse Primer</b>	<b>FAM probe</b>	<b>VIC probe</b>
GTGGAATAAAGAGAAGGGATAA ATACAAGACA	TCTGGAACATCTTCTTCACTGCTTT	TCACTTTGTTTCCTCCATG C	CACTTTGTTTCCGCCATG C

Each assay was carried out in 4 x 384-well plates, using 10ng dried template DNA for each individual.

Reactions were performed according to manufacturer's instructions, using the following thermal cycling profile:

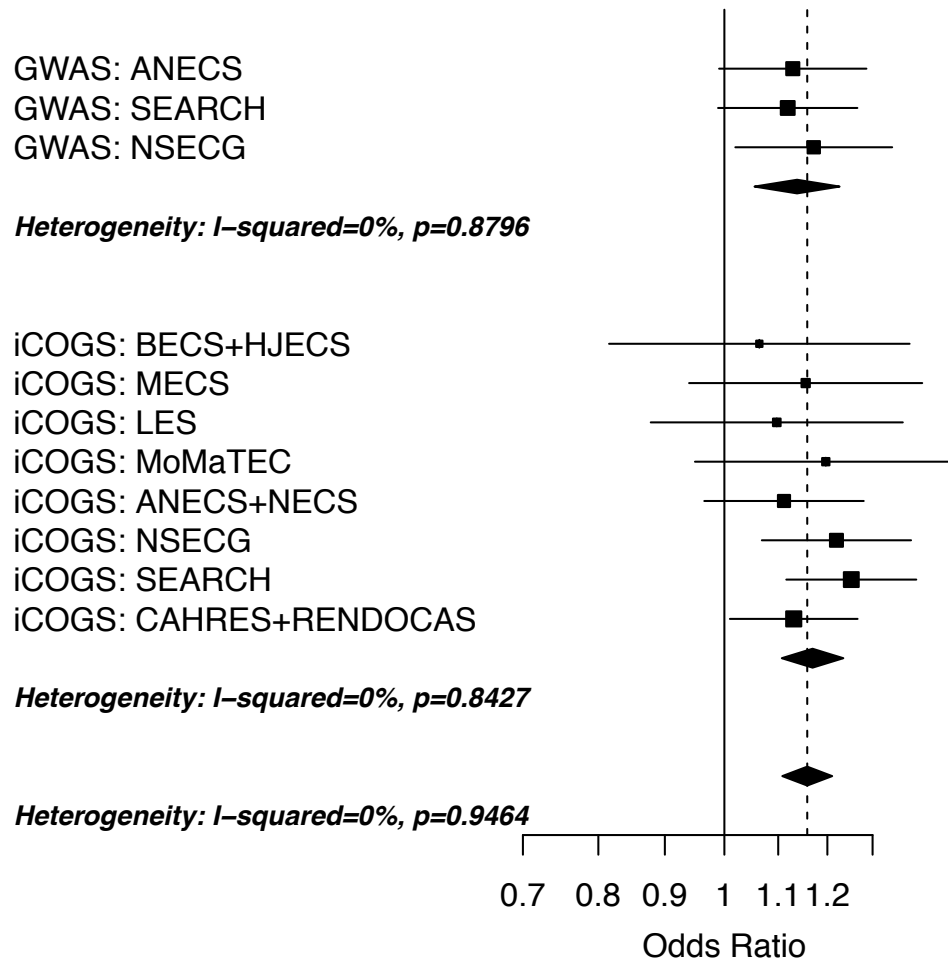
95°C for 10 mins followed by: [92°C for 15 secs, 60°C for 1 min] for 40 cycles.

Plates were read on the ABI Prism 7900 using the Sequence Detection Software (Applied Biosystems).

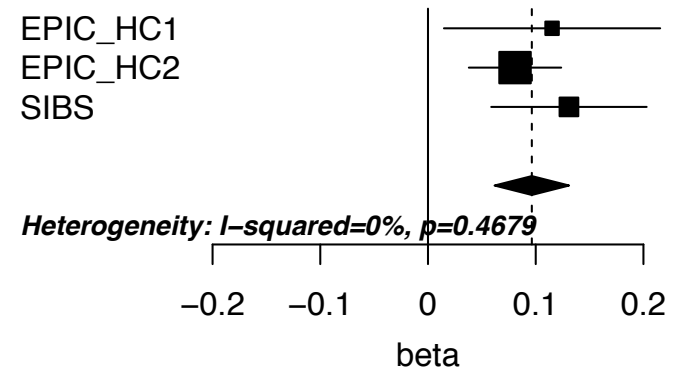
Each plate included 2-3 negative controls (no template controls) and 4 selected samples were chosen from each 384-well plate and duplicated on the fourth 384-well plate.

There was 100% duplicate concordance (n=13).

Supplementary Figure 1a: Association between rs727479 and endometrial cancer in each of the study sets included in the analysis

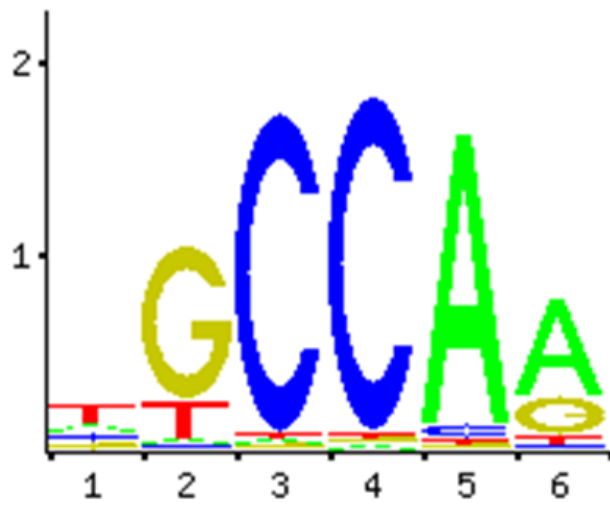


Supplementary Figure 1b: Association between rs727479 and estradiol levels in each of the study sets included in the analysis



Details of study acronyms are given in Supplementary Table 1.

**Supplementary Figure 2. rs28490942 SNP locus shows homology to NFIC position weight matrix (PWM).** The NFIC PWM was retrieved from JASPAR CORE database (<http://jaspar.genereg.net/>).



**C T C C A A** rs28490942-C  
**G T C C A A** rs28490942-G