

Table 1. SNPs associated with serum E2 and E1 concentrations: genome-wide results of meta-analysis

		Chr	Gene	Location	EA	FREQ	Effect	SE	p	N		
E2	<i>Model 1</i>											
	rs727479	15	CYP19A1	51242350	A	0.63	1.39	0.12	8.2×10^{-30}	11,097		
	rs5934505	X	FAM9B	8945785	C	0.26	0.67	0.12	3.4×10^{-8}	8,953		
	<i>Model 2</i>											
	rs727479	15	CYP19A1	51242350	A	0.64	1.42	0.10	3.1×10^{-43}	10,816		
	rs2899472*	15	CYP19A1	51223858	A	0.25	1.13	0.12	$1.1 \times 10^{-8} \dagger$	10,816		
	rs16964258*	15	CYP19A1	51313211	G	0.05	2.13	0.25	$8.2 \times 10^{-15} \dagger$	10,816		
	rs5951794	X	MIR	147350670	G	0.34	0.68	0.11	3.1×10^{-10}	7,794		
	E1	<i>Model 1</i>										
		rs2899472	15	CYP19A1	51223858	A	0.25	2.41	0.24	5.5×10^{-23}	7,570	
rs727479*		15	CYP19A1	51242350	A	0.65	2.09	0.22	$3.5 \times 10^{-10} \dagger$	7,570		
rs17277546		7	TRIM4	99891948	G	0.95	3.59	0.48	5.8×10^{-14}	7,570		
rs10093796		8	CYP11B1/B2	142897008	T	0.43	1.17	0.20	1.2×10^{-8}	7,570		

EA = Effect Allele, FREQ = Frequency of effect allele; Effect size is given per effect allele as pg/ml. Location is given according to Human GRCh38/hg38. All cohorts (n= 11,097) were included in the E2 GWAS of chromosomes 1-22. The E1 GWAS of chromosomes 1-22 included FHS, GOOD, MrOS Sweden Gothenburg, MrOS Sweden Malmö, MrOS US and RS1. X-chromosome data were available for FHS, GOOD, LURIC, MrOS Sweden Gothenburg, MrOS Sweden Malmö and MrOS US. Model 1 = adjusted for age and BMI, Model 2 = adjusted for age, BMI, testosterone and SHBG, * = secondary signal from GCTA analysis, † = conditional p-value from GCTA-analysis. Fixed effects meta-analysis p-values for secondary signals from GCTA analysis: rs2899472 (E2, model 2): p-value 4.3×10^{-21} ; rs16964258 (E2, model 2): p-value 2.3×10^{-17} ; rs727479 (E1, model 1): p-value 2.1×10^{-22} .

Table 2. Look-up of genome-wide significant lead SNPs and testosterone in men

Chr	Gene	SNP	EA	FREQ	Testosterone, adjusted for SHBG			
					Effect	SE	p	n ^a
15	CYP19	rs727479	A	0.64	-4.86	2.49	0.051	8,366
15	CYP19	rs2899472	A	0.26	-0.030	2.82	0.99	8,366
15	CYP19	rs16964258	G	0.05	-6.85	6.07	0.26	8,366
X	FAM9B	rs5934505	C	0.26	18.10	3.20	1.6 x 10⁻⁸	4,599
X	MIR	rs5951794	G	0.34	-7.68	3.05	1.2 x 10⁻²	4,599

EA = Effect Allele, *i.e.* the allele associated with increased serum E2; FREQ = Frequency of effect allele; Effect size is given per effect allele as ng/dl. ^aTotal number of study participants, information for individual SNPs not available; numbers in bold represent statistical significance. Testosterone levels were retrieved from our previous GWAS of testosterone levels (30).

Table 3. Look-up of genome-wide significant lead SNPs and BMD in men

Chr	Gene	SNP	EA	FREQ	BMD							
					Lumbar Spine				Femoral Neck			
					Effect	SE	p	n ^a	Effect	SE	p	n ^a
15	CYP19	rs727479	A	0.70	0.068	0.015	1.1 x 10⁻⁵	9,980	0.059	0.015	1.2 x 10⁻⁴	9,980
15	CYP19	rs2899472	A	0.28	0.047	0.017	7.4 x 10⁻³	9,980	0.052	0.018	2.4 x 10⁻³	9,980
15	CYP19	rs16964258	G	0.06	0.10	0.039	1.0 x 10⁻²	9,980	0.065	0.029	0.09	9,980
X	FAM9B	rs5934505	C	0.26	0.059	0.012	7.2 x 10⁻⁶	9,980	0.031	0.012	1.2 x 10⁻²	9,980
X	MIR	rs5951794	G	0.34	0.016	0.012	0.19	9,980	0.005	0.012	0.67	9,980

EA = Effect Allele; FREQ = Frequency of effect allele, taken from HapMap Genome Browser release #24; Effect size for BMD is given as standardized values per copy of the SNP allele from fixed-effects meta-analysis. ^aTotal number of study participants, information for individual SNPs not available; numbers in bold represent statistical significance after Bonferroni correction for two phenotypes (LS BMD and FN BMD).