

**Supplementary Table 1 Questions on variables related to hormonal and reproductive factors.**

Variable	Original question	Field ID
Age at menarche	How old were you when your periods started?	2714
Number of live births	How many children have you given birth to? (Please include live births only)	2734
Ever had stillbirth, spontaneous miscarriage or termination	Have you ever had any stillbirths, spontaneous miscarriages or terminations?	2774
Had menopause	Have you had your menopause (periods stopped)	2724
Age at menopause	How old were you when your periods stopped?	3581
Ever had hysterectomy	Have you had a hysterectomy (womb removed)?	3591
Bilateral oophorectomy	Have you had both ovaries removed	2834
Ever taken oral contraceptive pill	Have you ever taken the contraceptive pill? (include the 'mini-pill')	2784
Age started oral contraceptive pill	About how old were you when you first went on the contraceptive pill?	2794
Age when last used oral contraceptive pill	How old were you when you last used the contraceptive pill?	2804
Ever used hormone-replacement therapy (HRT)	Have you ever used hormone replacement therapy (HRT)?	2814
Age started hormone-replacement therapy (HRT)	How old were you when you first used HRT?	3536
Age last used hormone-replacement therapy (HRT)	How old were you when you last used HRT?	3546

**Supplementary Table 2 Hazard ratios for comparing individual and combined associations between hormonal and reproductive factors and the risk of rheumatoid arthritis.**

Characteristics	Total population (n=190574)	Number Incidence cases (n=2622)	Model 1		Model 2		Model 3	
			HR (95%CI)	P Value	HR (95%CI)	P Value	HR (95%CI)	P Value
<b>Age at menarche, years</b>								
<12	36640	558	1.15(1.02, 1.28)	<b>0.020</b>	1.05(0.94, 1.18)	0.385	1.04(0.92, 1.16)	0.555
12	36214	460	0.97(0.86, 1.09)	0.587	0.94(0.84, 1.06)	0.339	0.94(0.83, 1.06)	0.310
13	47690	619	Reference		Reference		Reference	
14	38168	503	0.99(0.88, 1.11)	0.830	0.98(0.87, 1.11)	0.774	0.98(0.87, 1.11)	0.771
>14	31862	482	1.15(1.02, 1.29)	<b>0.023</b>	1.11(0.99, 1.25)	0.078	1.11(0.98, 1.25)	0.089
<b>Ever been pregnant</b>								
No	28811	348	Reference		Reference		Reference	
Yes	161763	2274	1.02(0.91, 1.14)	0.755	1.01(0.90, 1.13)	0.886	0.99(0.89, 1.12)	0.924
<b>Menopause</b>								
No	59781	463	Reference		Reference		Reference	
Yes	130793	2159	1.09(0.94, 1.26)	0.236	1.08(0.93, 1.24)	0.316	1.00(0.86, 1.16)	0.983
<b>History of hysterectomy</b>								
No	176087	2259	Reference		Reference		Reference	
Yes	14487	363	1.52(1.36, 1.71)	<b>&lt; 0.001</b>	1.42(1.27, 1.59)	<b>&lt; 0.001</b>	1.53(1.33, 1.75)	<b>&lt; 0.001</b>
<b>History of oophorectomy</b>								
No	183127	2474	Reference		Reference		Reference	
Yes	7447	148	1.18(1.00, 1.39)	0.054	1.09(0.93, 1.29)	0.292	0.71(0.58, 0.87)	<b>&lt; 0.001</b>
<b>Ever used oral contraceptive pills</b>								
No	34290	594	Reference		Reference		Reference	
Yes	156284	2028	0.95(0.86, 1.04)	0.272	1.01(0.92, 1.12)	0.786	0.97(0.88, 1.07)	0.533

<b>Ever used HRT</b>							
No	126232	1351	Reference		Reference		Reference
Yes	64342	1271	1.38(1.27, 1.50)	< <b>0.001</b>	1.4(1.28, 1.52)	< <b>0.001</b>	1.36(1.25, 1.48) < <b>0.001</b>

Model 1: adjusted for age.

Model 2: Adjusted for age, Townsend deprivation index, ethnicity, smoking status, alcohol drinker status, body mass index, physical activity, vitamin D supplement, fracture history, diabetes, systolic blood pressure, diastolic blood pressure.

Model 3: Adjusted for age, Townsend deprivation index, ethnicity, smoking status, alcohol use, body mass index, physical activity, vitamin D supplement, fracture history, diabetes, systolic blood pressure, diastolic blood pressure, age at menarche, pregnant, menopause, history of hysterectomy, history of oophorectomy, contraceptive pill use, HRT use.

HR: Hazard ratio; CI: Confidence interval; HRT: Hormone replacement therapy.

**Supplementary Table 3 Associations between hormonal and reproductive factors and the risk of rheumatoid arthritis after excluding those who were diagnosed with rheumatoid arthritis for two years.**

Characteristics	Total population (n=223054)	Number Incidence cases (n=2841)	Model 1		Model 2	
			HR (95%CI)	P Value	HR (95%CI)	P Value
<b>Age at menarche, years</b>						
<12	43039	619	1.18(1.05, 1.31)	<b>0.004</b>	1.08(0.96, 1.20)	0.198
12	41211	486	0.97(0.87, 1.10)	0.666	0.95(0.84, 1.07)	0.385
13	53487	640	Reference		Reference	
14	42980	515	0.97(0.87, 1.09)	0.643	0.97(0.86, 1.09)	0.588
>14	36341	505	1.14(1.02, 1.28)	<b>0.026</b>	1.11(0.98, 1.24)	0.094
<b>Ever been pregnant</b>						
No	33150	363	Reference		Reference	
Yes	189061	2469	1.04(0.93, 1.16)	0.493	1.02(0.91, 1.14)	0.715
<b>Number of children</b>						
None	42358	464	1.06(0.95, 1.18)	0.334	1.01(0.91, 1.13)	0.832
1	29738	385	1.16(1.03, 1.30)	0.012	1.08(0.96, 1.21)	0.188
2	97959	1197	Reference		Reference	
3	39164	529	1.07(0.96, 1.18)	0.221	1.01(0.91, 1.12)	0.880
≥4	13690	264	1.47(1.29, 1.69)	<b>&lt; 0.001</b>	1.20(1.04, 1.37)	<b>0.010</b>
Each child	222909	2839	1.04(1.01, 1.08)	<b>0.006</b>	1.02(0.99, 1.05)	0.272
<b>Menopause</b>						
No	62239	408	Reference		Reference	
Yes	160593	2429	1.25(1.08, 1.44)	<b>0.002</b>	1.20(1.04, 1.39)	<b>0.010</b>
<b>Age at menopause, years</b>						
<45	16305	330	1.65(1.42, 1.91)	<b>&lt;0.001</b>	1.48(1.28, 1.72)	<b>&lt;0.001</b>

45-49	30319	409	1.11(0.96, 1.28)	0.146	1.06(0.92, 1.22)	0.434
50-51	29507	375	Reference		Reference	
52-54	31378	382	0.94(0.82, 1.09)	0.408	0.95(0.83, 1.10)	0.501
>54	19365	284	1.04(0.89, 1.21)	0.623	1.03(0.88, 1.20)	0.712
<b>Reproductive years, years</b>						
<33	21999	416	1.44(1.25, 1.67)	< 0.001	1.31(1.13, 1.52)	< 0.001
33-35	18916	251	1.02(0.87, 1.21)	0.799	0.98(0.83, 1.16)	0.806
36-37	21078	252	0.90(0.76, 1.06)	0.198	0.89(0.76, 1.05)	0.176
38-39	23474	316	Reference		Reference	
40-42	25267	319	0.91(0.78, 1.06)	0.233	0.91(0.78, 1.07)	0.255
>42	13615	198	0.98(0.82, 1.18)	0.864	0.96(0.80, 1.15)	0.660
<b>History of hysterectomy</b>						
No	182456	2009	Reference		Reference	
Yes	15834	334	1.47(1.30, 1.65)	< 0.001	1.37(1.21, 1.54)	<0.001
<b>History of oophorectomy</b>						
No	202871	2453	Reference		Reference	
Yes	17316	313	1.28(1.14, 1.44)	< 0.001	1.21(1.07, 1.36)	0.002
<b>Ever used oral contraceptive pills</b>						
No	40766	666	Reference		Reference	
Yes	181781	2165	0.92(0.83, 1.01)	0.066	0.97(0.88, 1.06)	0.480
<b>Duration of oral contraceptive pills use, per year</b>	159331	1868	1.00(0.99, 1.01)	0.812	1.00(0.99, 1.01)	0.760
<b>Ever used HRT</b>						
No	138800	1321	Reference		Reference	
Yes	83653	1508	1.44(1.33, 1.56)	< 0.001	1.43(1.32, 1.55)	< 0.001
<b>Duration of HRT use, per year</b>	61475	1070	1.02(1.01, 1.03)	0.002	1.02(1.01, 1.03)	0.002

Model 1: adjusted for age.

Model 2: Adjusted for age, Townsend deprivation index, ethnicity, smoking status, alcohol drinker status, body mass index, physical activity, vitamin D supplement, fracture history, diabetes, systolic blood pressure, diastolic blood pressure.

HR: Hazard ratio; CI: Confidence interval; HRT: Hormone replacement therapy.

**Supplementary Table 4 Associations between hormonal and reproductive factors and the risk of rheumatoid arthritis after excluding those who had hysterectomy or oophorectomy.**

Characteristics	Total population (n=181627)	Number Incidence cases (n=2326)	Model 1		Model 2	
			HR (95%CI)	P Value	HR (95%CI)	P Value
<b>Age at menarche, years</b>						
<12	33301	467	1.13(1.00, 1.28)	0.053	1.04(0.92, 1.18)	0.555
12	33656	400	0.97(0.85, 1.10)	0.611	0.94(0.83, 1.07)	0.358
13	44588	542	Reference		Reference	
14	35550	433	0.97(0.86, 1.11)	0.688	0.97(0.86, 1.10)	0.640
>14	29571	432	1.19(1.05, 1.35)	<b>0.008</b>	1.15(1.02, 1.31)	<b>0.026</b>
<b>Ever been pregnant</b>						
No	28560	332	Reference		Reference	
Yes	152370	1987	0.99(0.88, 1.11)	0.822	0.98(0.87, 1.10)	0.676
<b>Number of children</b>						
None	36693	426	1.12(1.00, 1.26)	0.052	1.07(0.95, 1.20)	0.267
1	24874	349	1.27(1.12, 1.43)	<b>&lt; 0.001</b>	1.17(1.04, 1.33)	<b>0.011</b>
2	78901	956	Reference		Reference	
3	30708	409	1.06(0.94, 1.19)	0.323	1.00(0.89, 1.13)	0.952
≥4	10345	184	1.37(1.17, 1.61)	<b>&lt; 0.001</b>	1.12(0.95, 1.31)	0.181
Each child	181521	2324	1.01(0.98, 1.05)	0.550	0.99(0.96, 1.02)	0.570
<b>Menopause</b>						
No	61755	475	Reference		Reference	
Yes	119710	1849	0.98(0.84, 1.14)	0.806	0.97(0.84, 1.13)	0.728
<b>Age at menopause, years</b>						
<45	10193	192	1.37(1.16, 1.63)	<b>&lt;0.001</b>	1.25(1.05, 1.48)	<b>0.012</b>

45-49	26495	401	1.09(0.95, 1.26)	0.201	1.04(0.91, 1.20)	0.568
50-51	27441	401	Reference		Reference	
52-54	29723	417	0.94(0.82, 1.08)	0.387	0.95(0.83, 1.09)	0.453
>54	18259	300	1.01(0.87, 1.17)	0.931	1.00(0.86, 1.16)	0.967
<b>Reproductive years, years</b>						
<33	15099	279	1.31(1.11, 1.54)	<b>&lt; 0.001</b>	1.2(1.03, 1.41)	<b>0.023</b>
33-35	16724	248	1.04(0.89, 1.23)	0.606	1.00(0.85, 1.18)	0.972
36-37	19385	280	0.99(0.84, 1.16)	0.871	0.98(0.84, 1.15)	0.840
38-39	21926	326	Reference		Reference	
40-42	23811	348	0.95(0.82, 1.11)	0.534	0.96(0.82, 1.11)	0.578
>42	12481	204	0.97(0.81, 1.16)	0.726	0.95(0.79, 1.13)	0.543
<b>Ever used oral contraceptive pills</b>						
No	31582	511	Reference		Reference	
Yes	149683	1809	0.94(0.85, 1.05)	0.272	1.01(0.91, 1.12)	0.844
<b>Duration of oral contraceptive pills use, per year</b>	131171	1575	1.00(0.99, 1.01)	0.735	1.00(1.00, 1.01)	0.441
<b>Ever used HRT</b>						
No	125824	1300	Reference		Reference	
Yes	55351	1017	1.31(1.20, 1.44)	<b>&lt; 0.001</b>	1.34(1.22, 1.46)	<b>&lt; 0.001</b>
<b>Duration of HRT use, per year</b>	41702	757	1.03(1.01, 1.04)	<b>0.002</b>	1.03(1.01, 1.04)	<b>&lt; 0.001</b>

Model 1: adjusted for age.

Model 2: Adjusted for age, Townsend deprivation index, ethnicity, smoking status, alcohol drinker status, body mass index, physical activity, vitamin D supplement, fracture history, diabetes, systolic blood pressure, diastolic blood pressure.

HR: Hazard ratio; CI: Confidence interval; HRT: Hormone replacement therapy.



**Supplementary Table 5 Associations between hormonal and reproductive factors and the risk of rheumatoid arthritis after counting missing data using MICE.**

Characteristics	Total population (n=270460)	Number Incidence cases (n=4329)	Model 1		Model 2	
			HR (95%)	P Value	HR (95%CI)	P Value
<b>Age at menarche, years</b>						
<12	52549	959	1.22(1.13, 1.31)	< <b>0.001</b>	1.10(1.01, 1.20)	<b>0.032</b>
12	49731	724	0.98(0.89, 1.08)	0.744	0.96(0.86, 1.05)	0.369
13	64015	936	Reference		Reference	
14	51747	787	1.01(0.99, 1.04)	0.797	0.99(0.90, 1.09)	0.893
>14	44211	786	1.04(1.10, 1.29)	< <b>0.001</b>	1.15(1.15, 1.16)	<b>0.004</b>
<b>Ever been pregnant</b>						
No	39909	561	Reference		Reference	
Yes	229427	3756	1.03(0.94, 1.12)	0.540	1.01(0.92, 1.10)	0.872
<b>Number of children</b>						
None	50722	704	1.05(0.96, 1.14)	0.279	1.00(0.91, 1.09)	0.945
1	36124	590	1.16(1.07, 1.25)	<b>0.002</b>	1.07(0.98, 1.17)	0.144
2	118178	1813	Reference		Reference	
3	47878	821	1.08(1.00, 1.16)	0.066	1.01(0.93, 1.10)	0.757
≥4	17309	396	1.40(1.29, 1.51)	< <b>0.001</b>	1.10(0.99, 1.22)	0.081
Each child	270211	4324	1.04(1.02, 1.07)	< <b>0.001</b>	1.01(0.99, 1.04)	0.375
<b>Menopause</b>						
No	73914	619	Reference		Reference	
Yes	196121	3701	1.31(1.19, 1.42)	< <b>0.001</b>	1.25(1.14, 1.37)	< <b>0.001</b>
<b>Age at menopause, years</b>						
<45	20218	523	1.70(1.58, 1.82)	< <b>0.001</b>	1.52(1.40, 1.64)	< <b>0.001</b>

45-49	36774	633	1.14(1.02, 1.25)	<b>0.027</b>	1.08(0.97, 1.19)	0.182
50-51	35538	560	Reference		Reference	
52-54	37550	563	0.94(0.82, 1.05)	0.269	0.95(0.83, 1.06)	0.363
>54	23069	396	0.99(0.86, 1.12)	0.907	0.98(0.85, 1.11)	0.787
<b>Reproductive years, years</b>						
<33	27127	663	1.59(1.47, 1.71)	<b>&lt; 0.001</b>	1.43(1.31, 1.55)	<b>&lt; 0.001</b>
33-35	22851	385	1.10(0.96, 1.24)	0.174	1.05(0.91, 1.19)	0.490
36-37	25346	377	0.95(0.81, 1.08)	0.441	0.94(0.81, 1.08)	0.404
38-39	28194	447	Reference		Reference	
40-42	30065	471	0.96(0.83, 1.09)	0.564	0.96(0.83, 1.09)	0.562
>42	16262	280	1.00(0.85, 1.15)	0.991	0.97(0.82, 1.12)	0.671
<b>History of hysterectomy</b>						
No	219586	3026	Reference		Reference	
Yes	19653	520	1.51(1.42, 1.61)	<b>&lt; 0.001</b>	1.40(1.30, 1.49)	<b>&lt; 0.001</b>
<b>History of oophorectomy</b>						
No	244974	3699	Reference		Reference	
Yes	21537	505	1.35(1.30, 1.41)	<b>&lt; 0.001</b>	1.26(1.17, 1.36)	<b>&lt; 0.001</b>
<b>Ever used oral contraceptive pills</b>						
No	50978	1037	Reference		Reference	
Yes	218651	3278	0.91(0.84, 0.99)	<b>0.016</b>	0.98(0.90, 1.05)	0.527
<b>Duration of Oral contraceptive pill use, per year</b>	189203	2764	1.00(0.99, 1.00)	0.178	1.00(0.99, 1.00)	0.641
<b>Ever used HRT</b>						
No	166759	2003	Reference		Reference	
Yes	102717	2303	1.44(1.38, 1.51)	<b>&lt; 0.001</b>	1.45(1.38, 1.51)	<b>&lt; 0.001</b>
<b>Duration of HRT use, per year</b>	74154	1604	1.01(1.00, 1.02)	<b>0.004</b>	1.01(1.00, 1.02)	<b>0.004</b>

Model 1: adjusted for age.

Model 2: Adjusted for age, Townsend deprivation index, ethnicity, smoking status, alcohol drinker status, body mass index, physical activity, vitamin D supplement, fracture history, diabetes, systolic blood pressure, diastolic blood pressure.

HR: Hazard ratio; CI: Confidence interval; HRT: Hormone replacement therapy.

**Supplementary Table 6 Adjusted hazard ratios for rheumatoid arthritis associated with hormonal and reproductive factors, by age, Townsend deprivation index, and BMI.**

Characteristics	Age			Townsend deprivation index			BMI		
	≤ 60 years	> 60 years	<i>P</i>	Below average	Above average	<i>P</i>	≤ 25 kg/m <sup>2</sup>	> 25 kg/m <sup>2</sup>	<i>P</i>
	HR (95%CI)	HR (95%CI)	Value	HR (95%CI)	HR (95%CI)	Value	HR (95%CI)	HR (95%CI)	Value
<b>Early menarche<sup>a</sup> vs. not</b>	1.13(1.00, 1.27)	1.01(0.90, 1.14)	0.071	1.06(0.95, 1.19)	1.07(0.95, 1.21)	0.690	1.12(0.95, 1.33)	1.05(0.95, 1.16)	0.793
<b>Pregnant vs. not</b>	1.16(1.00, 1.33)	0.93(0.80, 1.08)	<b>0.031</b>	0.89(0.77, 1.02)	1.24(1.06, 1.44)	<b>&lt; 0.001</b>	0.98(0.83, 1.17)	1.09(0.96, 1.24)	0.082
<b>Each child</b>	1.06(0.92, 1.24)	1.14(0.98, 1.33)	<b>0.011</b>	0.96(0.92, 1.00)	1.06(1.03, 1.10)	<b>0.006</b>	0.98(0.93, 1.04)	1.04(1.00, 1.07)	<b>0.025</b>
<b>Early menopause<sup>b</sup> vs. not</b>	1.48(1.23, 1.78)	1.43(1.24, 1.65)	0.675	1.27(1.09, 1.50)	1.66(1.42, 1.93)	<b>&lt;0.001</b>	1.40(1.13, 1.72)	1.48(1.30, 1.69)	0.084
<b>Hysterectomy vs. not</b>	1.63(1.34, 1.98)	1.32(1.16, 1.50)	<b>0.005</b>	1.36(1.17, 1.58)	1.45(1.23, 1.70)	0.379	1.49(1.21, 1.82)	1.37(1.21, 1.56)	0.457
<b>Oophorectomy vs. not</b>	1.32(1.11, 1.57)	1.14(0.99, 1.31)	<b>0.007</b>	1.15(0.99, 1.34)	1.27(1.08, 1.48)	0.257	1.38(1.13, 1.69)	1.14(1.00, 1.30)	0.063
<b>Oral contraceptive pill use vs. not</b>	1.07(0.91, 1.25)	0.95(0.86, 1.06)	0.423	0.98(0.87, 1.10)	1.00(0.88, 1.13)	0.168	0.97(0.83, 1.13)	0.99(0.90, 1.10)	0.350
<b>Duration of oral contraceptive pill use (per year)</b>	0.99(0.99, 1.00)	1.01(1.00, 1.02)	<b>&lt; 0.001</b>	1.00(0.99, 1.01)	1.00(0.99, 1.01)	0.634	1.00(0.99, 1.01)	1.00(0.99, 1.01)	0.463
<b>HRT use vs. not</b>	1.51(1.35, 1.69)	1.42(1.28, 1.57)	0.055	1.37(1.24, 1.51)	1.57(1.41, 1.76)	0.323	1.42(1.24, 1.62)	1.47(1.35, 1.61)	0.157
<b>Duration of HRT use (per year)</b>	1.03(1.01, 1.05)	1.02(1.00, 1.03)	0.446	1.02(1.00, 1.03)	1.02(1.01, 1.03)	0.361	1.03(1.01, 1.05)	1.01(1.00, 1.02)	<b>0.019</b>

Adjusted for age, Townsend deprivation index, ethnicity, smoking status, alcohol drinker status, body mass index, physical activity, vitamin D supplement, fracture history, diabetes, systolic blood pressure, diastolic blood pressure.

HR: Hazard ratio; CI: Confidence interval; HRT: Hormone replacement therapy; BMI: body mass index.

<sup>a</sup> Early menarche was defined as age at first menstrual period before the age of 12 years.

<sup>b</sup> Early menopause was defined as the permanent absence of menstrual periods before the age of 45 years.