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Supplementary Material

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Table S1. Baseline characteristics between Chinese and Japanese women living in the country of origin and Western countries

Baseline characteristics	Chinese in China (n=145,571)	Chinese in Western countries* (n=437)	Japanese in Japan (n=8965)	Japanese in Western countries* (n=96)
Median (IQR) age at baseline, years	58 (54-65)	56 (53-60)	51 (46-55)	58 (53-61)
Birth cohort				
Born before 1940	29921 (20.6)	6 (1.4)	84 (0.9)	<5
Born 1940-49	58181 (40.0)	159 (36.4)	3327 (37.1)	40 (41.7)
Born 1950 or later	57469 (39.5)	272 (62.2)	5554 (62.0)	55 (57.3)
Education level				
No formal education	53974 (37.1)	11 (2.5)	0 (0)	0 (0)
≤10 years	76360 (52.5)	139 (31.8)	0 (0)	7 (7.3)
11-12 years	11444 (7.9)	51 (11.7)	140 (1.6)	17 (17.7)
>12 years	3793 (2.6)	236 (54.0)	8825 (98.4)	72 (75.0)
Smoking status				
Never smoker	134818 (92.6)	380 (87.0)	6586 (73.5)	54 (56.3)
Former smoker	2327 (1.6)	44 (10.1)	1111 (12.4)	38 (39.6)
Current smoker	8426 (5.8)	13 (3.0)	1268 (14.1)	<5
Body mass index				
Underweight (<18.5 kg/m ²)	7996 (5.5)	19 (4.3)	492 (5.5)	9 (9.4)
Normal weight (18.5-22.9 kg/m ²)	52632 (36.2)	196 (44.9)	5210 (58.1)	52 (54.2)
Overweight (23-27.4 kg/m ²)	61680 (42.4)	175 (40.0)	2819 (31.4)	31 (32.3)
Obese (≥27.5 kg/m ²)	23263 (16.0)	47 (10.8)	444 (5.0)	<5
Mean ± SD, kg/m ²	23.9±3.6	23.4±3.4	22.4±2.8	22.3±3.0
Age at menarche				
≤11 years	776 (0.5)	56 (13.2)	1225 (13.8)	11 (11.8)
12-13 years	16217 (11.2)	224 (52.7)	4650 (52.3)	54 (58.1)
14-15 years	42575 (29.3)	112 (26.4)	2752 (31.0)	27 (29.0)
≥16 years	85921 (59.1)	33 (7.8)	266 (3.0)	<5
Mean ± SD, years	16.0±2.0	13.1±1.6	12.9±1.4	12.8±1.3
Number of children				
0	373 (0.3)	88 (20.2)	1200 (14.0)	38 (39.6)
1	22347 (15.5)	99 (22.7)	877 (10.2)	19 (19.8)
2	43925 (30.5)	173 (39.7)	3946 (45.9)	24 (25.0)
3	37573 (26.0)	61 (14.0)	2276 (26.5)	14 (14.6)
≥4	40025 (27.7)	15 (3.4)	298 (3.5)	<5
Mean ± SD, children	2.9±1.5	1.6±1.1	2.0±1.0	1.2±1.1
MHT use				
Never	N/A†	340 (77.8)	8506 (96.6)	82 (85.4)
Ever	N/A†	97 (22.2)	298 (3.4)	14 (14.6)

Age at natural menopause				
<40 years	4000 (2.8)	5 (1.1)	84 (0.9)	<5
40-44 years	14890 (10.2)	24 (5.5)	350 (3.9)	<5
45-49 years	60846 (41.8)	108 (24.7)	2705 (30.2)	17 (17.7)
50-51 years	33525 (23.0)	116 (26.5)	2752 (30.7)	30 (31.3)
52-54 years	24755 (17.0)	120 (27.5)	2613 (29.1)	27 (28.1)
≥55 years	7555 (5.2)	64 (14.6)	461 (5.1)	18 (18.8)
Mean ± SD, years	48.6±4.0	50.4±4.0	50.1±3.2	51.3±3.6
Incident type 2 diabetes				
No	137661 (94.6)	395 (90.4)	8513 (95.0)	92 (95.8)
Yes	7910 (5.4)	42 (9.6)	452 (5.0)	<5

IQR: interquartile range; SD: standard deviation; MHT: menopausal hormone therapy; N/A: not applicable.

* Chinese and Japanese in Western countries are Chinese and Japanese women living in the UK and Australia.

† China Biobank did not have data on MHT use.

Table S2. The association between age at natural menopause and risk of type 2 diabetes in Chinese, South/Southeast Asian, Black, and Mixed/Other women, using menopause at age 45-49 years as reference

Age at natural menopause (years)	Sample N	Person-years	T2DM n	IR /10 ³ p-ys	BMI at baseline Mean ± SD	Model 1* HR (95% CI)	Model 2† HR (95% CI)	Model 3‡ HR (95% CI)
Chinese (n=146,008)								
<40	4005	237892	219	0.92	23.5±3.7	0.98 (0.85-1.12)	0.99 (0.86-1.14)	1.02 (0.89-1.17)
40-44	14914	881962	794	0.90	23.4±3.6	0.99 (0.91-1.07)	0.99 (0.92-1.07)	1.02 (0.95-1.10)
45-49	60954	3568550	3136	0.88	23.8±3.6	Ref	Ref	Ref
50-51	33641	1987149	1832	0.92	24.0±3.6	1.01 (0.95-1.07)	1.00 (0.95-1.06)	0.99 (0.94-1.05)
52-54	24875	1484307	1433	0.97	24.4±3.6	1.00 (0.94-1.06)	0.98 (0.92-1.04)	0.94 (0.88-1.00)
≥55	7619	478974	538	1.12	24.4±3.8	0.99 (0.90-1.08)	0.98 (0.89-1.07)	0.93 (0.85-1.02)
South/Southeast Asian (n=2,228)								
<40	63	3907	18	4.61	28.1±5.3	1.76 (1.08-2.87)	1.67 (1.02-2.72)	1.52 (0.93-2.48)
40-44	232	14917	49	3.28	27.4±4.6	1.15 (0.83-1.58)	1.14 (0.82-1.57)	1.08 (0.78-1.50)
45-49	740	48982	151	3.08	26.9±5.1	Ref	Ref	Ref
50-51	544	36659	127	3.46	27.2±5.0	1.07 (0.83-1.36)	1.07 (0.85-1.36)	1.04 (0.82-1.32)
52-54	405	27912	82	2.94	27.0±4.7	0.85 (0.65-1.11)	0.86 (0.65-1.12)	0.85 (0.65-1.11)
≥55	244	17417	52	2.99	26.9±4.4	0.80 (0.58-1.11)	0.79 (0.57-1.09)	0.78 (0.57-1.08)
Black (n=1,838)								
<40	54	3348	13	3.88	30.9±5.0	1.70 (0.96-3.03)	1.64 (0.92-2.93)	1.54 (0.86-2.74)
40-44	207	12907	39	3.02	31.1±4.8	1.22 (0.84-1.76)	1.16 (0.80-1.68)	1.17 (0.81-1.70)
45-49	596	38804	108	2.78	30.3±4.5	Ref	Ref	Ref
50-51	380	25804	72	2.79	30.2±4.5	0.92 (0.68-1.24)	0.90 (0.66-1.22)	0.89 (0.66-1.21)
52-54	345	23597	59	2.50	30.1±4.6	0.80 (0.58-1.11)	0.80 (0.58-1.10)	0.82 (0.60-1.14)
≥55	256	18275	61	3.34	30.0±4.8	1.01 (0.73-1.41)	0.98 (0.71-1.37)	1.01 (0.73-1.41)
Mixed/Other (n=1,250)								
<40	26	1534	5	3.26	27.8±6.5	3.07 (1.20-7.84)	3.07 (1.19-7.92)	3.02 (1.16-7.86)
40-44	108	7028	12	1.71	26.8±4.7	1.04 (0.54-1.99)	1.02 (0.53-1.96)	0.99 (0.52-1.92)
45-49	376	24733	38	1.54	26.9±5.5	Ref	Ref	Ref
50-51	306	20529	47	2.29	27.3±4.8	1.42 (0.93-2.18)	1.43 (0.93-2.19)	1.40 (0.91-2.16)
52-54	299	20481	32	1.56	27.2±5.2	0.84 (0.52-1.35)	0.84 (0.52-1.36)	0.83 (0.51-1.33)
≥55	135	9585	23	2.40	27.2±4.9	1.26 (0.74-2.14)	1.23 (0.73-2.10)	1.22 (0.72-2.08)

BMI: body mass index; SD: standard deviation; T2DM: type 2 diabetes; IR: incidence rate (per 1000 person-years); HR: hazard ratio; CI: confidence interval.

* Cox proportional hazard models were used to estimate HR and 95% CI in the overall sample and then separately for each ethnicity (each ethnic group was a different model), with study as a random effect. Model 1 was adjusted for age (continuous) at baseline.

† Model 2 was adjusted for age (continuous) at baseline, ethnicity (only in the overall sample), education level, and smoking status, and stratified by birth year (as a strata variable).

‡ Model 3 included all covariates in Model 2 and BMI (using ethnicity-specific cut-offs: <18.5, 18.5-24.9, 25-29.9, ≥30 kg/m² for Black and Mixed/Other; <18.5, 18.5-22.9, 23-27.4, ≥27.5 kg/m² for Chinese and South/Southeast Asian).

Table S3. The association between age at natural menopause and risk of type 2 diabetes in the overall sample and each ethnic group, adjusting for age at menarche and number of children (10 studies)*

Age at natural menopause (years)	Sample N	Person-years	T2DM n	IR /10 ³ p-ys	Early menarche† %	No children %	Model 3‡ HR (95% CI)	Model 4§ HR (95% CI)
Overall (n=329,069)								
<40	7051	445160	523	1.17	11.0	10.4	1.31 (1.20-1.43)	1.30 (1.19-1.43)
40-44	27917	1779025	1781	1.00	10.3	9.0	1.16 (1.10-1.23)	1.15 (1.09-1.22)
45-49	105423	6612396	6054	0.92	8.0	7.9	1.09 (1.05-1.13)	1.09 (1.05-1.13)
50-51	78385	5108899	4378	0.86	10.0	9.2	Ref	Ref
52-54	74094	4945843	4217	0.85	11.6	9.3	0.95 (0.91-0.99)	0.95 (0.91-0.99)
≥55	36199	2552503	2402	0.94	14.8	9.5	0.94 (0.90-0.99)	0.94 (0.90-0.99)
White (n=171,144)								
<40	2992	203750	272	1.33	23.1	22.3	1.55 (1.37-1.76)	1.53 (1.35-1.74)
40-44	12375	860088	901	1.05	21.2	18.6	1.27 (1.18-1.37)	1.26 (1.16-1.36)
45-49	40963	2837784	2570	0.91	18.3	18.3	1.17 (1.11-1.24)	1.17 (1.10-1.24)
50-51	41254	2912704	2232	0.77	17.4	16.1	Ref	Ref
52-54	45967	3262039	2518	0.77	17.5	13.9	0.98 (0.92-1.04)	0.98 (0.92-1.04)
≥55	27593	2007024	1714	0.85	18.8	12.0	0.96 (0.90-1.03)	0.96 (0.90-1.03)
Chinese (n=144,630)								
<40	3852	229504	212	0.92	15.2	0.7	1.02 (0.89-1.18)	1.03 (0.89-1.18)
40-44	14728	870827	779	0.89	15.2	0.4	1.03 (0.94-1.12)	1.02 (0.94-1.11)
45-49	60385	3534636	3112	0.88	11.6	0.3	1.01 (0.96-1.07)	1.01 (0.96-1.07)
50-51	33394	1972138	1815	0.92	11.2	0.3	Ref	Ref
52-54	24704	1473973	1425	0.97	11.2	0.3	0.95 (0.88-1.01)	0.95 (0.88-1.01)
≥55	7567	475707	534	1.12	9.8	0.4	0.94 (0.85-1.03)	0.95 (0.86-1.04)
Chinese born ≥1950 (n=57,225)								
<40	1348	65707	54	0.82	20.4	0.5	2.80 (2.10-3.72)	2.76 (2.07-3.67)
40-44	5690	287660	182	0.63	18.8	0.4	1.88 (1.57-2.25)	1.85 (1.54-2.21)
45-49	26411	1370590	688	0.50	15.1	0.4	1.28 (1.12-1.45)	1.27 (1.12-1.44)
50-51	14316	760668	367	0.48	14.0	0.2	Ref	Ref
52-54	8786	478238	236	0.49	13.9	0.3	0.82 (0.70-0.97)	0.82 (0.69-0.96)
≥55	674	38240	20	0.52	16.5	1.0	0.64 (0.41-1.01)	0.63 (0.40-1.00)
Japanese (n=8,636)								
<40	80	4003	8	2.00	23.8	17.5	4.23 (2.06-8.66)	4.04 (1.97-8.30)
40-44	333	17360	17	0.98	13.8	25.8	2.00 (1.20-3.33)	2.00 (1.20-3.32)
45-49	2581	141226	129	0.91	16.1	15.9	1.37 (1.07-1.75)	1.36 (1.06-1.74)
50-51	2658	150690	126	0.84	14.3	13.1	Ref	Ref
52-54	2526	147648	133	0.90	11.5	12.5	0.86 (0.67-1.10)	0.87 (0.68-1.11)
≥55	458	28183	28	0.99	9.4	11.6	0.69 (0.46-1.05)	0.70 (0.46-1.06)

South/Southeast Asian (n=2,013)									
<40	55	3422	16	4.68	18.2	21.8	1.48 (0.87-2.51)	1.55 (0.91-2.63)	
40-44	211	13612	46	3.38	16.1	16.1	1.11 (0.78-1.57)	1.10 (0.78-1.56)	
45-49	652	43299	126	2.91	15.0	15.2	0.95 (0.73-1.22)	0.97 (0.75-1.25)	
50-51	487	32937	110	3.34	13.8	12.3	Ref	Ref	
52-54	373	25750	76	2.95	12.3	11.0	0.85 (0.64-1.15)	0.89 (0.66-1.19)	
≥55	235	16768	51	3.04	16.6	6.4	0.78 (0.56-1.09)	0.80 (0.57-1.12)	
Black (n=1,633)									
<40	51	3205	11	3.43	13.7	19.6	1.49 (0.78-2.85)	1.51 (0.79-2.88)	
40-44	184	11526	30	2.60	16.9	14.1	1.18 (0.76-1.85)	1.18 (0.75-1.86)	
45-49	530	34726	90	2.59	13.4	13.0	1.11 (0.79-1.54)	1.10 (0.79-1.54)	
50-51	341	23327	60	2.57	10.3	10.6	Ref	Ref	
52-54	296	20442	47	2.30	14.9	12.2	0.91 (0.62-1.33)	0.91 (0.62-1.33)	
≥55	231	16545	57	3.45	14.3	3.5	1.27 (0.88-1.84)	1.26 (0.87-1.83)	
Mixed/Other (n=1,013)									
<40	21	1276	4	3.13	33.3	28.6	2.04 (0.70-5.95)	2.34 (0.78-7.00)	
40-44	86	5612	8	1.43	17.4	19.8	0.80 (0.37-1.75)	0.82 (0.37-1.79)	
45-49	312	20725	27	1.30	22.8	22.4	0.72 (0.43-1.19)	0.75 (0.45-1.26)	
50-51	251	17103	35	2.05	18.3	17.1	Ref	Ref	
52-54	228	15991	18	1.13	20.6	15.8	0.48 (0.27-0.84)	0.51 (0.29-0.91)	
≥55	115	8276	18	2.17	20.9	11.3	0.89 (0.50-1.60)	1.05 (0.59-1.89)	

BMI: body mass index; SD: standard deviation; T2DM: type 2 diabetes; IR: incidence rate (per 1000 person-years); HR: hazard ratio; CI: confidence interval.

* Three studies (HOW, WHITEHALL, and SABRE) were excluded as they did not collect data on both age at menarche and parity.

† Age at menarche ≤ 11 years was defined as early menarche, while in Chinese women age at menarche ≤ 13 years was defined as early menarche.

‡ Cox proportional hazard models were used to estimate HR and 95% CI in the overall sample and then separately for each ethnicity (each ethnic group was a different model), with study as a random effect. Model 3 was adjusted for age (continuous) at baseline, ethnicity (only in the overall sample), education level, smoking status, and BMI, and stratified by birth year (as a strata variable).

§ Model 4 included all covariates in Model 3 and age at menarche and number of children.

Table S4. The association between age at natural menopause and risk of type 2 diabetes in the overall sample and each ethnic group, adjusting for use of menopausal hormone therapy (12 studies)*

Age at natural menopause (years)	Sample N	Person-years	T2DM n	IR /10 ³ p-ys	Ever used MHT [†] %	Model 3 [‡] HR (95% CI)	Model 4 [§] HR (95% CI)
Overall (n=191,318)							
<40	3342	224716	331	1.47	54.3	1.58 (1.41-1.78)	1.59 (1.41-1.78)
40-44	13707	942415	1057	1.12	45.2	1.26 (1.18-1.36)	1.26 (1.18-1.36)
45-49	46934	3202315	3121	0.97	33.5	1.15 (1.10-1.21)	1.15 (1.10-1.21)
50-51	46781	3257316	2721	0.84	31.0	Ref	Ref
52-54	51037	3582763	2908	0.81	30.6	0.95 (0.90-1.00)	0.95 (0.90-1.00)
≥55	29517	2139338	1931	0.90	39.3	0.94 (0.89-1.00)	0.94 (0.89-1.00)
White (n=176,759)							
<40	3113	211545	286	1.35	55.7	1.54 (1.36-1.74)	1.53 (1.36-1.74)
40-44	12799	888433	940	1.06	46.9	1.27 (1.18-1.37)	1.27 (1.18-1.37)
45-49	42468	2937826	2685	0.91	35.9	1.16 (1.10-1.23)	1.17 (1.10-1.23)
50-51	42709	3011903	2341	0.78	33.1	Ref	Ref
52-54	47315	3353345	2601	0.78	32.4	0.97 (0.92-1.03)	0.97 (0.92-1.03)
≥55	28355	2061081	1763	0.86	40.2	0.95 (0.89-1.01)	0.95 (0.89-1.01)
Japanese (n=8,900)							
<40	82	4134	8	1.94	18.3	4.08 (2.00-8.36)	4.56 (2.22-9.39)
40-44	342	17823	17	0.95	11.4	2.06 (1.24-3.43)	2.13 (1.28-3.55)
45-49	2666	145857	132	0.90	3.8	1.39 (1.09-1.78)	1.39 (1.09-1.78)
50-51	2742	155437	127	0.82	3.1	Ref	Ref
52-54	2596	151770	132	0.87	2.3	0.85 (0.66-1.08)	0.84 (0.66-1.07)
≥55	472	28987	29	1.00	2.5	0.72 (0.48-1.08)	0.71 (0.47-1.07)
South/Southeast Asian (n=2,222)							
<40	63	3907	18	4.61	46.0	1.46 (0.89-2.40)	1.61 (0.97-2.67)
40-44	231	14862	49	3.30	27.3	1.05 (0.76-1.47)	1.07 (0.77-1.49)
45-49	738	48872	150	3.07	23.0	0.96 (0.76-1.22)	0.97 (0.76-1.22)
50-51	542	36517	126	3.45	21.4	Ref	Ref
52-54	404	27858	82	2.94	20.8	0.82 (0.62-1.08)	0.81 (0.62-1.08)
≥55	244	17417	52	2.99	27.1	0.75 (0.54-1.04)	0.75 (0.54-1.04)
Black (n=1,834)							
<40	53	3293	12	3.64	39.6	1.60 (0.87-2.97)	1.60 (0.86-2.97)
40-44	207	12907	39	3.02	17.4	1.31 (0.88-1.96)	1.31 (0.88-1.96)
45-49	594	38689	107	2.77	16.5	1.12 (0.82-1.51)	1.12 (0.82-1.51)
50-51	380	25804	72	2.79	15.3	Ref	Ref
52-54	344	23536	58	2.46	14.5	0.91 (0.64-1.29)	0.91 (0.64-1.29)
≥55	256	18275	61	3.34	24.2	1.14 (0.80-1.61)	1.14 (0.80-1.61)

Mixed/Other (n=1,166)							
<40	26	1534	5	3.26	53.9	2.07 (0.80-5.37)	2.20 (0.84-5.76)
40-44	104	6775	12	1.77	43.3	0.74 (0.39-1.42)	0.77 (0.40-1.49)
45-49	360	23754	36	1.52	30.3	0.70 (0.45-1.08)	0.71 (0.45-1.10)
50-51	292	19684	46	2.34	25.7	Ref	Ref
52-54	258	17975	21	1.17	28.3	0.46 (0.27-0.77)	0.46 (0.27-0.76)
≥55	126	9017	20	2.22	34.1	0.81 (0.47-1.38)	0.81 (0.48-1.39)

BMI: body mass index; T2DM: type 2 diabetes; IR: incidence rate (per 1000 person-years); MHT: menopausal hormone therapy; HR: hazard ratio; CI: confidence interval.

* China Biobank was excluded as they did not collect data on MHT use, so the analysis for Chinese women was not performed.

† MHT use at baseline at categorised as never and ever.

‡ Cox proportional hazard models were used to estimate HR and 95% CI in the overall sample and then separately for each ethnicity (each ethnic group was a different model), with study as a random effect. Model 3 was adjusted for age (continuous) at baseline, ethnicity (only in the overall sample), education level, smoking status, and BMI, and stratified by birth year (as a strata variable).

§ Model 4 included all covariates in Model 3 and age at menarche and number of children.

Table S5. The association between age at natural menopause and risk of type 2 diabetes in the overall sample and each ethnic group, excluding incident diabetes cases occurring within two years of menopause (13 studies)

Age at natural menopause (years)	Sample N	Person-years	T2DM n	IR /10 ³ p-ys	BMI at baseline Mean ± SD	Model 1* HR (95% CI)	Model 2† HR (95% CI)	Model 3‡ HR (95% CI)
Overall (n=335,915)								
<40	7337	462491	535	1.16	25.1±5.0	1.46 (1.33-1.59)	1.41 (1.29-1.55)	1.41 (1.29-1.55)
40-44	28598	1823832	1800	0.99	25.0±4.7	1.27 (1.21-1.35)	1.24 (1.17-1.31)	1.25 (1.18-1.32)
45-49	107517	6754172	5784	0.86	24.8±4.4	1.16 (1.11-1.20)	1.14 (1.09-1.18)	1.13 (1.09-1.18)
50-51	80057	5227053	4073	0.78	25.2±4.5	Ref	Ref	Ref
52-54	75556	5049421	3829	0.76	25.7±4.5	0.94 (0.90-0.98)	0.95 (0.91-1.00)	0.92 (0.88-0.97)
≥55	36850	2602360	2135	0.82	26.4±4.8	0.92 (0.87-0.97)	0.92 (0.87-0.97)	0.87 (0.83-0.92)
White (n=176,918)								
<40	3117	212033	281	1.33	27.1±5.5	1.96 (1.73-2.22)	1.80 (1.59-2.04)	1.62 (1.43-1.84)
40-44	12814	889893	920	1.03	26.8±5.1	1.49 (1.38-1.60)	1.41 (1.30-1.52)	1.33 (1.23-1.44)
45-49	42515	2942759	2547	0.87	26.4±4.9	1.25 (1.18-1.33)	1.22 (1.16-1.30)	1.19 (1.12-1.26)
50-51	42801	3019389	2195	0.73	26.3±4.8	Ref	Ref	Ref
52-54	47387	3359914	2398	0.71	26.5±4.8	0.97 (0.91-1.03)	0.98 (0.93-1.04)	0.96 (0.90-1.01)
≥55	28284	2058130	1571	0.76	26.9±4.9	0.95 (0.89-1.02)	0.96 (0.90-1.03)	0.90 (0.84-0.96)
Chinese (n=144,823)								
<40	3995	237530	212	0.89	23.5±3.7	1.05 (0.91-1.21)	1.07 (0.92-1.23)	1.11 (0.96-1.28)
40-44	14886	880754	766	0.87	23.4±3.7	1.07 (0.98-1.16)	1.08 (0.99-1.18)	1.13 (1.03-1.23)
45-49	60629	3552892	2865	0.81	23.7±3.6	1.05 (0.99-1.12)	1.06 (1.00-1.13)	1.07 (1.01-1.14)
50-51	33307	1970145	1565	0.79	23.9±3.6	Ref	Ref	Ref
52-54	24526	1465691	1169	0.80	24.4±3.6	0.94 (0.87-1.02)	0.93 (0.86-1.01)	0.90 (0.83-0.97)
≥55	7480	471109	426	0.90	24.4±3.8	0.87 (0.78-0.97)	0.86 (0.77-0.96)	0.83 (0.74-0.92)
Chinese born ≥1950 (n=57,009)								
<40	1424	69361	51	0.74	23.7±3.5	4.34 (3.20-5.89)	4.33 (3.19-5.88)	4.43 (3.26-6.01)
40-44	5734	290008	164	0.57	23.5±3.4	2.82 (2.30-3.45)	2.82 (2.30-3.45)	2.91 (2.38-3.57)
45-49	26391	1370402	516	0.38	23.8±3.4	1.63 (1.39-1.92)	1.63 (1.39-1.92)	1.66 (1.41-1.94)
50-51	14186	754233	218	0.29	24.0±3.4	Ref	Ref	Ref
52-54	8624	469717	97	0.21	24.4±3.4	0.55 (0.44-0.70)	0.55 (0.44-0.70)	0.53 (0.42-0.68)
≥55	650	36905	6	0.16	25.0±3.6	0.30 (0.13-0.67)	0.30 (0.13-0.67)	0.27 (0.12-0.61)
Japanese (n=8,962)								
<40	84	4213	8	1.90	21.9±3.6	5.22 (2.53-10.8)	5.33 (2.58-11.0)	5.73 (2.78-11.8)
40-44	354	18460	17	0.92	22.1±3.1	2.80 (1.67-4.69)	2.82 (1.68-4.75)	2.82 (1.67-4.73)
45-49	2696	147663	110	0.74	22.1±2.8	1.59 (1.21-2.09)	1.60 (1.22-2.11)	1.57 (1.19-2.07)
50-51	2748	155992	96	0.62	22.3±2.8	Ref	Ref	Ref
52-54	2609	152628	104	0.68	22.6±2.7	0.88 (0.66-1.16)	0.88 (0.67-1.16)	0.85 (0.64-1.12)
≥55	471	28987	22	0.76	23.0±2.9	0.75 (0.47-1.20)	0.75 (0.47-1.20)	0.65 (0.41-1.04)

South/Southeast Asian (n=2,175)								
<40	62	3868	17	4.40	28.3±5.3	1.81 (1.09-3.01)	1.72 (1.03-2.87)	1.62 (0.97-2.70)
40-44	230	14834	47	3.17	27.3±4.6	1.19 (0.85-1.67)	1.18 (0.84-1.66)	1.16 (0.82-1.63)
45-49	724	48228	135	2.80	26.8±5.0	0.96 (0.75-1.23)	0.96 (0.75-1.23)	0.99 (0.77-1.27)
50-51	529	35905	112	3.12	27.1±5.0	Ref	Ref	Ref
52-54	395	27381	72	2.63	27.0±4.7	0.78 (0.58-1.05)	0.79 (0.59-1.06)	0.80 (0.60-1.08)
≥55	235	16903	43	2.54	26.9±4.4	0.69 (0.48-0.98)	0.68 (0.48-0.97)	0.70 (0.49-0.99)
Black (n=1,804)								
<40	54	3348	13	3.88	30.9±6.0	2.09 (1.15-3.80)	2.09 (1.15-3.81)	1.96 (1.08-3.58)
40-44	206	12863	38	2.95	31.0±7.3	1.46 (0.97-2.18)	1.43 (0.95-2.15)	1.46 (0.97-2.20)
45-49	581	38090	93	2.44	30.2±6.0	1.04 (0.76-1.43)	1.07 (0.78-1.47)	1.08 (0.78-1.48)
50-51	374	25500	66	2.59	30.2±5.4	Ref	Ref	Ref
52-54	342	23433	56	2.39	30.1±6.1	0.90 (0.63-1.28)	0.91 (0.64-1.31)	0.95 (0.66-1.36)
≥55	247	17759	52	2.93	29.9±5.3	1.01 (0.70-1.46)	1.00 (0.69-1.44)	1.04 (0.72-1.51)
Mixed/Other (n=1,233)								
<40	25	1499	4	2.67	27.1±5.6	2.25 (0.80-6.35)	2.19 (0.77-6.24)	2.20 (0.76-6.34)
40-44	108	7028	12	1.71	26.8±4.7	0.87 (0.45-1.67)	0.85 (0.44-1.64)	0.84 (0.44-1.63)
45-49	372	24540	34	1.39	27.0±5.5	0.76 (0.48-1.21)	0.76 (0.48-1.20)	0.77 (0.48-1.22)
50-51	298	20122	39	1.94	27.2±4.8	Ref	Ref	Ref
52-54	297	20374	30	1.47	27.2±5.3	0.66 (0.41-1.06)	0.65 (0.40-1.05)	0.64 (0.40-1.04)
≥55	133	9472	21	2.22	27.2±4.9	0.96 (0.56-1.64)	0.93 (0.54-1.59)	0.93 (0.54-1.59)

BMI: body mass index; SD: standard deviation; T2DM: type 2 diabetes; IR: incidence rate (per 1000 person-years); MHT: menopausal hormone therapy; HR: hazard ratio; CI: confidence interval.

* Cox proportional hazard models were used to estimate HR and 95% CI in the overall sample and then separately for each ethnicity (each ethnic group was a different model), with study as a random effect. Model 1 was adjusted for age (continuous) at baseline.

† Model 2 was adjusted for age (continuous) at baseline, ethnicity (only in the overall sample), education level, and smoking status, and stratified by birth year (as a strata variable).

‡ Model 3 included all covariates in Model 2 and BMI (using ethnicity-specific cut-offs: <18.5, 18.5-24.9, 25-29.9, ≥30 kg/m² for White, Black, and Mixed/Other; <18.5, 18.5-22.9, 23-27.4, ≥27.5 kg/m² for Chinese, Japanese, and South/Southeast Asian).

Table S6. The association between age at natural menopause and risk of type 2 diabetes in the overall sample and each ethnic group, excluding women with a history of gestational diabetes (6 studies)*

Age at natural menopause (years)	Sample N	Person-years	T2DM n	IR /10 ³ p-ys	BMI at baseline Mean ± SD	Model 1† HR (95% CI)	Model 2‡ HR (95% CI)	Model 3§ HR (95% CI)
Overall (n=163,813)								
<40	2743	186242	256	1.37	27.2±5.6	1.97 (1.73-2.25)	1.76 (1.55-2.00)	1.57 (1.38-1.79)
40-44	11688	813025	850	1.05	26.8±5.2	1.40 (1.29-1.52)	1.31 (1.21-1.42)	1.24 (1.14-1.34)
45-49	39298	2730881	2544	0.93	26.5±5.0	1.24 (1.17-1.31)	1.18 (1.12-1.25)	1.15 (1.09-1.22)
50-51	39454	2797531	2226	0.80	26.3±4.8	Ref	Ref	Ref
52-54	43869	3127403	2421	0.77	26.5±4.8	0.95 (0.90-1.01)	0.98 (0.93-1.04)	0.95 (0.90-1.01)
≥55	26761	1954364	1693	0.87	26.9±4.9	0.99 (0.93-1.05)	1.00 (0.94-1.07)	0.94 (0.88-1.00)
White (n=158,438)								
<40	2607	177750	224	1.26	27.1±5.6	1.95 (1.70-2.24)	1.77 (1.55-2.04)	1.58 (1.37-1.81)
40-44	11160	779147	762	0.98	26.8±5.1	1.41 (1.29-1.53)	1.33 (1.22-1.44)	1.25 (1.15-1.36)
45-49	37604	2618618	2267	0.87	26.4±5.0	1.24 (1.16-1.31)	1.20 (1.13-1.28)	1.17 (1.10-1.24)
50-51	38187	2711152	1999	0.74	26.3±4.8	Ref	Ref	Ref
52-54	42794	3052813	2259	0.74	26.5±4.8	0.98 (0.93-1.05)	1.00 (0.94-1.06)	0.97 (0.91-1.03)
≥55	26086	1905971	1561	0.82	26.9±4.9	1.00 (0.94-1.07)	1.02 (0.95-1.09)	0.95 (0.88-1.01)
South/Southeast Asian (n=2,116)								
<40	58	3653	15	4.11	28.5±5.4	1.45 (0.85-2.49)	1.37 (0.80-2.35)	1.28 (0.75-2.20)
40-44	219	14145	48	3.39	27.3±4.5	1.14 (0.82-1.60)	1.15 (0.82-1.61)	1.12 (0.80-1.56)
45-49	697	46390	142	3.06	26.9±5.0	0.95 (0.75-1.22)	0.96 (0.75-1.22)	0.97 (0.76-1.25)
50-51	514	34825	118	3.39	27.2±5.0	Ref	Ref	Ref
52-54	387	26756	77	2.88	27.0±4.6	0.80 (0.60-1.07)	0.82 (0.61-1.09)	0.83 (0.62-1.10)
≥55	241	17214	51	2.96	26.9±4.4	0.76 (0.55-1.06)	0.75 (0.54-1.04)	0.76 (0.54-1.05)
Black (n=1,692)								
<40	51	3205	11	3.43	31.1±6.0	1.64 (0.87-3.12)	1.61 (0.85-3.07)	1.51 (0.79-2.87)
40-44	192	12024	32	2.66	31.3±7.3	1.29 (0.84-1.99)	1.26 (0.81-1.94)	1.22 (0.79-1.89)
45-49	556	36365	96	2.64	30.4±6.1	1.12 (0.81-1.55)	1.13 (0.82-1.56)	1.12 (0.81-1.54)
50-51	350	23948	63	2.63	30.3±5.5	Ref	Ref	Ref
52-54	307	21214	52	2.45	30.1±6.3	0.91 (0.63-1.32)	0.90 (0.62-1.30)	0.94 (0.65-1.36)
≥55	236	16968	55	3.24	30.0±5.4	1.08 (0.75-1.56)	1.11 (0.77-1.60)	1.16 (0.80-1.68)
Mixed/Other (n=1,041)								
<40	22	1331	4	3.01	28.1±7.0	1.68 (0.59-4.75)	1.62 (0.57-4.62)	1.67 (0.58-4.83)
40-44	89	5807	8	1.38	27.0±4.9	0.66 (0.31-1.42)	0.65 (0.30-1.39)	0.66 (0.31-1.43)
45-49	317	21107	27	1.28	27.0±5.4	0.60 (0.37-0.98)	0.58 (0.36-0.96)	0.61 (0.37-1.00)
50-51	259	17638	39	2.21	27.5±4.8	Ref	Ref	Ref
52-54	235	16523	18	1.09	27.5±5.3	0.45 (0.25-0.78)	0.44 (0.25-0.78)	0.45 (0.26-0.79)
≥55	119	8537	19	2.23	27.4±4.7	0.86 (0.49-1.50)	0.83 (0.47-1.46)	0.86 (0.49-1.50)

BMI: body mass index; SD: standard deviation; T2DM: type 2 diabetes; IR: incidence rate (per 1000 person-years); HR: hazard ratio; CI: confidence interval.

* Six studies (ALSWH, HOW, WLHS, NCDS, Prospect-EPIC, and UK Biobank) provided data on history of gestational diabetes, with only small sample for Chinese and Japanese. Thus, the analyses for Chinese and Japanese women were not performed.

† Cox proportional hazard models were used to estimate HR and 95% CI in the overall sample and then separately for each ethnicity (each ethnic group was a different model), with study as a random effect. Model 1 was adjusted for age (continuous) at baseline.

‡ Model 2 was adjusted for age (continuous) at baseline, ethnicity (only in the overall sample), education level, and smoking status, and stratified by birth year (as a strata variable).

§ Model 3 included all covariates in Model 2 and BMI (using ethnicity-specific cut-offs: <18.5, 18.5-24.9, 25-29.9, ≥ 30 kg/m² for White, Black, and Mixed/Other; <18.5, 18.5-22.9, 23-27.4, ≥ 27.5 kg/m² for Chinese, Japanese, and South/Southeast Asian).

Table S7. The association between age at natural menopause and risk of type 2 diabetes in the overall sample and each ethnic group, using diabetes cases identified through linked health data (4 studies)*

Age at natural menopause (years)	Sample N	Person-years	T2DM n	IR /10 ³ p-ys	BMI at baseline Mean ± SD	Model 1† HR (95% CI)	Model 2‡ HR (95% CI)	Model 3§ HR (95% CI)
Overall (n=162,103)								
<40	2706	184412	231	1.25	27.2±5.6	2.00 (1.74-2.29)	1.77 (1.55-2.03)	1.57 (1.37-1.80)
40-44	11551	805839	781	0.97	26.9±5.2	1.44 (1.33-1.57)	1.35 (1.24-1.46)	1.26 (1.16-1.37)
45-49	38632	2696592	2244	0.83	26.5±5.0	1.23 (1.16-1.31)	1.18 (1.11-1.25)	1.14 (1.08-1.22)
50-51	39124	2781210	1986	0.71	26.3±4.8	Ref	Ref	Ref
52-54	43260	3096766	2154	0.70	26.5±4.8	0.95 (0.90-1.01)	0.98 (0.92-1.05)	0.96 (0.90-1.02)
≥55	26830	1959660	1509	0.77	26.9±4.9	0.98 (0.91-1.04)	1.00 (0.93-1.07)	0.93 (0.87-1.00)
White (n=156,741)								
<40	2570	175935	199	1.13	27.1±5.6	1.95 (1.68-2.26)	1.76 (1.52-2.04)	1.56 (1.35-1.80)
40-44	11026	772141	695	0.90	26.8±5.1	1.44 (1.32-1.57)	1.36 (1.24-1.48)	1.27 (1.16-1.38)
45-49	36941	2584397	1990	0.77	26.4±5.0	1.23 (1.15-1.31)	1.20 (1.12-1.28)	1.16 (1.09-1.24)
50-51	37855	2694677	1778	0.66	26.3±4.8	Ref	Ref	Ref
52-54	42198	3022877	2014	0.67	26.5±4.8	0.99 (0.93-1.06)	1.01 (0.94-1.07)	0.97 (0.91-1.04)
≥55	26151	1910979	1388	0.73	26.9±4.9	0.99 (0.92-1.06)	1.01 (0.94-1.09)	0.94 (0.87-1.00)
South/Southeast Asian (n=2,123)								
<40	60	3748	16	4.27	28.5±5.4	1.66 (0.98-2.81)	1.54 (0.91-2.61)	1.42 (0.84-2.41)
40-44	220	14205	46	3.24	27.3±4.5	1.17 (0.83-1.65)	1.17 (0.83-1.66)	1.13 (0.80-1.60)
45-49	701	46659	135	2.89	26.9±5.0	0.97 (0.75-1.24)	0.97 (0.76-1.25)	0.99 (0.77-1.28)
50-51	514	34857	110	3.16	27.2±5.0	Ref	Ref	Ref
52-54	386	26726	68	2.54	27.0±4.6	0.76 (0.56-1.03)	0.78 (0.58-1.06)	0.79 (0.58-1.07)
≥55	242	17293	44	2.54	26.9±4.4	0.70 (0.49-1.00)	0.68 (0.48-0.97)	0.70 (0.49-1.00)
Black (n=1,691)								
<40	51	3205	11	3.43	31.1±6.0	1.80 (0.94-3.42)	1.77 (0.93-3.38)	1.65 (0.86-3.16)
40-44	191	11958	32	2.68	31.4±7.4	1.43 (0.92-2.21)	1.37 (0.88-2.13)	1.34 (0.86-2.09)
45-49	553	36210	84	2.32	30.4±6.1	1.07 (0.76-1.50)	1.08 (0.77-1.51)	1.07 (0.76-1.50)
50-51	352	24065	58	2.41	30.2±5.5	Ref	Ref	Ref
52-54	306	21174	46	2.17	30.1±6.3	0.88 (0.60-1.30)	0.87 (0.59-1.29)	0.90 (0.61-1.33)
≥55	238	17084	51	2.99	30.0±5.4	1.10 (0.75-1.61)	1.11 (0.76-1.63)	1.16 (0.79-1.70)
Mixed/Other (n=1,016)								
<40	20	1221	4	3.28	27.5±6.5	2.19 (0.77-6.26)	2.15 (0.74-6.19)	2.22 (0.76-6.50)
40-44	86	5633	8	1.42	27.0±4.9	0.83 (0.38-1.81)	0.82 (0.37-1.79)	0.84 (0.38-1.84)
45-49	313	20925	26	1.24	27.0±5.4	0.71 (0.42-1.20)	0.70 (0.42-1.18)	0.74 (0.44-1.24)
50-51	257	17521	32	1.83	27.5±4.8	Ref	Ref	Ref
52-54	223	15833	16	1.01	27.5±5.3	0.50 (0.27-0.91)	0.50 (0.27-0.91)	0.50 (0.28-0.92)
≥55	117	8416	19	2.26	27.4±4.8	1.05 (0.59-1.87)	1.02 (0.57-1.82)	1.04 (0.58-1.85)

BMI: body mass index; SD: standard deviation; T2DM: type 2 diabetes; IR: incidence rate (per 1000 person-years); HR: hazard ratio; CI: confidence interval.

* Four studies (ALSWH, WLHS, Prospect-EPIC, and UK Biobank) provided health administrative data, with only small sample for Chinese and Japanese. Thus, the analyses for Chinese and Japanese women were not performed.

† Cox proportional hazard models were used to estimate HR and 95% CI in the overall sample and then separately for each ethnicity (each ethnic group was a different model), with study as a random effect. Model 1 was adjusted for age (continuous) at baseline.

‡ Model 2 was adjusted for age (continuous) at baseline, ethnicity (only in the overall sample), education level, and smoking status, and stratified by birth year (as a strata variable).

§ Model 3 included all covariates in Model 2 and BMI (using ethnicity-specific cut-offs: <18.5, 18.5-24.9, 25-29.9, ≥ 30 kg/m² for White, Black, and Mixed/Other; <18.5, 18.5-22.9, 23-27.4, ≥ 27.5 kg/m² for Chinese, Japanese, and South/Southeast Asian).

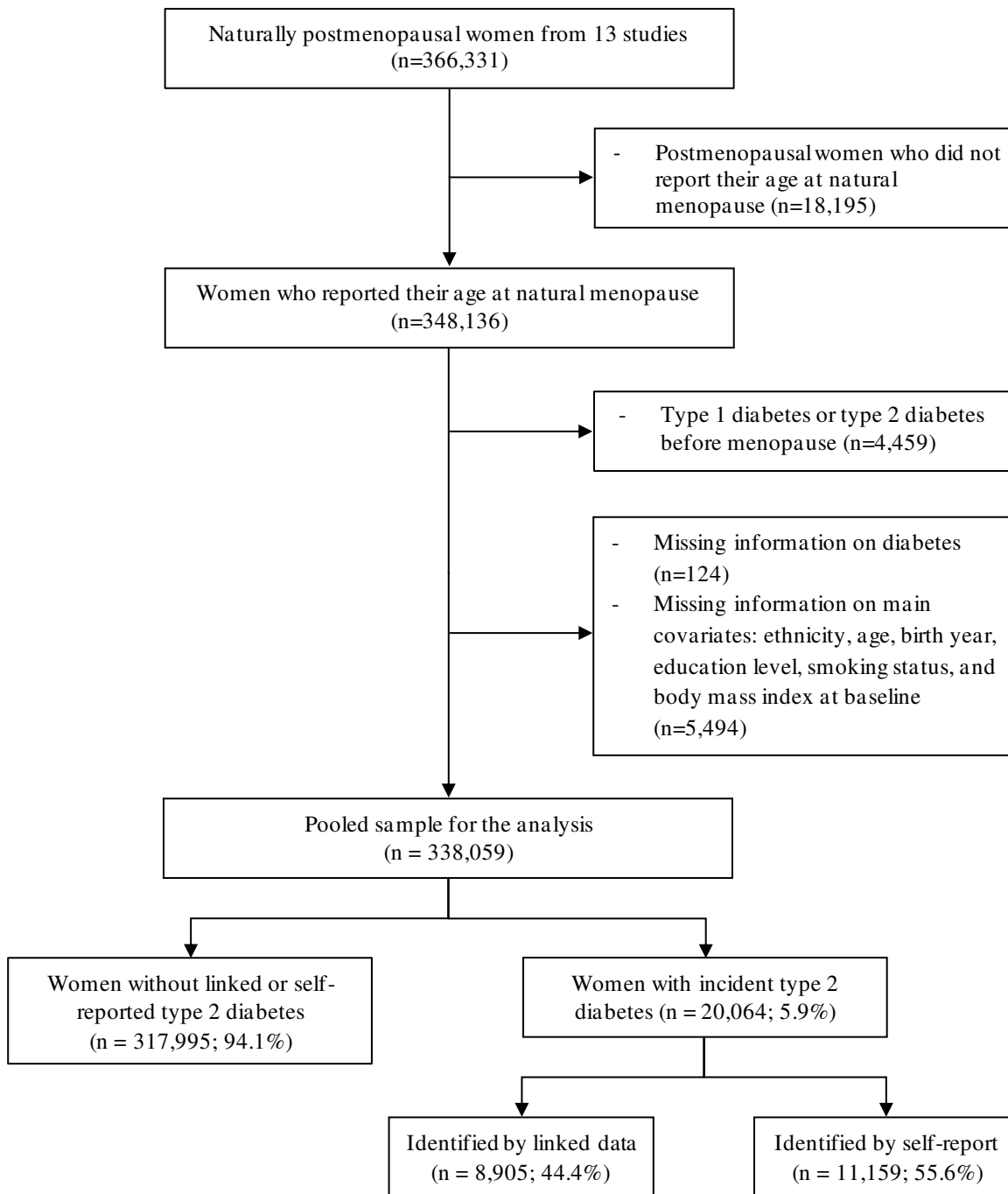


Figure S1. Flow diagram of sample for analysis of the association between age at natural menopause and risk of type 2 diabetes in the InterLACE consortium

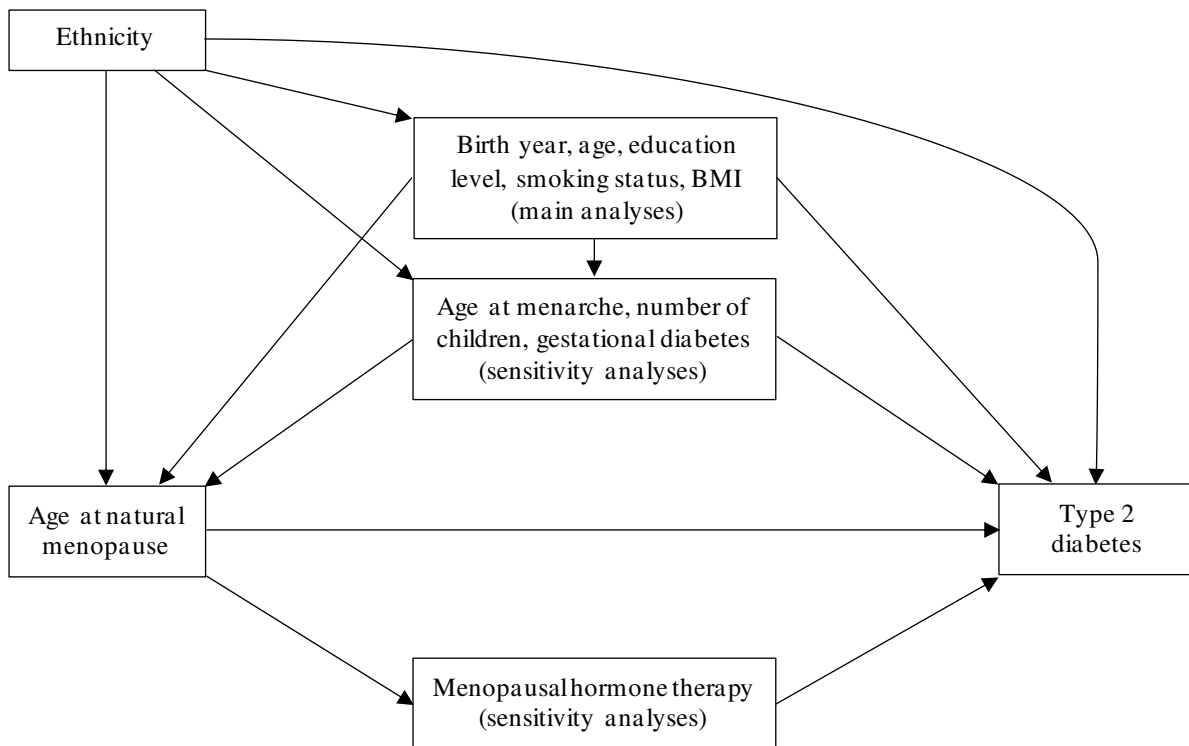
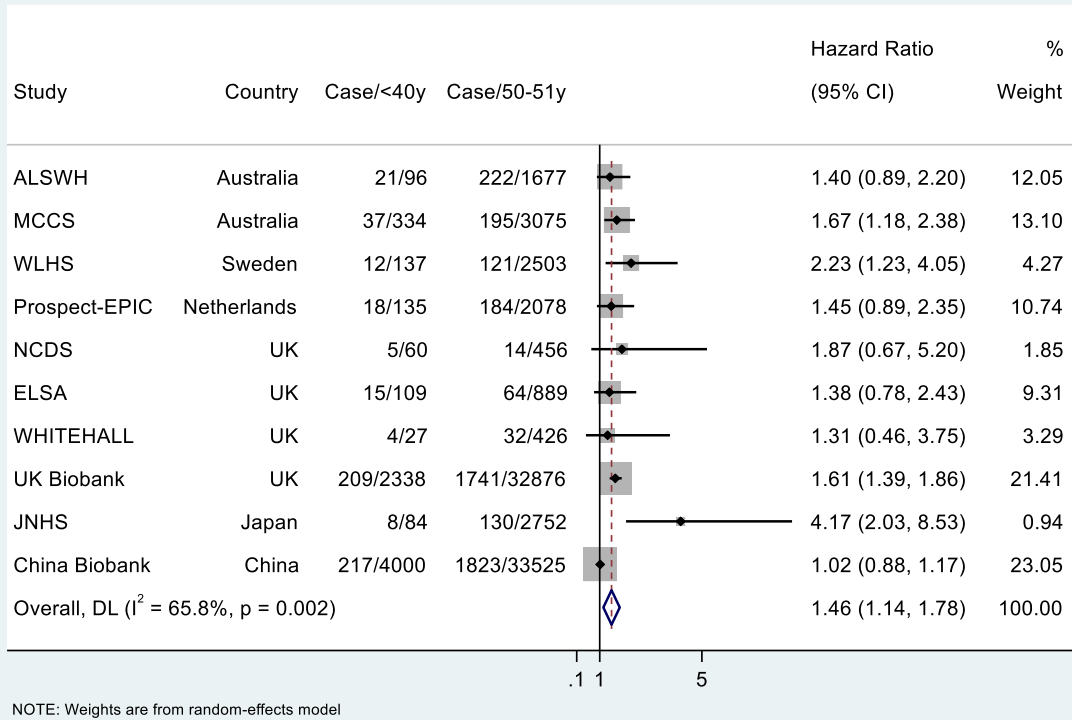


Figure S2. Directed acyclic graph for the association between ethnicity, age at natural menopause type 2 diabetes, and their confounding factors.

(A) POI <40 vs menopause at 50-51 years



(B) Early menopause 40-44 vs menopause at 50-51 years

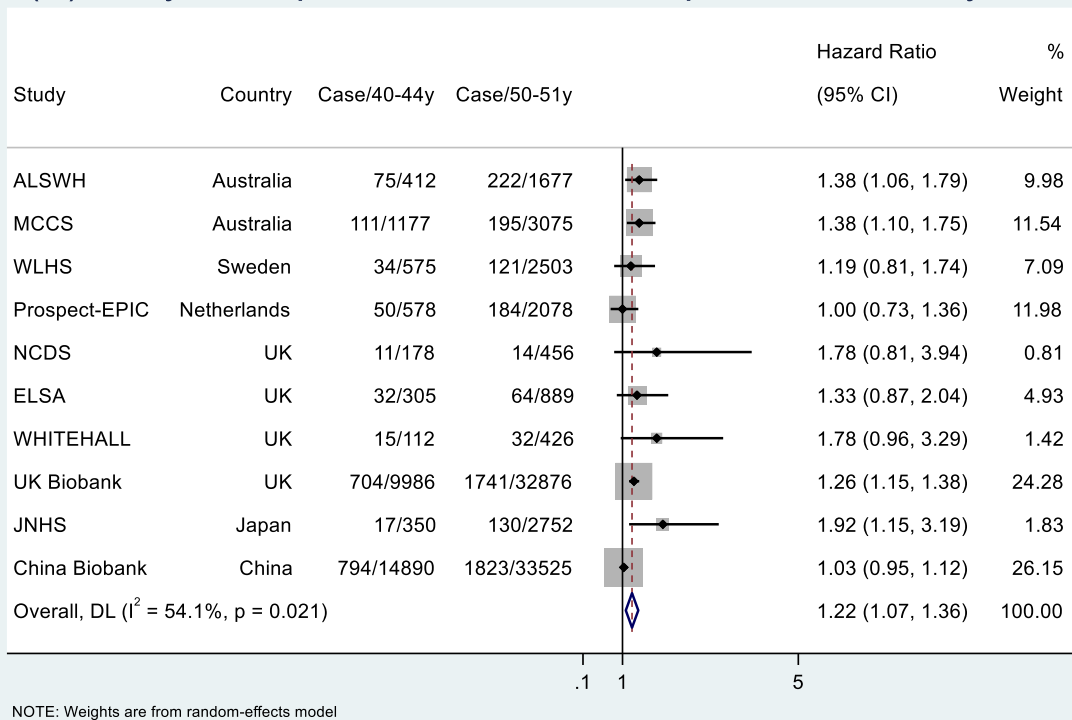
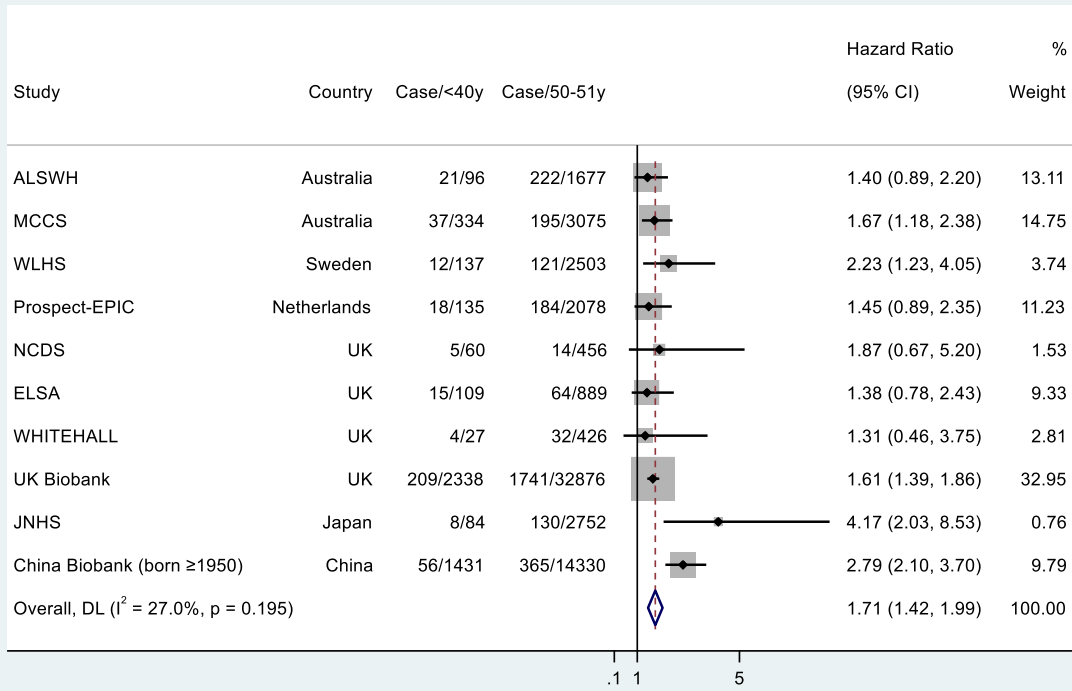


Figure S3. Meta-analysis of the association between (A) POI <40 years and (B) early menopause 40-44 years and the risk of type 2 diabetes, using 10 studies with sufficient data (excluding HOW, NSHD, and SABRE). Hazard ratios were fully adjusted for age (continuous) at baseline, education level, smoking status, and body mass index, and stratified by birth years (as a strata variable).

(A) POI <40 vs menopause at 50-51 years



(B) Early menopause 40-44 vs menopause at 50-51 years

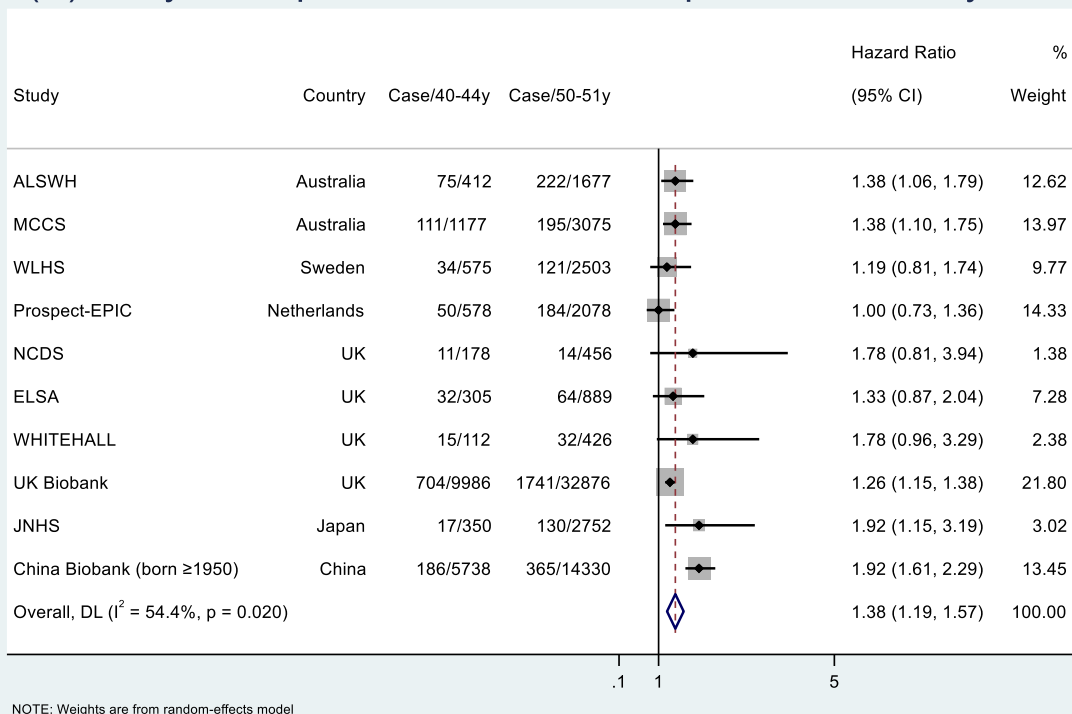


Figure S4. Meta-analysis of the association between (A) POI <40 years and (B) early menopause 40-44 years and the risk of type 2 diabetes, including younger generations of China Biobank (born in 1950 or later). Hazard ratios were fully adjusted for age (continuous) at baseline, education level, smoking status, and body mass index, and stratified by birth years (as a strata variable).