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Timing and type of menopause are not risk factors for the onset of diabetes: a UK Biobank cohort study

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Abstract

Objectives: Early and premature menopause are positively associated with coronary heart disease and stroke, but there is less evidence regarding its relationship with the onset of diabetes. The primary objective of this study is to assess the association between the timing and type of menopause and the possible development of type 1 or 2 diabetes.

Methods: Participants from the UK Biobank were enrolled between 2006 and 2010, with follow-up to the end of 2023. The outcome variable was diagnosis of type 1 or 2 diabetes during follow-up, and the main explanatory variable was age at menopause (normal above 45 y, early 40-45 y, and premature below 40 y). Behavioral factors, comorbidities, and blood tests were also collected. Survival models with Weibull distribution were fitted to the time of diabetes onset.

Results: Of the 146,764 women analyzed over a mean follow-up of 14.5 years, 6,598 women developed diabetes (cumulative incidence 4.5%). Rates were higher in women with earlier menopause (4.2% at age above 45 y, 5.2% at ages 40-45 y, and 7.4% before age 40); however, the multivariate analysis showed no independent association (40-45 y: hazard ratio: 1.00; <40 y, hazard ratio: 0.97), taking the normal age of menopause as the reference. Surgical menopause was likewise not associated with a greater risk of diabetes compared with natural menopause.

Conclusions: In a large cohort of women with long-term follow-up, no independent or clinically significant relationship between age or type of menopause and the onset of diabetes was observed.

Key Words: Cardiovascular disease, Cardiovascular risk, Diabetes, Premature menopause.

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Women who experience menopause before the age of 45 are at higher risk of coronary heart disease and stroke,[1] and the postmenopause period is also marked by a higher risk of altered glucose metabolism in women who had both natural and surgical menopause. Among women with early or premature menopause, cardiovascular risk is higher in those with diabetes than in those without.[2] However, there is no strong evidence to suggest whether early or premature menopause clearly and directly promotes the development of diabetes.

The menopause transition is associated with an increase in fat, especially in the trunk region, which—like estrogen suppression—is associated with insulin resistance. Hypothetically, then, this would lead to an increased risk of developing diabetes and dyslipidemia.[3] The decrease in estrogen could also lead to an underproduction of insulin by pancreatic cells and its decrease in muscle tissue, suggesting a plausible relationship with the development of diabetes in menopausal women.[4,5] Likewise, an increase in visceral fat could favor greater inflammation due to the effect of adipokines. This could further contribute to the development of insulin resistance,[6] on top of

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the added resistance generated by the increased availability of testosterone.[7]

Not only natural menopause, but menopause with a surgical cause has also been associated with a higher risk of alterations in glucose metabolism in postmenopause.[8]

Thus, the hormonal and metabolic changes triggered by menopause can potentially increase the risk of diabetes due to insulin resistance, increased inflammation due to increased visceral fat, and increased surrounding insulin,[9] despite decreased pancreatic production and lower presence in muscles. However, there is a paucity of direct evidence for this association, as acknowledged in the 2021 European Guidelines on the Prevention of Cardiovascular Disease in Clinical Practice.[10] The main objective of this study is to assess the relationship between early onset (40-45 y) or premature menopause (below 40 y), including surgical menopause, with the risk of type 1 or 2 diabetes.

METHODS

This cohort study drew data from the UK Biobank database, which includes longitudinal health data (encompassing behaviors, comorbidities, and blood tests) for 502,129 volunteer participants (228,973 men and 273,156 women) aged 40 years or older and living in the United Kingdom at enrollment. Participants consented to long-term health monitoring through record linkage. They were enrolled from 2006 to 2010 and followed to 2023. The study design and data collection methods for the UK Biobank cohort have been described in detail elsewhere[11]; the database project was approved by the North West Multi-Centre Research Ethics Committee, the National Board for Information Governance in Health and Social Care in England and Wales, and the Community Health Index Advisory Group in Scotland. All participants provided written informed consent before data collection.

The present study complies with the Declaration of Helsinki and was approved by the University Miguel Hernández Office for Responsible Research on November 11, 2023 (reference AUT.DMC.JAQR.231109).

Participants

Inclusion criteria were female sex and having menopause at the time of enrollment, that is, those who answered "yes" to the question "Have you had menopause (periods stopped)?" (data field 2,724) when completing the touchscreen questionnaire at baseline. Women were excluded if they had been diagnosed with diabetes mellitus before inclusion in the study or before menopause, were lost to follow-up due to a change of address, or who chose to drop out of the cohort. Women with missing values for menopause, age at menopause, or type of menopause were also excluded.

Variables and data collection

The outcome variable was a diagnosis of type 1 or 2 diabetes mellitus (International Classification of Diseases, 10th revision [ICD-10]: E10-E14) during follow-up, along with the date of diagnosis. The main explanatory variables of interest were age at menopause, categorized as normal (above 45 y), early (40-45 y), or premature (below 40 y), and type of menopause (natural vs. surgical).

In addition, a wide variety of explanatory variables were collected for analysis. Their categorizations are detailed below; a category for "missing" was also considered for each variable.

- *Sociodemographics*: age at recruitment (years), Townsend Deprivation Index (unit), educational level (A level/AS levels (Advanced Baccalaureate) or equivalent/college or university degree/Certificate of Secondary Education or equivalent/NVQ, HND or HNC (vocational qualifications) Level or General Certificate of Secondary Education or equivalent/other: nursing, teaching/none of the above).
- *Behavioral factors*: frequency of alcohol intake (never/previous/current), tobacco use (no/only occasionally/yes, most days), daily hours of sleep (<7 h/7-9 h/>9 h), International Physical Activity Questionnaire activity (low/moderate/high).
- *Anthropometric variables*: total metabolic equivalent of task per week (high $>6{,}272$ kJ/moderate 5,027-6,272 kJ/low $<5{,}027$ kJ), waist circumference (<80 cm/80-88 cm/>88 cm), body mass index (normal <25 kg/m^2/overweight 25-30 kg/m^2/obese >30 kg/m^2), percentage of fat mass (normal $<21\%$/moderate 21%-32%/high $>32\%$).
- *Physiological variables*: forced vital capacity: calculated as normal or high if the observed value was greater than the theoretical value ($>0.041\times\text{height}-0.018\times\text{age}-2.69$), and reduced if it was lower, diastolic blood pressure (normal <90 mm Hg/high ≥ 90 mm Hg), systolic blood pressure (normal <140 mm Hg/high ≥ 140 mm Hg), blood type (AA/AB/AO/BB/BO/OO).
- *Dietary variables*: cooked vegetable intake, tablespoons per day (none /1-2/3-4/>4), raw vegetable intake, tablespoons per day (none/1-2/3-4/>4), fresh fruit intake, pieces per day (none/1-2/3-4/>4), salt added to food (never or rarely/sometimes/frequently/always), cups of coffee consumed per day (none/<1/1-2/3-4/>4), glasses of water consumed per day (none/<1/1-2/3-4/>4), sugar intake (no/yes).
- *Health status*: overall self-perceived health (excellent/good/fair/poor), asthma, bronchitis, emphysema or lung clot (no/yes), cancer (no/yes), acute myocardial infarction (AMI), angina or stroke (no/yes), diabetes (no/yes), anxiety, nervous tension or depression (no/yes), cholesterol medication (no/yes), insulin use (no/yes), dental problems (no/yes).
- *Female-specific factors*: age at menarche in years (<10/10-12/13-14/>14); ever taken oral contraceptive pills (no/yes), use of hormone therapy (HT) (no/yes), hysterectomy (no/yes).
- *Family history*: father with diabetes (no/yes), father with hypertension (no/yes), mother with diabetes (no/yes), mother with hypertension (no/yes).
- *Analytical variables*: total cholesterol in mmol/L (normal <5.2/high >5.2), high-density lipoprotein (HDL) cholesterol in mmol/L (high ≥ 1.6/normal 1.3-1.6/low <1.3), low-density lipoprotein (LDL) cholesterol in mmol/L (normal <3/high ≥ 3), creatinine μmol/L (low

< 61.9/normal 61.9-106.1/high > 106.1), glucose in mmol/L (low < 4.1/normal 4.1-5.9/high > 5.9), hemoglobin A1c (HbA1c) (low < 5.7%/normal 5.7-6.49%/ high > 6.49%), vitamin D in nmol (normal > 50/low ≤ 50), albumin in g/L (low < 35/normal 35-50/high > 50), triglycerides in mmol/L (normal < 1.7/high > 1.7), urate in µmol/L (low < 202/normal 202-416/ high > 416), urea in mmol/L (low < 2.8/normal 2.8-8.2/ high > 8.2), lipoprotein (a) in nmol/L (normal < 120/ high > 120), calcium in nmol/L (low < 2.1/normal 2.1-2.6/ high > 2.6).

The study period was from the date of inclusion (between March 2006 and December 2010) until the end of follow-up, measured on December 31, 2023.

Statistical analysis

For the only quantitative variable (deprivation index) with missing data (247 cases, 0.1%), a simple imputation process was performed with the mean and stratified according to the presence of diabetes. For the remaining variables, a "missing" category was created. A descriptive analysis was performed by calculating frequencies for qualitative variables and means and standard deviations for quantitative variables.

Factors associated with the onset of diabetes were analyzed using the χ^2 test for qualitative variables and the Student *t* test for quantitative variables. To analyze the association between age at menopause and type of menopause with the onset of diabetes, the χ^2 test was applied, calculating the diabetes rate per 1,000 women-years, and survival models with a Weibull distribution were fitted to the time to diabetes onset. Crude and age-adjusted analyses were performed for all variables, and a multivariate model was fitted using a variable selection process based on the Akaike Information Criterion, until an optimal model was reached. Multicollinearity was assessed based on the variance inflation factor criterion. The crude and age-adjusted analyses were performed on the full sample, and the multivariate adjustment was performed on a random training sample of 70% of the total sample size. The predictive index *C*-index, along with its 95% confidence interval (CI), was calculated using a testing sample of 30% of the total sample size. The goodness-of-fit of the Weibull distribution was assessed by plotting the log (- log()) of the estimated survival against the log () of the follow-up time, fitting a regression line, and showing the adjusted R^2. Points located on the line, and an $R^2 > 0.9$, were indicative of a good fit.[12,13] Analyses were performed with the R v.4.4.1 program.[14]

RESULTS

The UK Biobank contained data for 273,156 women. After excluding 56,335 (20.6%) due to missing variables related to menopause, 62,265 (22.8%) for not being menopausal at the time of inclusion, and 7,792 (2.8%) for having diabetes before inclusion or before menopause, a sample of 146,764 women was included in the analysis (Fig. 1). Their mean age was 60 years (range: 40-71); 38% were overweight, 22% were obese, 29% had a university education, 12% showed low physical activity, 25% slept < 7 hours a day, 10% had a history of cancer, 25% had high blood pressure, 39% had anxiety, nervous tension or depression, and 3.6% had had an AMI, angina pectoris or stroke. Regarding variables specific to women, 38% had menarche before the age of 12, 78% were taking birth control pills, and 10% were on HT. Indicators related to diabetes control showed that 6.6% had high basal blood glucose, and 16.6% had a glycosylated hemoglobin level > 5.7%. Supplemental Table S1, Supplemental Digital Content 1, http://links.lww.com/MENO/B468 shows the proportions of all baseline variables for each type of premature, early, or normal menopause.

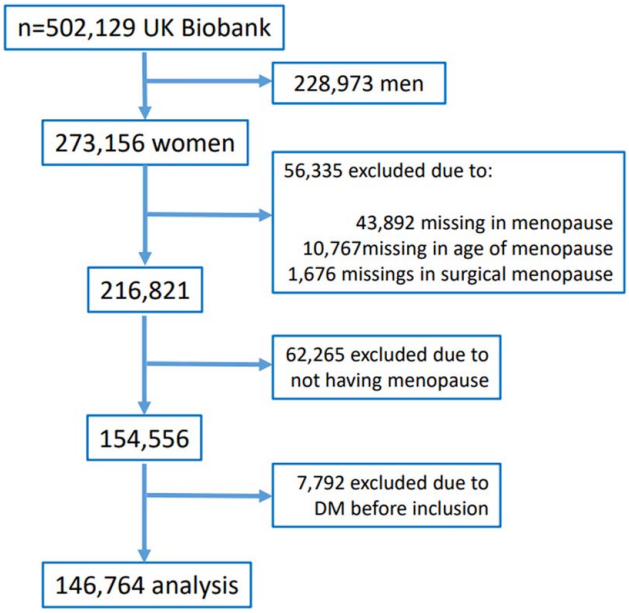

FIG. 1. Flow chart of participants included in the study. DM, diabetes mellitus.

As for the two study factors of interest, 81.9% had menopause after age 45, 14.3% between 40 and 45 years of age, and 3.8% before age 40. In addition, 5.5% of women had surgical menopause resulting from bilateral oophorectomy.

Over a median follow-up of 14.8 years (mean: 14.5 y), 6,598 women were diagnosed with diabetes (cumulative incidence: 4.5%, incidence: 3.1 cases per 1,000 woman-years). Of these, 94% had type 2 diabetes and 1% type 1; for the remaining 5%, the type of diabetes was unspecified. The earlier the onset of menopause, the higher the incidence of diabetes, with cumulative rates of 4.2% in women with normal menopause (2.90 cases per 1,000 woman-years), 5.2% in early menopause (3.61 cases per 1,000 woman-years), and 7.4% in premature menopause (5.13 cases per 1,000 woman-years) (χ^2 test, $P < 0.001$). The group with surgical menopause also showed a higher incidence of diabetes (6.6%, with 4.59 cases per 1,000 woman-years) than women with normal menopause (4.4%, with 2.99 cases per 1,000 woman-years) (χ^2 test, $P < 0.001$) (Table 1).

TABLE 1. Prevalence of premature menopause and type of menopause, and incidence of diabetes

	n (%)				
	Total	**DM no**	**DM yes**	***P***	**DM rate[a]**
Age at menopause					
Normal >45 y	120,188 (81.9)	115,103 (95.8)	5,085 (4.2)	<0.001	2.90
Precocious 40-45 y	20,940 (14.3)	19,843 (94.8)	1,097 (5.2)		3.61
Premature <40 y	5,636 (3.8)	5,220 (92.6)	416 (7.4)		5.13
Type of menopause					
Natural	138,733 (94.5)	132,666 (95.6)	6,067 (4.4)	<0.001	2.99
Surgical	8,031 (5.5)	7,500 (93.4)	531 (6.6)		4.59

DM, diabetes mellitus.
[a]Diabetes incidence rate × 1,000 woman/years.

A significantly higher incidence of diabetes was also observed in women with other risk factors: smoking (7.5%); obesity (10.8%); high basal metabolic rate (11.3%); no intake of vegetables (6.8%) or fruit (6.6%); high intake of added salt (7.0%); worse self-perceived health (13.1%); AMI, angina or stroke (11.6%); hypertension (8.1%); cholesterol medication (10.0%); father (6.8%) or mother (8.7%) with diabetes; blood type BB (7.9%); low HDL cholesterol (11.7%); high urate levels (16.2%); high basal glucose levels (13.9%); and HbA1c levels between 4.5% and 5.7% (13.8%) or >6.5% (74.4%) (Table S1, Supplemental Digital Content 1, http://links.lww.com/MENO/B468).

Table 2 shows the hazard ratios (HR) for the onset of diabetes. The crude analysis showed a significant association between menopause categories (age and type) and diabetes (early menopause HR: 1.19, premature menopause HR: 1.52, surgical menopause HR: 1.41; $P<0.001$), as did the age-adjusted model (early menopause HR: 1.20, premature menopause HR: 1.58, surgical menopause HR: 1.37; $P<0.001$). However, the significance disappeared in the multivariate model (early menopause HR: 1.01, $P=0.88$; premature menopause HR: 0.97, $P=0.56$; surgical menopause HR: 1.01, $P=0.82$). Thus, neither age at menopause nor type of menopause were independently associated with the onset of diabetes. The full model is shown in Table S2 of the Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/MENO/B468. The model showed a good fit to the data (Fig. S1, Supplemental Digital Content 2, http://links.lww.com/MENO/B469), with a *C*-index of 0.850 (95% CI: 0.841-0.858) in the testing sample. The full fitted model is shown in Supplemental Table S2, Supplemental Digital Content 1, http://links.lww.com/MENO/B468.

DISCUSSION

This large study, involving more than 146,000 women who were followed for an average of over 14 years, showed that age at menopause and type of menopause had no clinical or statistical association with the onset of diabetes. The associations observed in the crude and age-adjusted analyses are spurious due to the presence of confounders. Our findings, therefore, do not support the initial hypothesis that menopause generates a metabolic change favorable to insulin resistance and the consequent development of diabetes.

These results address the evidence gap mentioned in the 2021 ESC Guidelines on Cardiovascular Disease Prevention in Clinical Practice,[10] corroborating the insufficiency of evidence to draw conclusions about any increased risk of diabetes due to characteristics of menopause. Our study sheds new light on this question, ruling out a direct association and suggesting that any association observed is likely due to the confounding effect of cardiovascular risk factors, which are more common in postmenopausal women, rather than the presence of menopause itself.

TABLE 2. Risks of diabetes onset, as estimated by Weibull models for age at menopause

Age and type of menopause	**HR (95% CI)**	***P***
Model I		
Normal >45 y	1	
Precocious 40-45 y	1.188 (1.116-1.264)	<0.001
Premature <40 y	1,521 (1.380-1.677)	<0.001
Natural	1	
Surgical	1.412 (1.297-1.537)	<0.001
Model II		
Normal >45 y	1	
Precocious 40-45 y	1.207 (1.134-1.284)	<0.001
Premature <40 y	1,576 (1.430-1.737)	<0.001
Natural	1	
Surgical	1.365 (1.254-1.485)	<0.001
Model III		
Normal >45 y	1	
Precocious 40-45 y	1.005 (0.946-1.066)	0.882
Premature <40 y	0.971 (0.880-1.071)	0.555
Natural	1	
Surgical	1.012 (0.916-1.117)	0.816

Model I: crude analysis in total sample (n = 146,764).
Model II: age-adjustment in total sample (n = 146,764).
Model III: multivariate model in training sample adjusted for age, deprivation index, alcohol consumption, body mass index, waist circumference, basal metabolic rate, education level, forced vital capacity, salad-vegetable consumption, cooked vegetable consumption, salt consumption, sugar consumption, self-rated health, asthma/bronchitis/emphysema/lung clot, nerves/anxiety/tension/depression, cholesterol medication, birth control pill use, hormone therapy use, hysterectomy, paternal and maternal history of diabetes, paternal and maternal history of hypertension, dental problems, blood type, systolic blood pressure, creatinine, glucose, HbA1c; HDL cholesterol, triglycerides, urate, vitamin D, and calcium. n = 102711; no. diabetes = 4576. *C*-index in testing sample: 0.850 95% CI (0.841-0.858), n = 44,053; no. diabetes = 2,022.
CI, confidence interval; HbA1c, hemoglobn A1c; HDL, high-density lipoprotein; HR, hazard ratio.

The absence of a direct relationship between diabetes and menopause in our study does not contradict the findings of another cohort study using UK Biobank data, which concluded that premature natural and surgical menopause (before age 40) was associated with a small but statistically significant increased risk of cardiovascular disease among postmenopausal women.[15] Although early and premature menopause are known to confer a higher long-term risk of developing cardiovascular disease,[16] only a few studies have linked it to a higher risk of diabetes. A meta-analysis of 13 studies investigating this question and involving 191,762 postmenopausal women found that both early menopause and premature ovarian failure were associated with a higher risk of developing diabetes; however, there was high, unexplained heterogeneity ($I^2 = 61\%$) and a small effect size (odds ratio: 1.15), so these results are not conclusive.[17] The child-bearing period, understood as the time between menarche and menopause, is not exactly the same indicator as age at menopause, but they are closely related. A large study of over 124,000 postmenopausal women found a relationship between a short child-bearing period and the onset of diabetes when adjusted for age, but the statistical association disappeared after adjusting for multiple variables, which is consistent with our findings.[18]

Our results contradict those obtained by Muka and colleagues, who proposed that the relationship between the age of menopause and diabetes is a continuum. They observed a 4% lower risk of diabetes (HR: 0.96) for each additional year before the onset of menopause. That is, the younger the age of menopause onset, the greater the risk of diabetes.[19] Although our initial findings are suggestive of an association between early menopause and a higher incidence of diabetes, the multivariate analysis indicates that this relationship is confounded by other underlying factors.

Despite what is known about menopause and cardiovascular risk, the main guidelines for the management of women with menopause do not recommend HT solely for the prevention of cardiovascular disease or diabetes. Instead, they simply highlight the relevance of general population-based preventive counselling.[20] Research on large population-based databases has not yet allowed decisions to be made regarding the treatment that women may need for cardiovascular risk prevention, despite the identification of specific risk factors in postmenopausal women.[21]

Our study reopens the debate in this field, as the data linking menopause as a risk factor for the development of cardiovascular morbidity and mortality have not clarified, to date, what direct role menopause plays in the development of other diseases, including diabetes. Indeed, it may be a combination of factors related to the onset of menopause that confer a higher risk, and which, in our analysis, we considered as confounders that could alter the direct relationship. Further studies are still needed to conclusively establish a relationship between these processes.

Our study has important strengths, including high statistical power and rich, standardized data, which enabled a comprehensive, longitudinal analysis of risk factors and their association with diabetes. However, certain limitations should also be considered, including the risk of selection bias inherent to a volunteer database like the UK Biobank (which may be systematically different from the general population) and a potential survival bias. Moreover, age at menopause was self-reported, introducing some potential for heterogeneity, as also occurs with the definition of diabetes. The possible existence of residual confounding, as well as the relatively homogeneous population of mainly European descent, are further limitations. Nevertheless, the study makes an important contribution to the body of evidence on the association between early menopause and diabetes, providing robust conclusions that future research can build on.

CONCLUSION

After adjusting for confounders, no clinically or statistically significant association was observed between the development of diabetes and the age at menopause or the type of menopause in a large cohort of 146,000 women who were followed for over 14 years. More studies are needed to elucidate the causal pathways between early or premature menopause and its association with morbidity and mortality, in order to implement more appropriate prevention and screening measures in this important segment of the population.

REFERENCES

1. Wellons M, Ouyang P, Schreiner PJ, Herrington DM, Vaidya D. Early menopause predicts future coronary heart disease and stroke: the multiethnic study of atherosclerosis. *Menopause* 2012;19:1081-1087. doi:10.1097/gme.0b013e3182517bd0
2. Yoshida Y, Chen Z, Baudier RL, et al. Early menopause and cardiovascular disease risk in women with or without type 2 diabetes: a pooled analysis of 9,374 postmenopausal women. *Diabetes Care* 2021;44:2564-2572. doi:10.2337/dc21-1107
3. Matthews KA, Crawford SL, Chae CU, et al. Are changes in cardiovascular disease risk factors in midlife women due to chronological aging or to the menopause transition? *J Am Coll Cardiol* 2009;54:2366-2373. doi:10.1016/j.jacc.2009.10.009
4. Xu B, Allard C, Alvarez-Mercado AI, et al. Estrogens promote misfolded proinsulin degradation to protect insulin production and delay diabetes. *Cell Rep* 2018;24:181-196. doi:10.1016/j.celrep.2018.06.019
5. Mandrup CM, Egelund J, Nyberg M, et al. Effects of menopause and high-intensity training on insulin sensitivity and muscle metabolism. *Menopause* 2018;25:165-175. doi:10.1097/GME.0000000000000981
6. Chedraui P, Escobar GS, Pérez-López FR, et al. Angiogenesis, inflammation and endothelial function in postmenopausal women screened for the metabolic syndrome. *Maturitas* 2014;77:370-374. doi:10.1016/j.maturitas.2014.01.014
7. Kalyani RR, Franco M, Dobs AS, et al. The association of endogenous sex hormones, adiposity, and insulin resistance with incident diabetes in postmenopausal women. *J Clin Endocrinol Metab* 2009;94:4127-4135. doi:10.1210/jc.2009-0910
8. Farahmand M, Ramezani Tehrani F, Bahri Khomami M, Noroozzadeh M, Azizi F. Surgical menopause versus natural menopause and cardio-metabolism disturbances: a 12-year population-based cohort study. *J Endocrinol Invest* 2015;38:761-767. doi:10.1007/s40618-015-0253-3
9. Stevenson JC, Tsiligiannis S, Panay N. Cardiovascular risk in perimenopausal women. *Curr Basque Pharmacol* 2019;17:591-594. doi:10.2174/1570161116666181002145340
10. Visseren FLJ, Mach F, Smulders YM, et al.; ESC National Cardiac Societies; ESC Scientific Document Group. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J* 2021;42:3227-3337. doi:10.1093/eurheartj /ehac458

11. UK Biobank. Protocol for a large-scale prospective epidemiological resource. 2006. Accessed November 23, 2025. https://www.ukbiobank.ac.uk/wp-content/uploads/2025/01/Main-study-protocol.pdf
12. Klein JP, Moeschberger ML. *Survival Analysis: Techniques for Censored and Truncated Data*, 2nd ed. New York: Springer; 2005:1. doi:10.1007/b97377
13. Moore DF. *Applied Survival Analysis Using R*. Springer; 2016. doi:10.1007/978-3-319-31245-3
14. R Core Team *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2024.
15. Honigberg MC, Zekavat SM, Aragam K, et al. Association of premature natural and surgical menopause with incident cardiovascular disease. *JAMA* 2019;322:2411-2421. doi:10.1001/jama.2019.19191
16. Liu J, Jin X, Liu W, et al. The risk of long-term cardiometabolic disease in women with premature or early menopause: a systematic review and meta-analysis. *Front Cardiovasc Med* 2023;10:1131251. doi:10.3389/fcvm.2023.1131251
17. Anagnostis P, Christou K, Artzouchaltzi AM, et al. Early menopause and premature ovarian insufficiency are associated with increased risk of type 2 diabetes: a systematic review and meta-analysis. *Eur J Endocrinol* 2019;180:41-50. doi:10.1530/EJE-18-0602
18. LeBlanc ES, Kapphahn K, Hedlin H, et al. Reproductive history and risk of type 2 diabetes mellitus in postmenopausal women: findings from the Women's Health Initiative. *Menopause* 2017;24:64-72. doi:10.1097/GME.0000000000000714
19. Muka T, Asllanaj E, Avazverdi N, et al. Age at natural menopause and risk of type 2 diabetes: a prospective cohort study. *Diabetology* 2017;60:1951-1960. doi:10.1007/s00125-017-4346-8
20. Hemachandra C, Taylor S, Islam RM, Fooladi E, Davis SR. A systematic review and critical appraisal of menopause guidelines. *BMJ Sex Reprod Health* 2024;50:122-138. doi:10.1136/bmjsrh-2023-202099
21. Doust J, Baneshi MR, Chung HF, Wilson LF, Mishra GD. Assessing the accuracy of cardiovascular disease prediction using female-specific risk factors in women aged 45 to 69 years in the UK Biobank Study. *Circ Cardiovascular Qual Outcomes* 2024;17:e010842. doi:10.1161/CIRCOUTCOMES.123.010842

