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RESEARCH

The U-curve associations of birth interval with prevalence of osteoarthritis in postmenopausal women

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Abstract

Background To explore associations of birth interval, age at first birth (AFB), age at last birth (ALB) with prevalence of osteoarthritis (OA) in United States (U.S.) postmenopausal women with two deliveries.

Methods Cross-sectional analysis of 3088 postmenopausal women with two deliveries from the National Health and Nutrition Examination Survey (1999–2018). Weighted multivariable logistic regression, subgroup analysis and restricted cubic spline (RCS) models were used to examine association of reproductive factors (birth interval, AFB and ALB) with OA risk.

Results The prevalence of OA was 30.6%. According to RCS, we found the U-shaped relationships were observed between AFB, ALB, birth interval and risk or OA in postmenopausal women. 24–25 years for AFB, 25–30 years for ALB, and 4–6 years for birth interval were associated with lowest OA risk. These associations persisted across various subgroups.

Conclusions AFB, ALB and birth interval shown the U-shaped associations with OA prevalence in postmenopausal women with two deliveries. These findings highlight the potential long-term impacts of reproductive history on musculoskeletal health and may inform strategies for OA prevention in U.S. postmenopausal women.

Keywords Postmenopausal women · Birth interval · Pregnancy · Osteoarthritis

Introduction

Osteoarthritis (OA) is a highly prevalent joint disorder that significantly impacts global health, particularly affecting postmenopausal women [1, 2]. As one of the leading causes of disability worldwide, OA affects over 500 million people globally and The United States of America has the highest prevalence and Disability-adjusted life years (DALYs) compared with other countries [1]. The condition is characterized by the degradation of articular cartilage, changes in subchondral bone, and inflammation of the synovial membrane, leading to pain, stiffness, and reduced joint function [3]. The dramatic increase in OA prevalence and severity among women aged after 40 years suggests a strong link between menopause-related hormonal changes and the development of OA [4].

Birth interval, defined as the time between consecutive deliveries, has been increasingly recognized as a factor influencing women's long-term health outcomes, including bone health and OA risk in postmenopausal years [5, 6]. Biologically, frequent pregnancies and short birth intervals can lead to maternal depletion syndrome, potentially impacting bone mineral density and joint health later in life [4, 5, 7]. Physically, the repeated stress on the musculoskeletal system during pregnancy and childbirth, especially with short intervals, may contribute to joint instability and increased OA risk [3, 4, 8]. From a societal perspective, shorter birth intervals often correlate with lower socioeconomic status and reduced access to healthcare, factors that can indirectly influence OA development and management in postmenopausal women [5, 9]. Therefore, this study aims to utilize the data from the National Health and Nutrition Examination Survey (NHANES) [10], to explore how birth interval associated with OA in United States (U.S.) postmenopausal women

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with two deliveries. Understanding these associations can contribute to a life-course approach to women's health, recognizing that reproductive choices and experiences may have long-term impacts on musculoskeletal health. This research can also bridge a gap in knowledge about sex-specific factors influencing OA risk, potentially leading to more personalized care for postmenopausal women. By elucidating the potential link between birth interval and OA, we can enhance our understanding of the complex interplay between reproductive factors and postmenopausal health outcomes.

Material and methods

Study population

All data are from NHANES data from 1999 to 2018. The survey, organized by the National Center for Health Statistics (NCHS) and the Centers for Disease Control and Prevention, is a continuous, systematic collection and analysis of health-related data [11]. A total of 96,811 individuals were included and 47,625 participants were excluded due to a lack of OA questionnaire. Additionally, we excluded 32,357 men and eliminated 10,718 female who only delivered once and more than three times. Furthermore, 3023 females without reproductive factors including age at first birth (AFB) and age at last birth (ALB) were also excluded. Finally, 3088 postmenopausal women with two deliveries only were included in the analysis (Fig. 1). The NCHS Ethics Review Board approved the protocol and obtained written informed consent from all participants.

Assessment of reproductive factors

The Reproductive Health Questionnaire was used to assess the reproductive factors in women. Researchers used the questionnaire to collect information on a woman's AFB, ALB, and number of deliveries. Birth interval in our study was only explored among postmenopausal women with 2 deliveries. In other words, birth interval in our study represented the year differences between ALB and AFB. Additionally, the researchers also collected participants' age at menarche, age at menopause, reproductive lifespan (difference between age at menarche to age at menopause), menopausal status, history of oral contraceptive use, history of gynecological surgery (including bilateral oophorectomy and hysterectomy).

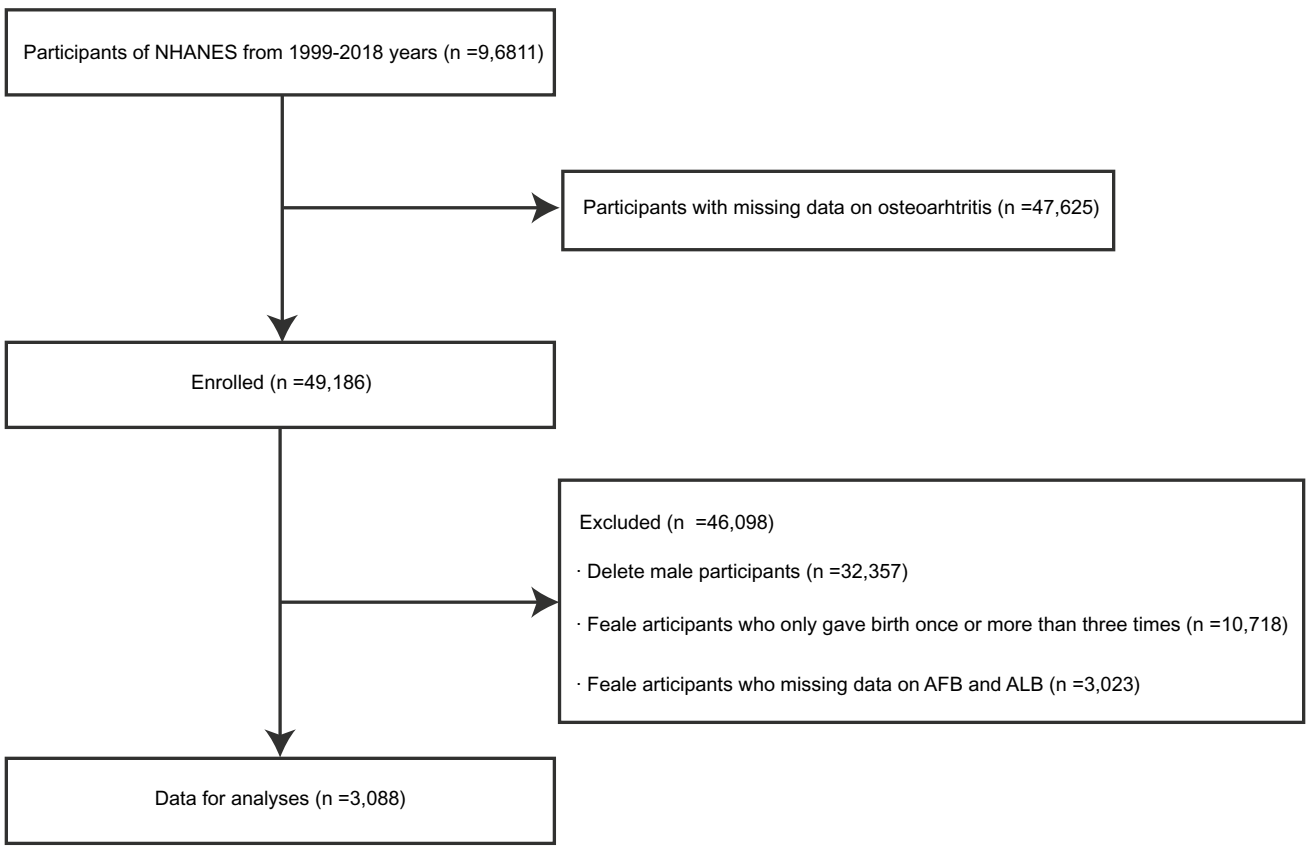

Fig. 1 Study flow chart. *NHANES* National Health and Nutrition Examination Surveys

Covariates

The covariates included in this study were age, race/ethnicity, education level, family income to poverty ratio (PIR), the complication of hypertension, marital status, alcohol use, waist circumference (WC), the complication of diabetes mellitus (DM), smoker, body mass index (BMI), mean energy intake, work activity, recreational activity, blood urea nitrogen (BUN), fast blood glucose (FBG), uric acid (UA), serum creatinine (Scr), estimated glomerular filtration rate (eGFR), total cholesterol (TC), triglyceride (TG), and high-density lipoprotein-cholesterol (HDL). Physical activity levels, including recreational activity and work activity, were assessed using questions from the separate questionnaires, including time spent sitting and time spent engaged in typical physical activity over the past week [12]. If the participant satisfied the vigorous physical activity recommendation (minimum 20 min of vigorous physical activity a day, at least three times a week), then it was coded as "Yes", or if he did not as "No", respectively, for work and recreational activity [13]. Detailed covariate information can be obtained from the NHANES database (https://www.cdc.gov/nchs/nhanes/index.htm).

Osteoarthritis ascertainment

The individuals with OA were identified based on the answers they provided to two continuous questions about their medical condition. Firstly, "Doctor ever said you had arthritis?" If the participants answered 'Yes', they were defined as having arthritis. Additionally, participants were then asked the following questions: "Which type of arthritis was it?". Only participants who answered "Osteoarthritis or degenerative arthritis" were considered OA.

Statistical analysis

According to data distribution characteristics, continuous variables use mean ± standard deviation or interquartile range to describe the trend of data concentration, and categorical variables use frequency to describe. Weighted T-tests or Mann–Whitney U test were used to compare between-group differences for continuous variables. Weighted multivariable logistic regression analysis explored the association between AFB, ALB, birth interval and OA. Model 1 adjusted for age and race/ethnicity, and Model 2 adjusted for age, race/ethnicity, education level, smoking, alcohol use, marriage status, family PIR, hypertension, and DM. Model 3 was based on Model 2 with adjustments for work activity, TC, mean energy intake, TG, recreational activity, HDL, menopause status, BUN, history of oral contraceptive use, UA, age at menarche, Scr, hysterectomy, eGFR, reproductive lifespan, bilateral oophorectomy, BMI, age at menopause and WC. Additionally, restricted cubic splines (RCS) were used to analyze the association between AFB, ALB, birth interval and OA. Finally, subgroup analyses were performed to examine whether the effects of AFB, ALB and birth interval on OA could be changed by race/ethnicity, education level, family PIR, hysterectomy, history of oral contraceptive use, and bilateral oophorectomy based on model 3. Statistical analysis was performed using R 4.2.2 Version 4 and SPSS 23.0. P-value < 0.05 was considered statistically significant.

Results

Baseline characteristics

The prevalence of OA among U.S. postmenopausal women with two deliveries was 30.6% (4,834/15,810). Table 1 presents the baseline characteristics of this cohort. Women with OA, compared to those without, exhibited distinct demographic and health profiles. They were more likely to be older, Non-Hispanic White, and smokers. Additionally, they had a higher prevalence of hypertension and history of contraceptive use. Anthropometric measurements revealed higher BMI and WC among women with OA. Biochemical markers showed elevated BUN and eGFR. Reproductive factors also differed, with OA-affected women experiencing later menopause and longer reproductive lifespans.

Association of AFB, ALB and birth interval with osteoarthritis

To investigate the relationship between OA risk and AFB, ALB, and birth interval, we employed RCS while adjusting for covariates. The RCS curves revealed U-shaped relationships for all three variables. The relationship between AFB and OA risk follows a U-shaped curve (Fig. 2A). The lowest risk appears to be around 24–25 years for AFB and this U-shaped association was statistically significant, with a P-value for nonlinearity = 0.028 (Fig. 2A). ALB also demonstrates a U-shaped relationship with OA risk (Fig. 2B). The risk is elevated for women who had their last birth at younger ages (before 25) or older ages (after 35). The lowest point of the curve around 25–30 years for ALB represented the lowest risk with statistical significance (P-value for nonlinearity = 0.024). The association between birth interval and OA risk follows a U-shaped curve as well (Fig. 2C). Both short (< 4 years) and long (> 6 years) birth intervals are associated with higher risks of OA. The approximate 4–6 years birth interval appears to be associated with the lowest OA risk. This U-shaped relationship is highly significant, with a P-value for nonlinearity = 0.032. Detailed

Table 1 Demographic characteristics of the study participants

Variables	Overall (n = 3,088)	Non-osteoarthritis (n = 2,406)	Osteoarthritis (n = 682)	*P*-value
Age, years	59.91 ± 0.26	58.31 ± 0.32	64.81 ± 0.43	< 0.001
Race, %				< 0.001
Mexican American	282 (9.1%)	240 (7.8%)	42 (1.4%)	
Other Hispanic	283 (9.2%)	245 (8.0%)	38 (1.2%)	
Non-Hispanic Black	583 (18.9%)	501 (16.2%)	82 (2.7%)	
Non-Hispanic White	1698 (55.0%)	1216 (39.4%)	482 (15.6%)	
Other race	242 (7.8%)	204 (6.6%)	38 (1.2%)	
Family PIR	3.33 ± 0.05	3.30 ± 0.05	3.42 ± 0.08	0.115
Education level, %				0.078
Less than high school	578 (18.7%)	473 (15.3%)	105 (3.4%)	
High school	348 (11.3%)	263 (8.5%)	85 (2.8%)	
More than high school	2162 (70.0%)	1670 (54.1%)	492 (15.9%)	
Marital status, %				0.178
Having a partner	1736 (56.2%)	1367 (44.3%)	369 (11.9%)	
No partner	1236 (40.0%)	935 (30.3%)	301 (9.7%)	
Unmarried	116 (3.8%)	104 (3.4%)	12 (0.4%)	
Hypertension, %				< 0.001
No	1229 (39.8%)	1024 (33.2%)	205 (6.6%)	
Yes	1859 (60.2%)	1382 (57.4%)	477 (15.4%)	
DM, %				0.058
No	2426 (78.6%)	1911 (61.9%)	515 (16.7%)	
Yes	662 (21.4%)	495 (16.0%)	167 (5.4%)	
Smoker, %				< 0.001
No	1794 (58.1%)	1426 (46.2%)	368 (11.9%)	
Former	777 (25.2%)	552 (17.9%)	225 (7.3%)	
Now	517 (16.7%)	428 (13.9%)	89 (2.9%)	
Alcohol user, %				0.043
No	597 (19.3%)	484 (15.7%)	113 (3.7%)	
Former	595 (19.3%)	462 (15.0%)	133 (4.3%)	
Mild	1080 (35.0%)	805 (26.1%)	275 (8.9%)	
Moderate	510 (16.5%)	398 (12.9%)	112 (3.6%)	
Heavy	306 (9.9%)	257 (8.3%)	49 (1.6%)	
Work activity, %				0.497
No	1885 (61.0%)	1469 (47.6%)	416 (13.5%)	
Yes	1203 (39.0%)	937 (30.3%)	266 (8.6%)	
Recreational activity, %				0.297
No	1964 (63.6%)	1519 (49.2%)	445 (14.4%)	
Yes	1124 (36.4%)	887 (28.7%)	237 (7.7%)	
Oral contraceptive use, %				< 0.001
No	999 (32.4%)	770 (24.9%)	229 (7.4%)	
Yes	2089 (67.6%)	1636 (53.0%)	453 (14.7%)	
Use female hormones, %				0.159
No	1800 (58.3%)	1487 (48.2%)	313 (10.1%)	
Yes	1288 (41.7%)	919 (29.8%)	369 (11.9%)	
Had a hysterectomy, %				0.033
No	1650 (53.4%)	1317 (42.6%)	333 (10.8%)	
Yes	1438 (46.6%)	1089 (35.3%)	349 (11.3%)	
Bilateral oophorectomy, %				0.619
No	2195 (71.1%)	1726 (55.9%)	469 (15.2%)	
Yes	893 (28.9%)	680 (28.3%)	213 (6.9%)	

Table 1 (continued)

Variables	Overall (n = 3,088)	Non-osteoarthritis (n = 2,406)	Osteoarthritis (n = 682)	*P*-value
BMI, kg/m^2	29.17 ± 0.16	28.84 ± 0.16	30.16 ± 0.36	< 0.001
Waist circumference, cm	98.11 ± 0.36	97.35 ± 0.38	100.44 ± 0.70	< 0.001
Mean energy intake (kcal/day)	1687.01 ± 12.46	1678.82 ± 14.82	1712.09 ± 26.61	0.295
Mean vitamin D intake (mcg)	4.04 ± 0.08	4.05 ± 0.09	4.01 ± 0.15	0.814
FBG, mg/dL	106.65 ± 0.59	105.61 ± 0.64	109.82 ± 1.41	0.008
TC, mg/dL	209.82 ± 1.01	210.41 ± 1.13	208.04 ± 2.04	0.302
TG, mg/dL	130.87 ± 1.79	130.64 ± 2.03	131.58 ± 3.39	0.807
HDL, mg/dL	60.40 ± 0.54	59.97 ± 0.49	61.72 ± 1.24	0.147
BUN, mg/dL	14.54 ± 0.14	14.21 ± 0.15	15.57 ± 0.27	< 0.001
UA, mg/dL	5.01 ± 0.03	4.97 ± 0.03	5.13 ± 0.06	0.017
Scr, mg/dL	0.81 ± 0.01	0.81 ± 0.01	0.83 ± 0.01	0.092
eGFR, ml/min/1.73m^2	82.96 ± 0.47	84.64 ± 0.55	77.81 ± 0.82	< 0.001
AFB, years	23.55 ± 0.14	23.50 ± 0.17	23.71 ± 0.26	0.507
ALB, years	27.77 ± 0.13	27.78 ± 0.15	27.72 ± 0.26	0.838
Birth interval, times	4.21 ± 0.07	4.28 ± 0.09	4.00 ± 0.12	0.060
Number of pregnancies, times	2.66 ± 0.03	2.66 ± 0.04	2.64 ± 0.05	0.755
Age at menarche, years	12.68 ± 0.04	12.72 ± 0.04	12.55 ± 0.08	0.050
Age at menopause, years	44.38 ± 0.23	43.92 ± 0.27	45.78 ± 0.36	< 0.001
Fertile lifespan, years	31.70 ± 0.24	31.20 ± 0.27	33.23 ± 0.38	< 0.001

Family PIR family poverty income ratio, *BMI* body mass index, *FBG* fast blood glucose, *BUN* blood urea nitrogen, *UA* uric acid, *Scr* serum creatinine, *TC* total cholesterol, *TG* triglycerides, *HDL-cholesterol* high density lipoprotein-cholesterol, *eGFR* estimated glomerular filtration rate, *AFB* age at first birth, *ALB* age at last birth

information regarding the associations between AFB, ALB, birth interval, and OA risk can be found in Table 2.

Subgroup analyses

Subgroup analyses stratified by race/ethnicity, education level, family PIR, hysterectomy, history of oral contraceptive use, and bilateral oophorectomy were further performed to explore associations of AFB, ALB and birth interval with OA (Supplementary Fig. 1, 2, and 3; Supplementary Table 1, 2, and 3). The U-shaped association between AFB and OA was consistent across various subgroups. This included participants from different racial and ethnic backgrounds such as Mexican American, Non-Hispanic Black, Non-Hispanic White, and other races. Additionally, this relationship held true regardless of family PIR being less than or greater than 1.3 and across educational levels of high school or higher. Furthermore, it was observed in women with a history of hysterectomy as well as those who had both ovaries removed or did not use oral contraceptives. For ALB, the relationship with OA varied among subgroups. Specifically, a J-shaped curve was observed in Mexican American participants and those from other races. Conversely, a U-shaped association was noted among Non-Hispanic Black women. This U-shaped relationship persisted across various family PIR categories (< 1.3 or ≥ 1.3), educational attainment (high school or more), history of hysterectomy, oral contraceptive use status, and regardless of ovarian removal. Finally, the association between birth interval and OA also exhibited variations across different subgroups. An L-shaped curve was identified among Mexican American participants and those from other races regardless of their education level. In contrast, a U-shaped association between birth interval and OA was found in women across both family PIR categories (< 1.3 or ≥ 1.3), irrespective of whether they had both ovaries removed or used oral contraceptives. These subgroup analyses underscore the complex interplay between reproductive factors and OA risk across diverse demographic and health profiles.

Discussion

In this study, we found a significant U-shaped association between birth interval and the prevalence of OA in postmenopausal women with two deliveries. The risk of OA was lowest for women with birth intervals between 4 to 6 years, while both shorter (< 4 years) and longer (> 6 years)

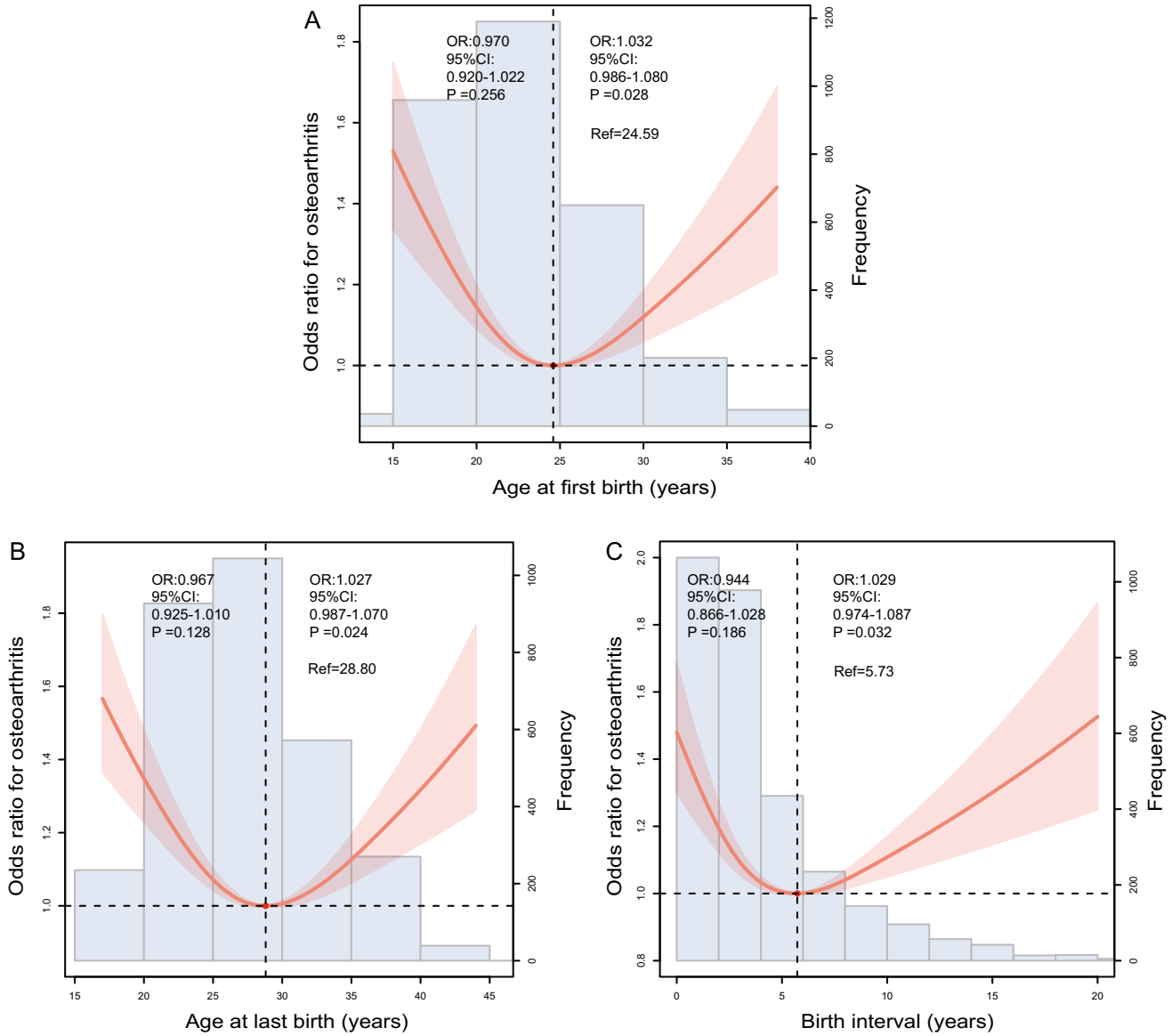

Fig. 2 Restricted cubic spline plots of associations between **A** age at first birth, **B** age at last birth, **C** birth interval and the prevalence of osteoarthritis in postmenopausal women

intervals were associated with increased risk. Additionally, we observed similar U-shaped relationships for AFB and ALB with OA risk. These associations persisted across various subgroups, including different racial/ethnic backgrounds, socioeconomic statuses, and medical histories, highlighting the robustness of our findings.

As populations age globally and postmenopausal women experience declining hormone levels, OA has emerged as a significant health concern among older adults [14]. Addressing this growing issue requires adopting a life-course perspective to develop effective prevention strategies. Previous research on the association between birth interval and OA in postmenopausal women has been limited and inconsistent [15–18] However, studies have explored the impact of reproductive factors on bone health more broadly [14, 17]. For example, studies have not established a direct link between age at first birth and the development of OA, however, chronic inflammatory arthritis, which can affect pregnancy outcomes, may indirectly influence the risk of developing OA later in life [19, 20]. The biological mechanisms underlying this relationship may involve the cumulative effects of pregnancy and lactation on bone mineral density, as well as the influence of hormonal changes during and after pregnancy on joint health [7, 21, 22]. Shorter birth intervals may not allow sufficient time for maternal bone recovery, while longer intervals might be associated with prolonged periods of low estrogen levels, both potentially contributing to increased OA risk [7, 23]. Social factors,

Table 2 Associations of AFB, ALB and birth interval with the prevalence of osteoarthritis in postmenopausal women

	Model 1 OR (95%CI)	*P* for trend	Model 2 OR (95%CI)	*P* for trend	Model 3 OR (95%CI)	*P* for trend
AFB		0.428		0.534		0.714
≤24	1.00		1.00		1.00	
25–27	0.77 (0.60, 0.98) *		0.73 (0.57, 0.94) *		0.77 (0.60, 0.99) *	
28–34	0.87 (0.67, 1.26)		0.97 (0.78, 1.29)		1.12 (0.87, 1.46)	
≥35	0.99 (0.50, 1.53)		1.00 (0.55, 1.71)		1.13 (0.63, 2.01)	
ALB		0.406		0.492		0.744
≤24	1.00		1.00		1.00	
25–29	0.90 (0.72, 1.12)		0.87 (0.70, 1.09)		0.91 (0.72, 1.14)	
30–34	0.83 (0.64, 1.06)		0.80 (0.62, 1.04)		0.88 (0.68, 1.15)	
≥35	0.96 (0.72, 1.28)		0.99 (0.74, 1.34)		1.14 (0.84, 1.56)	
Birth interval		0.143		0.138		0.207
<3	1.00		1.00		1.00	
3	0.92 (0.71, 1.18)		0.90 (0.70, 1.16)		0.88 (0.68, 1.14)	
4–6	0.81 (0.65, 1.01)		0.80 (0.63, 1.00)		0.79 (0.63, 0.99) *	
>6	0.89 (0.69, 1.14)		0.89 (0.69, 1.15)		0.92 (0.71, 1.19)	

Model 1: age and race/ethnicity. Model 2: model 1 variables plus education level, marital status, family poverty-income ratio, hypertension, diabetes mellitus, smoker, alcohol user; Model 3 was adjusted for model 2 variables plus work activity, recreational activity, oral contraceptive use, use female hormones, had a hysterectomy, both ovaries removed, body mass index, waist circumference, mean energy intake, fast glucose, blood urea nitrogen, uric acid, serum creatinine, estimated glomerular filtration rate, total cholesterol, triglyceride, high-density lipoprotein-cholesterol, age at menarche, age at menopause, and fertile lifespan

AFB age at first birth, *ALB* age at last birth, *OR* odd ratio, *CI* confidence interval

* $P < 0.05$

such as socioeconomic status and access to healthcare, may also play a role in mediating this relationship, as they can influence both reproductive choices and long-term health outcomes [4, 24]. Though later ALB has been associated with both positive and negative health effects in different studies, suggesting a complex relationship that may extend to OA risk, early childbearing has been associated with lower bone mineral density in some populations, potentially due to the competing calcium demands of pregnancy and lactation during a critical period of bone mass accrual [18, 25, 26]. The U-shaped relationships observed in the current study for AFB, ALB, and birth interval with OA risk suggest that there may be optimal ranges for these reproductive factors that are associated with lower OA risk in postmenopausal women.

The exploration of female-specific factors and their impact on OA, provide us a unique perspective in improving postmenopausal women's health. By examining the association between reproductive history and OA risk, we contribute to bridging the gap in understanding sex differences in musculoskeletal health [4]. This research highlights the importance of considering reproductive factors in assessing and managing OA risk in postmenopausal women. Our findings may inform the development of more tailored preventive strategies and clinical guidelines that take into account a woman's reproductive history when evaluating her risk for OA and other bone health issues. For example, future research is warranted to explore the potential benefit of additional intervention such as vitamin D and hormonal therapy for women with suboptimal birth interval, as vitamin D and hormonal therapy have been considered as protector factors of musculoskeletal health. A major strength of this study is its use of a large, nationally representative dataset, which enhances the generalizability of our findings [27]. The comprehensive nature of the data allowed us to control for numerous potential confounding factors and conduct detailed subgroup analyses.

However, our study also has limitations. Firstly, we only include women with two deliveries only, therefore limiting our interpretation on how the birth interval impacts women with fewer or more children or pregnancies. Secondly, the average age of our included women was around 60 years old, which may limit the representative of postmenopausal women and underestimate the impact of the age on OA. Thirdly. the cross-sectional design precludes the establishment of causal relationships between birth interval and OA [28]. Additionally, the reliance on self-reported reproductive history and OA diagnosis may introduce recall bias [29, 30]. Future longitudinal studies with objective measures of joint health and more detailed reproductive histories could further elucidate the temporal relationship between birth interval and OA development in postmenopausal women.

Conclusion

This study reveals significant U-shaped associations between birth interval, AFB, ALB and OA prevalence in postmenopausal women with two deliveries. Our findings suggest that reproductive timing may be linked to OA risk later in life. By adopting a life-course perspective on women's health, we may be able to better mitigate OA risk and improve quality of life for postmenopausal women.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40520-025-03057-w.

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Data availability Data from the NHANES survey are publicly available online for users and researchers around the world at the following URL: https://www.cdc.gov/nchs/nhanes/.

Declarations

Conflict of interest The authors declare no competing interests.

Ethics approval and consent to participate The NHANES 1999–2018 was approved by the NCHS Research Ethics Review Board (Continuation of Protocol #1999–2018), and each participant signed the written informed consent, which can be found at https://www.cdc.gov/nchs/nhanes/.

Consent for publication Not applicable.

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