

Reproductive History and Infertility Risk: Insights from the 2017–2020 National Health and Nutrition Examination Survey

Yao Zhao¹, Mofan Tian², Hongyu Xie³

¹Medical Genetics and Genomics, Medical, Veterinary, and Life Sciences Education Hub, University of Glasgow, Glasgow, G12 8LE, UK; ²Medical, Veterinary, and Life Sciences Education Hub, University of Glasgow, Glasgow, G12 8LE, UK; ³James Watt School of Engineering, University of Glasgow, Glasgow, G12 8LE, UK

Correspondence: Yao Zhao, Medical Genetics and Genomics, Medical, Veterinary, and Life Sciences Education Hub, University of Glasgow, Glasgow, G12 8LE, UK, Email zhaoyao981013@outlook.com

Background: Infertility is a significant public health issue in global women's health. As the trend of delayed childbearing among women increases, the associated risks have garnered growing attention. Previous studies have indicated a potential association between reproductive factors and infertility, although the precise nature of this relationship remains unclear. Therefore, investigating the relationship between reproductive factors and infertility is of considerable academic and practical significance.

Methods: This study is based on data from the US National Health and Nutrition Examination Survey (NHANES) collected between 2017 and 2020, and includes 1,891 women. Multiple regression analyses and restricted cubic spline (RCS) curves were employed to evaluate the relationships of age at first birth (AFB), age at last birth (ALB), and number of live births (NLB) with infertility. Potential confounders such as age and race were controlled for in the analysis.

Results: The results indicated that increases in AFB and ALB were significantly associated with a heightened risk of infertility, whereas an increase in NLB was significantly linked to a reduced risk. Specifically, a J-shaped relationship was observed between AFB and infertility, a U-shaped association between ALB and infertility, and a linear negative correlation between NLB and infertility. Subgroup analysis revealed that living alone was significantly associated with infertility risk, with certain subgroups exhibiting a lower risk.

Conclusion: This study elucidates the critical relationship between reproductive factors and the risk of infertility. Delays in AFB and ALB were found to significantly increase the risk of infertility, whereas an increase in NLB markedly reduced the risk. These findings provide a basis for the early screening and intervention of infertility, and offer scientific support for the evaluation of women's reproductive health and policy-making. Future research should further explore the underlying mechanisms of these factors across different populations and conduct in-depth analyses using longitudinal data.

Keywords: infertility, reproductive history, NHANES, age at first birth, age at last birth

Introduction

Infertility is an important public health issue in global women's health, affecting approximately 15% of couples of reproductive age.¹ With socioeconomic development and rising levels of female education, an increasing number of women are choosing to delay childbearing.² According to the 2024 World Fertility Report, delayed childbearing (particularly a later age at first birth) has become increasingly common in recent years, directly impacting women's reproductive health.^{3,4} Although the potential impact of delayed childbearing on fertility has attracted widespread attention, the specific mechanisms by which it affects female infertility remain unclear.^{5,6} Furthermore, infertility not only imposes significant stress on women's physical and mental health,^{7,8} but also exerts far-reaching effects on society and the economy.^{9,10} Therefore, investigating the relationship between reproductive timing and infertility, particularly the

age at first birth (AFB), age at last birth (ALB), and number of live births (NLB), has become a critical topic in contemporary gynecological research.

Existing literature reveals a degree of controversy regarding the relationship between specific reproductive factors and infertility.¹¹ Some studies have suggested that delayed childbearing is associated with an increased risk of infertility,¹² which may be attributed to factors such as declining physiological function and reduced ovarian reserve in women.^{13,14} However, a few studies have indirectly indicated that a later age at first birth and having multiple births may be linked to greater physiological maturity and improved reproductive health in women, thereby reducing the risk of infertility.^{15,16} In addition, the number of live births, as an important indicator of reproductive experience, is also thought to potentially affect a woman's fertility.¹⁷ Currently, research on the relationship between the number of live births and infertility is limited, and no clear consensus has been reached regarding a direct association between them. However, some studies have noted that women who have experienced more deliveries may exhibit a higher prevalence of depression.⁴ Therefore, a unified conclusion regarding the relationship between certain reproductive factors and infertility has not yet been reached, and further studies with large sample sizes and proper control of confounding factors are urgently needed to clarify the actual impact of these factors on infertility.

In this study, we employed multiple regression analyses and restricted cubic spline (RCS) curves, while controlling for several potential confounders (such as age, race, and BMI), to reveal the independent effects of reproductive factors on infertility. This approach not only allows us to validate the perspectives presented in the existing literature regarding these reproductive factors, but also to elucidate their complex impact mechanisms on infertility, thereby providing more precise evidence for early diagnosis, risk assessment, and preventive interventions. Furthermore, the innovative aspect of this study lies in its use of the large-scale NHANES dataset to conduct a comprehensive and in-depth analysis of the relationships between age at first birth, age at last birth, and the number of live births and female infertility. Compared to many studies that focus on single factors or utilize small sample analyses, this study systematically evaluates the effects of multiple reproductive factors and, in conjunction with findings from the existing literature, provides a clearer direction for infertility risk prediction and the formulation of public health strategies.

Materials and Methods

Study Population

The NHANES is conducted by the National Center for Health Statistics (NCHS) and the Centers for Disease Control and Prevention (CDC) to systematically and continuously collect and analyze health-related data. This survey employs a complex, multistage sampling design and collects data biennially to ensure national representativeness, covering the civilian, non-institutionalized US population. NHANES data encompass various aspects, including demographic information, dietary status, laboratory test results, physical examination indices, and questionnaire responses. All participants in the NHANES survey provided written informed consent, and the data used in this study were de-identified and publicly available. Therefore, this secondary data analysis was exempt from additional ethical review.

This study utilized data from the 2017–2020 NHANES survey cycle, with an initial sample comprising 15,561 participants from the United States. During the data cleaning process, 10,247 women who had not completed the RHQ074 or RHQ076 questionnaire were excluded. Subsequently, 2,482 individuals under the age of 20 were excluded. Additionally, 885 women with missing reproductive data (including age at first childbirth), 5 women with missing age at last childbirth, and 16 participants with missing menarche age data were excluded. Further exclusions included 13 individuals missing BMI data, 1 individual missing marital status data, 21 individuals missing pelvic inflammatory disease data, and participants missing any of the aforementioned key variables. Ultimately, 1,891 women were included in the final analysis. The data selection process is illustrated in [Figure 1](#).

Reproductive Factors

Data on female reproductive factors were obtained from the reproductive health questionnaire, which included detailed information on pregnancy history, menstrual history, and other related reproductive health conditions. Researchers collected data on variables such as age at menarche and history of pelvic inflammatory disease. Data on AFB (age at

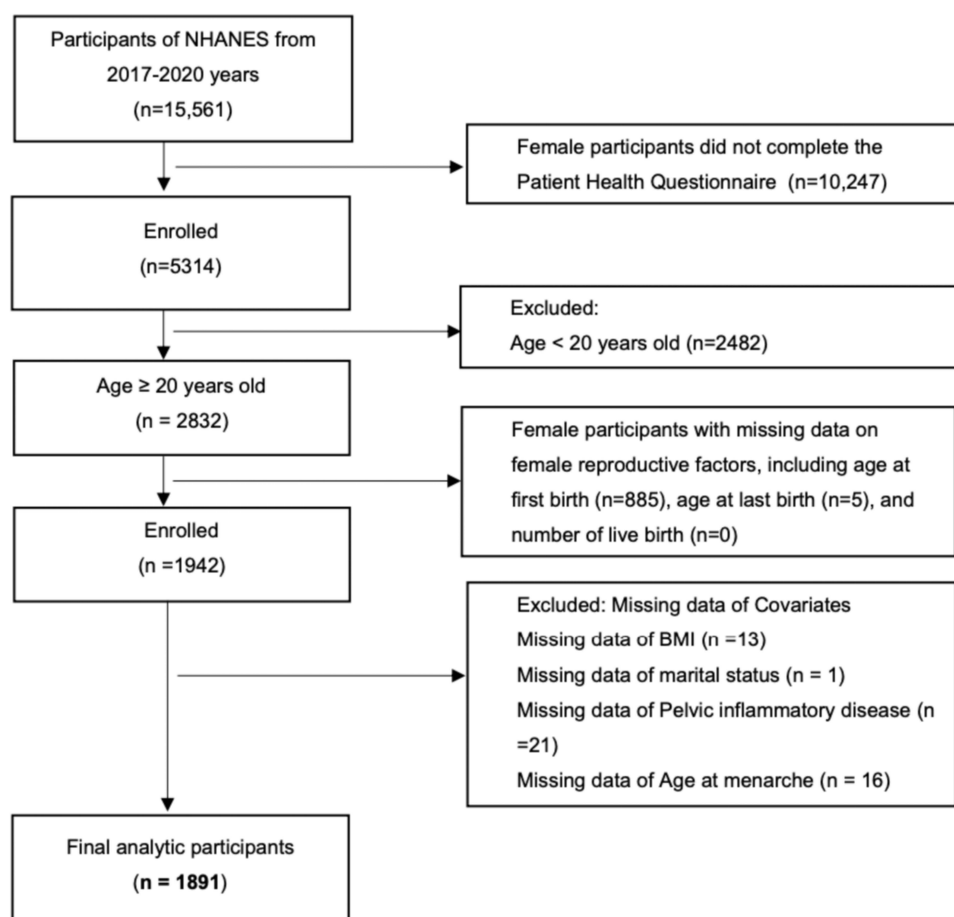


Figure 1 Study flow chart.

Notes: The chart illustrates the screening process of NHANES data from 2017 to 2020. Starting with 15,561 participants, multiple exclusion steps were applied, resulting in a final analytic sample of 1,891 women.

Abbreviations: NHANES, National Health and Nutrition Examination Surveys; PHQ074, Patient Health Questionnaire-074; PHQ078, Patient Health Questionnaire-078.

first birth), ALB (age at last birth), and NLB (total number of births, rather than live births) were collected through self-reported questionnaires.

Covariates

The covariates included in this study were age, race, body mass index (BMI), education level, smoking status, marital status, age at menarche, and history of pelvic inflammatory disease. Race, education level, smoking status, marital status, and history of pelvic inflammatory disease were classified as categorical variables, whereas age, BMI, and age at menarche were analyzed as continuous variables. Detailed definitions and measurement methods for the covariates can be found in the NHANES database (<https://www.cdc.gov/nchs/nhanes/index.htm>).

Definition of Infertility

Infertility status in this study was assessed based on two questions from the reproductive health questionnaire: (1) RHQ074: “Have you ever tried to become pregnant for at least a year without success?” and (2) RHQ076: “Have you ever sought help from a doctor or other healthcare provider because you were unable to become pregnant?” Participants who self-reported “yes” to either of these questions were classified as having a history of infertility.

Statistical Analysis

Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as counts (percentages). For comparisons between groups, analysis of variance (ANOVA) was used for continuous variables if homogeneity of variance was met; otherwise, Welch's *t*-test was applied. For categorical variables, Fisher's exact test was used if more than 20% of the expected frequencies were <5 or if any theoretical frequency was <1 ; otherwise, the chi-square test was performed.

To assess the association between AFB, ALB, and NLB with infertility, a multivariable logistic regression model was constructed with stepwise adjustment for confounders. Model 1 included AFB, ALB, and NLB. Model 2 further adjusted for pelvic inflammatory disease and age at menarche. Model 3 additionally adjusted for age, race/ethnicity, education level, smoking, alcohol consumption, and marital status.

A RCS with four default knots was used to explore the nonlinear relationship between reproductive factors and infertility, with the likelihood ratio test employed to assess the significance of nonlinearity. Subgroup analyses were conducted based on age, race, and reproductive history, with interaction terms (eg, age $\times$ AFB) introduced to examine effect modification. All analyses were performed using R software (version 4.2.2) and Stata software (version 17.0; StataCorp LLC, USA), with a two-sided $P < 0.05$ considered statistically significant.

Results

Baseline Characteristics

A total of 1,891 participants were included in this study, and their baseline characteristics are presented in Table 1. The mean age of participants was 43 ± 10 years, the mean age at menarche was 12.58 ± 1.87 years, and the mean BMI was 31 ± 9 kg/m².

Table 1 Demographical Characteristics of the Study Population

Characteristic	Overall, N = 1,891 ^a	Female Infertility		p-value
		Yes, N = 243 ^a	No, N = 1,648 ^a	
AFB, years	22.8 $\pm$ 5.2	25.0 $\pm$ 6.4	22.5 $\pm$ 4.9	<0.001 ^b
ALB, years	28 $\pm$ 6	30 $\pm$ 6	28 $\pm$ 6	<0.001 ^b
NLB, times				<0.001 ^c
1	420 (22.2%)	87 (35.8%)	333 (20.2%)	
2	681 (36.0%)	88 (36.2%)	593 (36.0%)	
3	438 (23.2%)	35 (14.4%)	403 (24.5%)	
4	238 (12.6%)	24 (9.9%)	214 (13.0%)	
5	114 (6.0%)	9 (3.7%)	105 (6.4%)	
Age, years	43 $\pm$ 10	41 $\pm$ 10	43 $\pm$ 11	0.009 ^b
Age at menarche, years	12.58 $\pm$ 1.87	12.44 $\pm$ 1.74	12.60 $\pm$ 1.89	0.190 ^b
BMI, kg/m²	31 $\pm$ 9	32 $\pm$ 8	31 $\pm$ 9	0.303 ^b
Race				0.004 ^c
Mexican American	276 (14.6%)	30 (12.3%)	246 (14.9%)	
Other Hispanic	209 (11.1%)	26 (10.7%)	183 (11.1%)	
Non-Hispanic White	556 (29.4%)	96 (39.5%)	460 (27.9%)	
Non-Hispanic Black	540 (28.6%)	50 (20.6%)	490 (29.7%)	
Non-Hispanic Asian	223 (11.8%)	28 (11.5%)	195 (11.8%)	
Other Race - Including Multi-Racial	87 (4.6%)	13 (5.3%)	74 (4.5%)	
Education level				0.009 ^c
Less than 9th grade	115 (6.1%)	9 (3.7%)	106 (6.4%)	
9-11th grade	222 (11.7%)	23 (9.5%)	199 (12.1%)	
High school graduate/GED or equivalent	438 (23.2%)	45 (18.5%)	393 (23.8%)	
Some college or AA degree	689 (36.4%)	93 (38.3%)	596 (36.2%)	
College graduate or above	427 (22.6%)	73 (30.0%)	354 (21.5%)	

(Continued)

Table 1 (Continued).

Characteristic	Overall, N = 1,891 ^a	Female Infertility		p-value
		Yes, N = 243 ^a	No, N = 1,648 ^a	
Marital status				0.014 ^c
Married or Living with partner	1,196 (63.2%)	171 (70.4%)	1,025 (62.2%)	
Living alone	695 (36.8%)	72 (29.6%)	623 (37.8%)	
Pelvic inflammatory disease				0.260 ^c
Yes	138 (7.3%)	22 (9.1%)	116 (7.0%)	
No	1,753 (92.7%)	221 (90.9%)	1,532 (93.0%)	
Alcohol user				0.665 ^c
Yes	1,673 (88.5%)	217 (89.3%)	1,456 (88.3%)	
No	218 (11.5%)	26 (10.7%)	192 (11.7%)	
Smoker				0.379 ^c
Yes	653 (34.5%)	90 (37.0%)	563 (34.2%)	
No	1,238 (65.5%)	153 (63.0%)	1,085 (65.8%)	

Notes: ^aMean $\pm$ SD; n (%); ^bWelch Two Sample t-test; ^cPearson's Chi-squared test.

Abbreviations: GED, General Educational Development; BMI, body mass index; AFB, age at first birth; ALB, age at last birth; NLB, number of live births.

Regarding racial distribution, non-Hispanic White (29.4%) and non-Hispanic Black (28.6%) participants had the highest proportions, whereas other racial groups (including multiracial individuals) had the lowest proportion (4.6%). In terms of education level, 36.4% of participants had some college education or an associate degree, while 22.6% held a bachelor's degree or higher. Marital status data showed that 63.2% of participants were married or cohabiting with a partner.

Regarding health-related characteristics, 88.5% of participants reported alcohol consumption, 34.5% were smokers, and 7.3% had a history of pelvic inflammatory disease. Additionally, 12.9% of participants reported a history of infertility. The results indicated significant differences between the infertility and non-infertility groups in several variables. The AFB was significantly higher in the infertility group compared to the non-infertility group (25.0 ± 6.4 vs 22.5 ± 4.9 , $p < 0.001$), and the ALB was also significantly higher (30 ± 6 vs 28 ± 6 , $p < 0.001$).

In terms of racial distribution, the proportion of non-Hispanic White participants was significantly higher in the infertility group than in the non-infertility group (39.5% vs 27.9%, $p = 0.004$). Regarding education level, the proportion of participants with a bachelor's degree or higher was significantly greater in the infertility group than in the non-infertility group (30.0% vs 21.5%, $p = 0.009$). Additionally, the proportion of married or cohabiting individuals was significantly higher in the infertility group than in the non-infertility group (70.4% vs 62.2%, $p = 0.014$). However, no significant differences were observed between the two groups in terms of BMI, age at menarche, alcohol consumption, and smoking habits.

The Association of AFB, ALB, and NLB with Infertility

AFB

In Model 1, each 1-year increase in age at first birth was significantly associated with the risk of infertility (OR = 1.08, 95% CI: 1.06–1.11, $p < 0.001$). However, after adjusting for confounders in Models 2 and 3, this association was no longer significant (Model 2: OR = 1.01, 95% CI: 0.97–1.06, $p = 0.497$; Model 3: OR = 1.01, 95% CI: 0.97–1.06, $p = 0.615$). The 24–26 age group showed a significant reduction in infertility prevalence in Model 3 (OR = 0.48, 95% CI: 0.26–0.89, $p = 0.021$). The 33–35 age group and the ≥ 36 age group showed a significant increase in infertility prevalence in Model 1 (Model 1: OR = 3.82, 95% CI: 2.16–6.76, $p < 0.001$; Model 1: OR = 4.55, 95% CI: 2.26–9.16, $p < 0.001$), but this association weakened after adjusting for confounders in Models 2 and 3 (Table 2).

ALB

In all models, ALB was positively associated with infertility; the higher the ALB, the greater the risk of infertility, especially in the ≥ 40 years age group (Model 3: OR = 5.22, 95% CI: 2.01–13.58, $p < 0.001$) (Table 2).

Table 2 Associations of Age at First Birth, Age at Last Birth and Number of Live Births with the Prevalence of Female Infertility

	Model 1		Model 2		Model 3	
	OR (95% CI)	P for Trend	OR (95% CI)	P for Trend	OR (95% CI)	P for Trend
AFB	1.08 (1.06,1.11)	<0.001	1.01 (0.97,1.06)	0.497	1.01 (0.97,1.06)	0.615
< 18	–	–	–	–	–	–
18-20	0.76 (0.45,1.29)	0.317	0.65 (0.38,1.11)	0.113	0.57 (0.33,0.99)	0.047
21-23	0.91 (0.56,1.47)	0.688	0.64 (0.38,1.07)	0.089	0.58 (0.34,0.99)	0.044
24-26	0.95 (0.56,1.59)	0.841	0.55 (0.31,0.99)	0.048	0.48 (0.26,0.89)	0.021
27-29	1.41 (0.84,2.36)	0.195	0.68 (0.36,1.28)	0.231	0.57 (0.29,1.12)	0.102
30-32	1.51 (0.85,2.66)	0.159	0.62 (0.30,1.29)	0.199	0.50 (0.23,1.11)	0.089
33-35	3.82 (2.16,6.76)	<0.001	1.28 (0.57,2.87)	0.544	1.10 (0.47,2.58)	0.825
≥ 36	4.55 (2.26,9.16)	<0.001	1.08 (0.39,2.98)	0.887	0.90 (0.31,2.58)	0.838
ALB	1.05 (1.02,1.07)	<0.001	1.06 (1.02,1.10)	0.002	1.08 (1.04,1.13)	<0.001
< 24	–	–	–	–	–	–
24-29	0.84 (0.56,1.26)	0.390	0.96 (0.61,1.51)	0.859	0.98 (0.62,1.56)	0.930
29-34	1.04 (0.70,1.56)	0.840	1.18 (0.69,1.99)	0.546	1.26 (0.73,2.17)	0.410
34-40	1.66 (1.11,2.48)	0.013	1.89 (1.01,3.53)	0.045	2.38 (1.24,4.55)	0.009
≥ 40	2.79 (1.44,5.41)	0.002	3.51 (1.40,8.76)	0.007	5.22 (2.01,13.58)	<0.001
NLB	0.71 (0.63,0.81)	<0.001	0.66 (0.54,0.81)	<0.001	0.67 (0.55,0.82)	<0.001
< 2	–	–	–	–	–	–
≥ 4	0.40 (0.26,0.61)	<0.001	0.29 (0.15,0.55)	<0.001	0.29 (0.15,0.56)	<0.001
2	0.57 (0.41,0.79)	<0.001	0.48 (0.33,0.71)	<0.001	0.48 (0.33,0.72)	<0.001
3	0.33 (0.22,0.51)	<0.001	0.26 (0.15,0.45)	<0.001	0.27 (0.16,0.47)	<0.001

Note: Model 1: Crude model; Model 2: model 1 variables plus pelvic inflammatory disease, age when first menstrual period occurred (age at menarche); Model 3 was adjusted for model 2 variables plus age and race/ethnicity, education level, smoking, alcohol user, marriage status, body mass index.

Abbreviations: AFB, age at first birth; ALB, age at last birth; NLB, number of live births; OR, Odds ratio; CI, Confidence interval.

NLB

The more live births, the lower the risk of infertility. In Model 1, the group with ≥ 4 live births had the lowest infertility prevalence (OR = 0.40, 95% CI: 0.26–0.61, $p < 0.001$). This association remained significant in Model 2 (OR = 0.29, 95% CI: 0.15–0.55, $p < 0.001$) and Model 3 (OR = 0.29, 95% CI: 0.15–0.56, $p < 0.001$) (Table 2).

In conclusion, age at first birth and age at last birth are significantly associated with infertility in certain age groups, while the number of live births is negatively correlated with the risk of infertility. After adjusting for confounders, the strength of these associations changed, particularly the relationship between age at first birth and infertility.

RCS Curves

Figure 2A shows a significant J-shaped curve relationship between AFB and infertility prevalence (P for nonlinearity = 0.002; overall $P < 0.001$). Specifically, infertility risk is relatively low at younger AFB values but rises sharply as AFB increases beyond a certain point, forming a characteristic “J” shape. The inflection point occurs at $\ln(\text{AFB}) = 3.025$

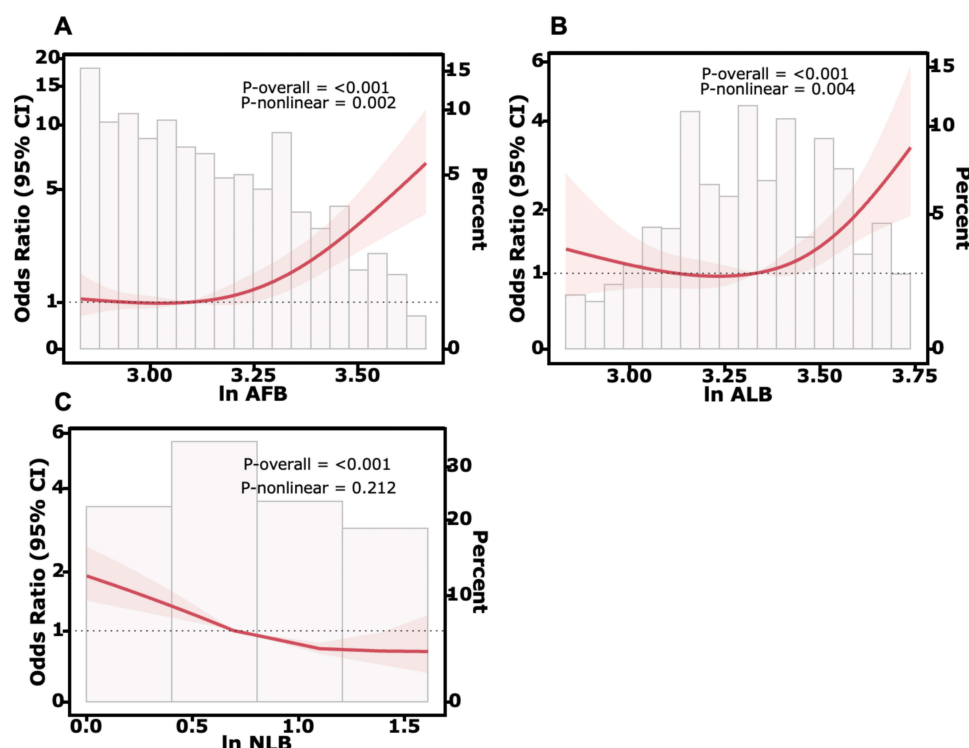


Figure 2 The restricted cubic spline (RCS) curves depict the relationship between the risk of female infertility and several reproductive factors.

Notes: (A) Shows a J-shaped relationship between ln AFB and infertility risk, indicating rising infertility risk with increasing AFB; (B) Shows a nonlinear positive correlation between ln ALB and infertility risk; (C) Shows a linear negative correlation between ln NLB and infertility risk.

Abbreviations: AFB, age at first birth; ALB, age at last birth; NLB, number of live births; OR, Odds ratio; CI, Confidence interval; Ln AFB is the natural logarithm of Age at First Birth (AFB). Ln ALB is the natural logarithm of Age at Last Birth (ALB). Ln NLB is the natural logarithm of the Number of Live Births (NLB).

(approximately 20.6 years), after which the risk of infertility increases more rapidly. Figure 2B reveals a typical U-shaped association between ALB and infertility (P for nonlinearity = 0.004; overall $P < 0.001$). Infertility risk is elevated at both lower and higher ALB values, while the lowest risk is observed at a moderate ALB level. The turning point is identified at $\ln(\text{ALB}) = 3.233$ (approximately 25.4 years), suggesting an optimal range for last birth age associated with minimal infertility risk. Figure 2C demonstrates a linear negative relationship between NLB and infertility prevalence (P for nonlinearity = 0.212; overall $P < 0.001$). As NLB increases, the risk of infertility consistently decreases, and no significant nonlinear pattern is observed. In summary, age at first birth and age at last birth exhibit significant nonlinear relationships with infertility prevalence, whereas the number of live births shows a gradually decreasing linear association with infertility prevalence. After adjusting for confounders, the effects of AFB and ALB on infertility remained significant.

Subgroup Analysis

In the overall population analysis, the prevalence of infertility was 14.3% among married or cohabiting individuals and 10.4% among those living alone, with an OR of 0.69 (95% CI: 0.52–0.93, $P = 0.014$), indicating a significant association between living alone and a reduced risk of infertility. In the subgroup analysis, no significant interactions were observed for race, education level, alcohol consumption, pelvic inflammatory disease, smoking, age at first birth, age at last birth, or the number of births (P for interaction > 0.05 for all). However, a significant interaction was found in the alcohol consumption subgroup (P for interaction = 0.048), where living alone was significantly associated with a reduced risk of infertility among alcohol consumers (OR = 0.63, 95% CI: 0.46–0.86, $P = 0.003$), whereas no significant difference was observed among non-drinkers. Additionally, the interaction for the number of births subgroup was borderline significant (P for interaction = 0.05), with a significantly reduced risk of infertility among those who had fewer than two births and lived alone (OR = 0.39, 95% CI: 0.23–0.66, $P < 0.001$) (Figure 3). Overall, the significant association between living

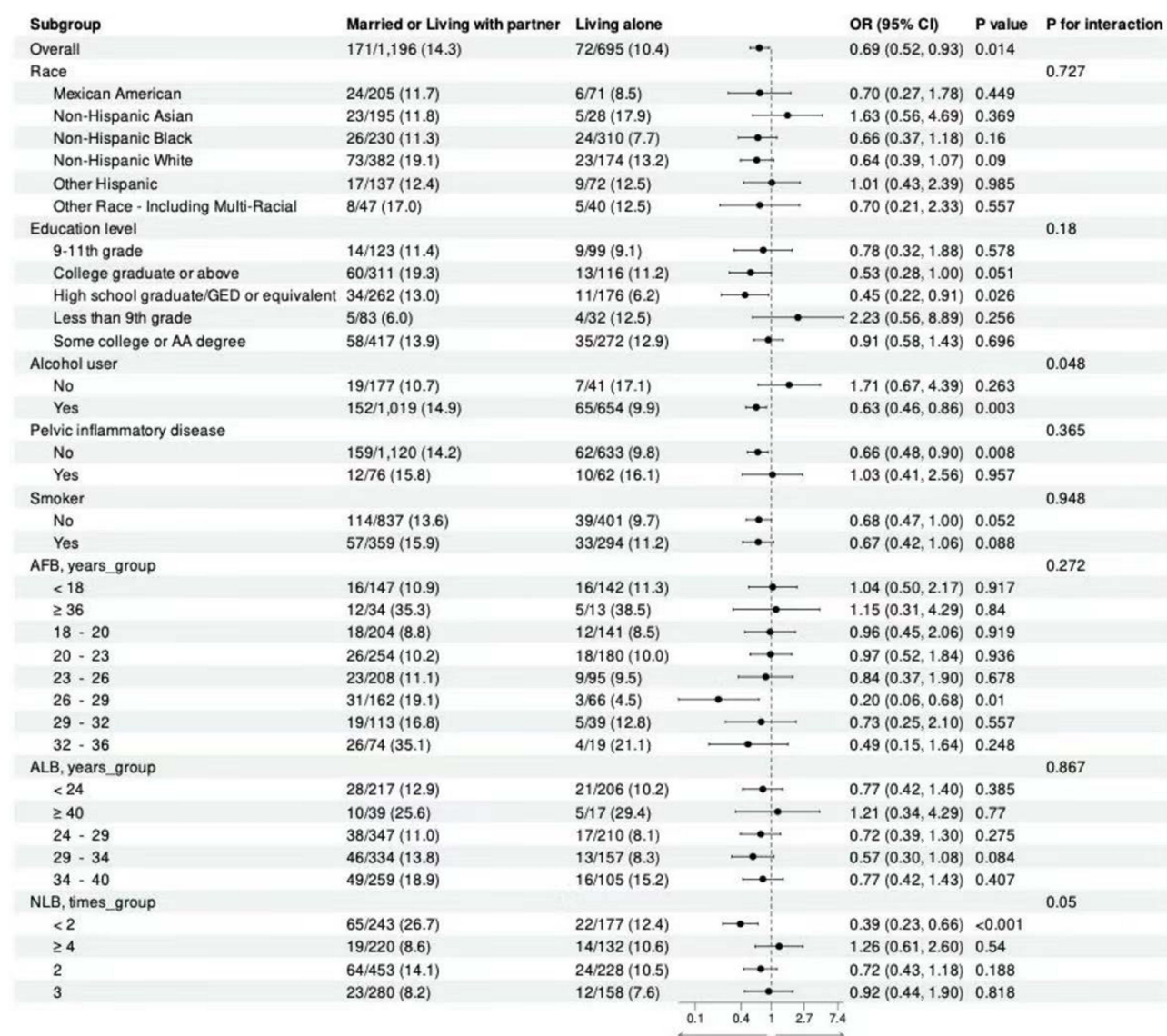


Figure 3 Subgroup analyses.

Notes: The chart displays the odds ratios (OR) and 95% confidence intervals (CI) for infertility risk in women married or living with a partner versus women living alone across different subgroups. P values indicate statistical significance, while P for interaction shows if there's a significant interplay between subgroups.

Abbreviations: AFB, age at first birth; ALB, age at last birth; NLB, number of live births; OR, Odds ratio; CI, Confidence interval.

alone and reduced infertility risk was confirmed in the overall population and certain subgroups, but differences in interactions among subgroups require further investigation.

Discussion

This study aims to investigate the relationship between AFB, ALB, and the NLB and female infertility by analyzing data on women from NHANES collected between 2017 and 2020. And this study, based on large-scale representative population data, systematically evaluated the relationship between female fertility-related factors and infertility. It was found that an increase in AFB and ALB significantly heightened the risk of infertility, whereas a higher NLB was significantly associated with a reduced risk of infertility. Further RCS curve analysis suggested a J-shaped relationship between AFB and infertility, a nonlinear positive association between ALB and infertility, and a linear negative correlation between NLB and infertility. In subgroup analyses, women living alone exhibited a lower risk of infertility in certain subgroups, suggesting that social and behavioral factors may also play a crucial role in reproductive health.

These findings provide novel evidence for understanding the complex relationship between the female reproductive trajectory and infertility risk.

Compared with previous cross-sectional studies with limited sample sizes, the NHANES dataset comprises a large number of samples and includes multidimensional information on various races, age groups, and socioeconomic backgrounds, thereby enhancing its representativeness. This enables us to explore the potential associations between these reproductive factors and infertility in a broader female population and to provide more reliable scientific evidence for the future formulation of screening and intervention strategies for infertility.

In recent years, an increasing number of studies have focused on the impact of female reproductive timing and fertility frequency on infertility risk.¹⁸ Several prospective and retrospective studies have indicated that delayed age at first birth and a reduced number of live births are closely associated with a decline in fertility.^{19,20} A woman's reproductive history is not only a crucial indicator for assessing her reproductive health but is also believed to be closely linked to ovarian reserve, endocrine function, and structural changes in reproductive organs.^{21,22} However, systematic studies on the effects of age at first birth, age at last birth, and number of live births on infertility remain relatively limited, particularly in large populations where confounding factors have been controlled. Therefore, this study holds significant practical implications and research value.

Delayed age AFB may affect female fertility through multiple biological mechanisms. First, as age increases, ovarian reserve gradually declines, and oocyte quality deteriorates, leading to impaired ovulatory function.^{23–25} Second, delayed childbirth may increase cumulative exposure to chronic diseases such as metabolic syndrome, endometriosis, and thyroid dysfunction, all of which are closely associated with infertility.^{26–28} Additionally, postponing first childbirth may be accompanied by social factors such as increased occupational stress, disrupted circadian rhythms, and unhealthy lifestyles, which can influence reproductive hormone secretion through hypothalamic-pituitary-ovarian axis regulation, thereby indirectly affecting fertility.^{16,29,30}

The association between delayed ALB and increased infertility risk may reflect the challenges of attempting conception at an advanced maternal age. In women over 40, the natural conception rate declines significantly, while the risks of miscarriage and pregnancy complications increase markedly, indicating a simultaneous decline in both the quantity and quality of oocytes at advanced maternal age.^{31–33} Currently, the reproductive mechanisms of women with a higher number of live births remain underexplored in academic research, and relevant literature is relatively scarce. However, some studies have suggested that multiple childbirths may have adverse effects on women's health, such as accelerating cellular aging and compromising overall well-being.^{34–36}

In the subgroup analysis of this study, we observed a significant negative correlation between living alone and infertility risk, particularly in the overall population analysis, where the infertility incidence was 14.3% among married or cohabiting individuals and 10.4% among those living alone. This finding suggests that living alone may have a protective effect on the occurrence of infertility. A current study in China indicates that social support has a significant impact on individual health, and living alone may result in a lack of emotional support and social connections, which can affect both physical and mental health.^{37,38} However, the relationship between living alone and infertility may be modulated by various factors, such as lifestyle, mental health, and physiological conditions. In addition, we found a significant interaction in the alcohol consumption subgroup, where living alone was particularly strongly associated with a reduced risk of infertility among alcohol drinkers. This phenomenon may be related to the impact of alcohol consumption on hormone levels. Previous studies have suggested a potential relationship between moderate alcohol intake and changes in female hormone levels.^{39,40} It is hypothesized that alcohol consumption may indirectly affect infertility risk by alleviating social stress or improving mental health status. However, no significant differences were observed among non-drinkers in this study, which may be due to the complex mechanisms by which alcohol influences reproductive health, involving various physiological and psychological factors. Furthermore, in the subgroup with fewer than two births, the risk of infertility was significantly lower among those living alone. This may be related to the tendency of individuals living alone to seek medical intervention in the absence of social support, or differences in their lifestyle and reproductive choices.⁴¹ Studies have shown that living alone may influence women's reproductive decisions and behavioral patterns, thereby affecting reproductive health.^{42,43} However, the interaction of factors such as race and education level did not show significance, which may indicate that these factors have a minimal effect on the relationship

between living alone and infertility risk. Existing studies suggest that while socio-economic factors may affect reproductive health,⁹ their role in the relationship between living alone and infertility is more complex and may be influenced by various individual lifestyle habits, social support systems, and health conditions.

Furthermore, this study found that there may be a J-shaped relationship between AFB and infertility, where the risk of infertility is higher at both lower and higher AFB levels, and lower or not significant at intermediate levels. This J-shaped relationship may reflect complex biological mechanisms. For example, lower AFB values may be associated with insufficient physiological or environmental factors that negatively affect fertility,⁴⁴ while higher AFB values may be linked to excessive fertility interventions or environmental exposures, leading to infertility.^{44,45}

This study has several strengths. First, based on a nationally representative sample and a large sample size, the study enhances the generalizability of the results. Second, by using multivariate logistic regression, restricted cubic spline analysis, and subgroup interaction analysis, the study's conclusions are more robust and reliable. Moreover, this study systematically evaluated the three core fertility indicators: AFB, ALB, and NLB, providing data support for future reproductive health policy development. However, this study also has certain limitations. First, due to its cross-sectional design, causal relationships cannot be established; second, the assessment of infertility in this study relies on self-reported questionnaire responses, which may introduce recall bias and misclassification. In particular, since infertility status was based on whether participants had attempted to conceive without success or had sought medical help, women who were not actively trying to conceive—especially those living alone—may have responded negatively, regardless of their underlying fertility status. This limitation could bias the observed association between living arrangement and infertility risk and should be interpreted with caution; third, there is a lack of differentiation between infertility types (primary/secondary) and specific causes; fourth, the study did not account for potential confounders, such as partner fertility factors and contraceptive history. Future research should incorporate longitudinal data and reproductive endocrine indicators, allowing for further exploration of mechanisms and intervention pathways, thus providing more effective guidance and recommendations for the future of reproductive health.

Conclusion

This study reveals the significant relationship between fertility factors and infertility risk through the analysis of large-scale, nationally representative population data. A delayed age at first birth and last birth increased the risk of infertility, whereas an increased number of live births significantly reduced the risk of infertility. These results provide valuable insights for assessing and intervening in women's reproductive health, particularly with significant implications for policy development and public health interventions. Future research should further explore the mechanisms of these factors in different populations across countries and regions, and incorporate longitudinal data for in-depth analysis to provide more precise guidance for women's reproductive health.

Abbreviations

NHANES, National Health and Nutrition Examination Survey; RCS, Restricted cubic spline; AFB, Age at first birth; ALB, Age at last birth; NLB, Number of live births; BMI, Body mass index; SD, Standard deviation.

Data Sharing Statement

The survey data are publicly available on the internet for data users and researchers throughout the world (www.cdc.gov/nchs/nhanes/).

Ethical Statement

The National Health and Nutrition Examination Survey was approved by the National Center for Health Statistics Research Ethics Review Board (<https://www.cdc.gov/nchs/nhanes/about/erb.html>). Patients/participants provided written informed consent to participate in the study. The Ethics Committee of the University of Glasgow in the UK waived ethical approval for this study because NHANES is a publicly accessible database.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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All authors declare that they have no competing interests in this work.

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