



## Original Article

## Parity and later life risk for coronary heart disease among slum-dwelling women in Mysore, India

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## ABSTRACT

**Background:** To examine the role of parity in coronary heart disease (CHD) among middle-aged Indian women living in government-designated slums in Mysore, India.**Methods:** Between October 2017 and May 2018, a cross-sectional study was carried out among women, 40–64 years of age, residing in government-designated slums in Mysore, India. In addition to socio-demographics, data were collected on CVD risk factors including use of tobacco and alcohol, diet, physical activity, sleep, quality of life, and personal and family history of chronic disease. Patients underwent a medical examination and a venous blood sample was taken for fasting lipid measurement. Resting electrocardiography was carried out by a trained medical technician. Multivariable logistic regression with associated 95% confidence intervals was used to examine the relationship between parity and coronary heart disease.**Results:** The prevalence of CHD in this sample of middle-aged women was 6.4%. Nulliparous women were at heightened risk for CHD compared to parous women with up to five live births. In the adjusted model, women who had 1–2 and 3–5 live births had 0.24 times lower odds (95% Confidence Interval [CI]: 0.05–1.29) and 0.38 times lower odds (95%CI: 0.178–0.87) of CHD, respectively, as compared to nulliparous women.**Conclusion:** Among a fairly homogenous population of slum-dwelling women reporting almost universal breastfeeding for three or more months following birth, parity up to five births appeared protective against CHD. Further studies are needed to evaluate whether near universal breastfeeding rates in this population mediated the relationship of parity and CHD.© 2021 Cardiological Society of India. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Cardiovascular disease (CVD) is the world's leading cause of mortality.<sup>1</sup> Over three quarters of CVD-related deaths occur in low- and middle-income countries (LMIC). Coronary Heart Disease (CHD) including angina pectoris, myocardial infarction (MI) and

silent myocardial ischemia<sup>2</sup> represent the largest single cause of deaths attributed to CVD.<sup>3</sup> In India, the probability of dying from CHD between the ages of 30 and 69 years increased from 10.4 to 13.1% among men, and 4.8–6.6% among women between 2000 and 2015.<sup>4</sup> The reasons for worsening cardiovascular health in India are unclear but include changing dietary habits and a significant decline in physical activity which have led to a higher prevalence of cardiometabolic risk factors.<sup>5</sup>

CHD has become a leading cause of death among Indian women.<sup>6</sup> As in other parts of the world, females present with heart disease about 10 years later than males, have lower overall

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knowledge about CVD and its risk factors, and generally have a poorer prognosis following acute MI compared to men of the same age.<sup>7–12</sup> Among Indian women, the prevalence and population attributable risk of smoking and alcohol use on heart disease is relatively low<sup>11,13</sup> while metabolic risk factors like dyslipidaemia, hypertension and diabetes contribute disproportionately to CVD risk.<sup>11,14,15</sup> Current risk algorithms like the Framingham Risk Score have a mixed record for CVD risk prediction in South Asians, underscoring the need for additional risk factors with clinical utility for predicting CVD risk in Indian women.<sup>16–18</sup>

A variety of studies have examined the relationship of parity with risk for later life CHD but findings are mixed.<sup>19–25</sup> Some research shows that parity increases CHD risk<sup>24</sup>; other studies report no association between number of live births and CHD<sup>25,26</sup>; while still others describe a nonlinear J-shaped dose–response relationship between parity and CHD outcomes.<sup>22</sup> Research also suggests that breastfeeding may mediate the effects of parity on CHD.<sup>23,27</sup> To our knowledge, this is one of the first studies to examine whether parity was associated with later life CHD in slum-dwelling Indian women.

## 2. Methods

Between October 2017 and May 2018, a cross-sectional study using non-probability sample of 607 women living in six government-designated slums was conducted in Mysore, India. About 19% of the city's population lives below the poverty line, and approximately 49,352 residents reside in slums (as defined by the Karnataka Slum Act). Study staff visited slums one day prior to recruitment and distributed brochures describing the purpose of the study, eligibility criteria, and study activities. Inclusion criteria for the study included being female, 40–64 years of age; resident of Mysore for six or more months, willing and able to undergo written informed consent and study procedures. Women were excluded if they had haemophilia or other medical conditions that put them at risk during sample collection. A study protocol was approved by Institutional Review Boards at Florida International University and Public Health Research Institute of India. All participants provided informed consent before data collection started.

Data were collected using an interviewer-administered questionnaire adapted from the Cardiometabolic Risk Reduction in South Asia (CARRS) Surveillance Study translated into the local language of *Kannada*.<sup>28</sup> Study variables included knowledge and beliefs about coronary heart disease (CHD), demographics, modifiable risk factors (smoking, use of alcohol, weight, physical activity, healthy diet, blood pressure, serum cholesterol, and blood glucose), and correlates of CHD (defined as previous physician-diagnosed CHD, ECG abnormalities suggestive of heightened risk for CHD including wide QRS/T angle, ECG-MI, high QRS nondipolar voltage, reduced heart rate variability, and QT prolongation) as interpreted by a Cardiologist at Apollo Hospital, Mysore,<sup>29</sup> or a finding of 'definite angina' on the Rose Angina Questionnaire (shown to have moderate sensitivity but high specificity for detection of CHD<sup>30</sup>).

The main independent variable was parity or number of biologically live births reported by a participant. Information about parity and gravida were obtained by personal interview and categorized into four groups (0, 1–2, 3–5 and  $\geq 6$ ). Selection of study covariates was based on a review of the literature.

Data were entered in an Access database (Microsoft Corporation, Redmond, WA). The primary outcome was CHD, analyzed as a binary variable. Univariate associations of baseline characteristics with CHD were made using Pearson chi-squared test, Fisher's exact test, and Mantel–Haenszel test for trend of odds. Data were adjusted for clustering based on slum residency. A series of logistic regression models were performed to calculate the adjusted odds

ratio (OR) and 95% Confidence Intervals (CI) for risk of CHD by parity. In order to avoid over-fitting, principal component analysis (PCA) was used to reduce variables in the following categories to a single index: sociodemographic factors, lifestyle factors, reproductive factors, and mediating factors (most of which were biological measurements—cholesterol, BMI category, etc). Variables included in the PCA index for somociodemographic factors included: marital status, education, income, and occupation. Lifestyle factors index included: having ever used tobacco or alcohol; currently alcohol or tobacco use; passive smoking; exercise for at least 150 min per week; self-reported quality of life; minutes of sedentarism; and diagnosis of diabetes, hypertension, or heart disease. The reproductive factors index included age at menarche; ever had abortion, miscarriage/stillbirth; early/late menarche, menopausal status, contraceptive/hormonal use, infant deaths, and number of pregnancies. Lastly, variables included in the mediating factors index were: family history of diabetes, family history of heart disease, family history of hypertension, LDL cholesterol, HDL cholesterol, total cholesterol, A1c, triglycerides, and BMI. The adjusted models included the following: Model 1 age; Model 2 age, sociodemographic and lifestyle factors indices; Model 3, all indices in Model 2 along with the reproductive factors index, and the final model, Model 4, included Model 3 factors along with the mediating factors index. In each model, clustering by slum was considered. Additional models explored whether age and tobacco use were confounders or effect modifiers. A *p*-value of 0.05 was considered statistically significant. Analysis was performed in Stata version 11.2 (Statacorp, College Station, Texas, US).

## 3. Results

### 3.1. Characteristics of the sample

A total of 734 women were screened, and 615 enrolled (83.7%). Eight women declined either to provide a blood sample or to undergo some study procedure, and were not included in the analysis. Of the 607 completing all procedures (98.7%), 39 met the criteria for CHD, for a prevalence of 6.4% (95% CI: 4.7–8.7) (Table 1). Average age at menarche was 13.2 years (SD  $\pm$  1.55) with 38.4% attaining it early (defined as at or before the first quartile of the age of menarche) and 39%, late (defined as at the third quartile of the age of menarche or later). Women had a median of three lifetime pregnancies and three live births [IQR: 2–4]. Six percent reported still births and 20.9% had at least one abortion/miscarriage. Almost 70% (68.9%) were post-menopausal.

### 3.2. Risk factors for CHD

Table 2 described associations between CHD risk factors and CHD. Household income was the only sociodemographic factor associated with CHD. The prevalence of CHD was lowest among women who had 1–2 live births, and highest among those who were nulliparous. The nulliparous group had higher percentages in each of the three categories (single–13.6%, widowed—52.3%, separated/divorced—11.4%). Among lifestyle factors, history of diabetes and heart disease were significantly associated with CHD; among reproductive factors, gravida and parity were significantly associated with CHD; and among mediating factors, family history of hypertension, family history of heart disease, and family history of diabetes were significantly associated with CHD (Table 3). The odds of having CHD increased with increasing monthly household income; a diagnosis of diabetes and heart disease; and a family history of diabetes, heart disease or hypertension. On the other hand, the odds of CHD were significantly lower with every unit increase in age at menarche.

**Table 1**  
Distribution of the socio demographic characteristics of the study population, Mysore, India (N = 607).

Characteristics	N	%
Age (in years)		
Mean (SD)	50.03	(±7.318)
Median (Q1, Q3)	50	(44, 55)
Education		
No schooling	361	59.5
Up to Class IV	67	11.0
Class V to IX	138	22.7
Class X and above including technical courses	41	6.8
Marital Status		
Single	7	1.2
Married	312	51.4
Other (Widow, separated)	288	47.5
Work Status		
Employed	373	61.5
Housewife	234	38.6
Monthly Household Income (INR)		
<3000	129	21.3
3000–10,000	321	53.0
>10,000	156	25.7
BMI		
Underweight	96	15.8
Normal	174	28.7
Overweight	91	15.0
Obese I	171	28.2
Obese II	75	12.4
CHD	39	6.4

SD, standard deviation; Q1, first quartile; Q3, third quartile; INR, Indian Rupees; BMI, body mass index.

Marital Status: "Other" includes separated, divorced, and widow/widower.

BMI: Underweight <18.5 kg/m<sup>2</sup>; Normal weight 18.5–22.9 kg/m<sup>2</sup>; Overweight 23–24.9 kg/m<sup>2</sup>; Obese I 25–29.9 kg/m<sup>2</sup>; Obese II ≥ 30 kg/m<sup>2</sup>.

The unadjusted and adjusted logistic regression models examining the association of parity and CHD are presented in Table 4. Both the unadjusted and adjusted multivariable models showed that women who had 1–2, and 3–5 live births had significantly lower odds of having CHD as compared to nulliparous women, although when adjusting for clustering, model 4 showed only a marginally significant effect for those with 1–2 live births. In the fully adjusted model (Model 4), after adjusting for age, socioeconomic factors, lifestyle factors, reproductive factors, and mediating factors, women who had 1–2 live births had 0.25 times lower odds (95%CI: 0.05–1.29) of CHD as compared to nulliparous women. Similarly, women with 3–5 live births had 0.37 times lower odds (95%CI: 0.16–0.85) of CHD as compared to nulliparous women. This relation was not seen among women with greater than five live births. The odds ratio for a woman with 5+ as compared to 4 or less children for CHD was 2.14 (95% CI: 0.94, 4.88) with a *p* value of 0.063 which was not statistically significant. The variance inflation factor for age and parity when included together was 5.51 for each factor, indicating that collinearity would be an issue if both variables were included in the model.

#### 4. Discussion

This study of slum-dwelling Indian women found a 6.4% CHD prevalence, markedly lower than rates found in other Indian urban female populations including Siliguri (9.4%),<sup>31</sup> Vellore (13.4%),<sup>32</sup> and urban Jaipur (10.8%).<sup>33</sup> We hypothesize that much of the population in Mysore slums were recent migrants from rural areas, and the detected prevalence likely a reflection of rates in those areas.

The sociodemographic factors index was significantly associated with CHD. The prevalence of CHD was lowest among women who had 1–2 live births and highest among those who were nulliparous. The lifestyle factors index was associated with lower odds of CHD although not significantly; tobacco and alcohol consumption were the primary influencing factors, although hypertension, diabetes, self-reported quality of life, and moderate physical activity also affected the index. Those with a higher reproductive factors index had marginally significantly lower odds of CHD, with age of menarche, whether menarche was late, gravida, and infant death driving the index. Nulliparous women were at heightened risk for CHD compared to parous women with up to five live births. In the full model, even after adjusting for the demographic factors index, the lifestyle index, the reproductive factors index, and the mediating factors index, the odds of CHD were about the same for each category, with the odds ratio ranging from 0.21 to 0.24 for 1–2 births, and 0.34 to 0.38 for 3–5 births.

Some studies suggest that multiparity is a risk factor for CHD outcomes, but our study does not provide evidence for that hypothesis. Our results are similar to others finding that 1–2 births were protective against CHD while being nulliparous or having more than five births either increased CHD risk or had no association, respectively.<sup>34</sup> It is possible, as Steenland has suggested, that positive associations between parity and CHD likely had uncontrolled or residual confounding by imperfectly controlled variables since studies with samples that were relatively homogenous for socioeconomic characteristics showed protective effects.<sup>19,25</sup> There is also recent evidence that breastfeeding may modify the relationship of CHD and multiparity. A study of more than 520,000 women in 10 countries found that while parity increased risk of CHD in later life, multiparous women who breastfed had significantly lower CHD risk compared to nulliparous women.<sup>23</sup> Breastfeeding was associated with an adjusted hazard ratio of 0.71 (95% CI: 0.52–0.98) for CHD compared to not breastfeeding. Another study of 139,681 postmenopausal parous women followed for an average of 7.9 years, showed that those who breastfed for 7–12 months were significantly less likely to develop CVD compared to women who never breastfed.<sup>35</sup> Other studies have shown similar effects.<sup>23,36</sup> In our population, 93% (563/607) of study participants reported breastfeeding all offspring for three or more months and this may have contributed to reduced odds of CHD among parous women in this study. Finally, while other studies reported that menopausal status was a contributing factor for CHD risk—particularly among women experiencing early menopause (before age 45 years).<sup>37</sup> Our results did not support these findings. We found no significant association between either menopausal status or premature menopause and risk for CHD in this population.

This study had several limitations. Since it was cross-sectional, it is not possible to establish temporality of some observed relationships. Although our anonymous surveys of women who declined to participate showed no significant demographic differences from participants, the study used a non-probability sample and this may have resulted in limited generalizability. Some factors were self-reported so there is a possibility of information bias. In addition, since the women were asked about the family history of some of the chronic diseases such as diabetes, hypertension etc, it is likely that there is an underestimation of the actual burden due to recall bias. It is also possible the observed associations may have been subject to unmeasured or residual confounding. For instance, involuntary childlessness is a stigmatized and stressful condition, and has been associated with depression in older age, a risk factor for CHD.<sup>38,39</sup> Other stressful life situations including widowhood, separation and divorce may also have impacted mental health and subsequent CHD outcomes.<sup>40</sup> Since the study did not measure mental health exposures, history of polycystic ovaries or hormonal

**Table 2**  
Sociodemographic characteristics and CHD among slum-dwelling women in Mysore, India (N = 607).

Characteristic	CHD			NC <i>p</i> -value	Clustering <i>p</i> -value
	N (%)	n	%		
Age Categories (in years)				0.635	0.291
40–49	292 (48.1)	16	5.48		
50–59	213 (35.1)	15	7.04		
>59	102 (16.8)	8	7.84		
Highest level of education				0.495	0.429
No formal education	361 (62.8)	21	5.82		
Upto Class IV	67 (11.0)	5	7.46		
Class V and above	179 (29.5)	13	7.26		
Marital status				0.339	<b>0.030</b>
Married	312 (51.4)	22	7.05		
Never married	7 (1.15)	1	14.29		
Other (widowed, separated)	288 (47.4)	16	5.56		
Monthly Household Income (INR)				<b>0.023</b>	<b>0.008</b>
<10,000	451 (74.3)	22	4.88		
10,001–20,000	119 (19.6)	12	10.08		
>20,000	37(6.10)	5	13.51		
h/o Hypertension				0.297	0.265
Yes	145 (23.9)	12	8.28		
No	462 (76.1)	27	5.84		
h/o Diabetes				<b>0.008</b>	<b>0.005</b>
Yes	107 (17.6)	13	12.15		
No	500 (82.4)	26	5.20		
h/o Heart Disease				<b>&lt;0.001</b>	<b>&lt;0.001</b>
Yes	14 (2.3)	7	50.00		
No	593 (97.7)	32	5.40		
Family h/o Hypertension				<b>&lt;0.001</b>	<b>0.001</b>
Yes	130 (21.4)	17	13.1		
No	477 (78.6)	22	4.6		
Family h/o Diabetes				<b>0.009</b>	<b>0.010</b>
Yes	145 (23.9)	16	11.0		
No	462 (76.1)	23	5.0		
Family h/o Heart Disease				<b>&lt;0.001</b>	<b>&lt;0.001</b>
Yes	79 (13.0)	15	19.0		
No	528 (87.0)	24	4.6		
Gravida				<b>0.003</b>	0.983*
0	26 (4.28)	5	19.23		
1–2	158 (26.03)	8	5.06		
3–5	341 (56.18)	16	4.69		
≥6	82 (13.51)	10	12.2		
Parity				<b>0.019</b>	0.815*
0	44 (7.25)	7	15.9		
1–2	252 (41.52)	10	3.97		
3–5	283 (46.62)	19	6.71		
≥6	28 (4.61)	3	10.71		

h/o, History of.

INR, Indian rupees.

Marital status: Other includes widowed (n = 257) and separated (n = 31).

disturbances, we were unable to determine whether these conditions contributed to elevated CHD outcomes in this population. Furthermore, the definition of CHD did not include ECG stress test and vascular imaging as this was not practical or feasible in a community based setting. It is possible that there may be some degree of misclassification in the outcome definition. Finally, no data were collected on several pregnancy-related factors that could have been shown to be associated with the risk of CVD in later life, including gestational diabetes, gestational obesity, preeclampsia and polycystic ovary syndrome. Despite these limitations, the study had several strengths. Biological and anthropometric data were collected in a clinical setting by trained medical personnel. Questionnaires were administered by trained interviewers familiar with target slum communities. Instruments were previously validated in similar Indian populations. Electrocardiograms were read by an expert and CHD outcomes were adjudicated by a trained cardiologist. Finally, the study sample was highly homogenous for

sociodemographic factors and this may have posed less potential risk of uncontrolled and residual confounding. Further studies should evaluate whether additional pregnancy-related variables including breastfeeding may mediate the relationship between parity and CVD.

In conclusion, CHD rates rise dramatically among women in middle to older age.<sup>41</sup> The epidemiological reasons for these changes are not completely understood or accounted for by traditional risk factors. In this sample, reproductive factors were associated with CHD, with nulliparous women at heightened risk for heart disease compared to parous women with up to five live births. These findings may have implications for CHD screening and well-woman care among older women. In addition, since pregnancy is associated with significant physiological changes, some of which may have lifelong consequences, further research is needed to better understand the implications of parity for later-life CHD in middle-aged women.

**Table 3**  
Logistic regression and odds of CHD in Urban Slum Dwelling Women in Mysore, India (N = 607).

Characteristic	Unadjusted			Adjusted for Clustering	
	OR	95% CI	p-value	95% CI	p-value
Age (Categories)					
40–49	Ref				
50–59	1.31	0.63–2.71	0.471	0.75–2.27	0.344
>59	1.47	0.61–3.54	0.393	0.96–2.25	<b>0.077</b>
Education in years	1.02	0.93–1.12	0.635	0.97–1.08	0.450
Marital status					
Married	Ref	–			
Never married	2.20	0.25–19.07	0.475	0.23–21.29	0.497
Other (widowed, separated)	<b>0.78</b>	0.40–1.51	0.453	<b>0.62–0.97</b>	<b>0.024</b>
Annual household income (INR)					
<10,000	Ref	–			
10,001–20,000	<b>2.19</b>	<b>1.05–4.56</b>	<b>0.037</b>	<b>1.29–3.70</b>	<b>0.003</b>
>20,000	<b>3.05</b>	<b>1.08–8.58</b>	<b>0.035</b>	<b>1.22–7.63</b>	<b>0.017</b>
Ever used tobacco					
Yes	Ref	–			
No	1.11	0.42–2.93	0.826	0.34–3.66	0.858
Currently using Tobacco					
Yes	Ref	–			
No	0.92	0.32–2.66	0.872	0.28–2.99	0.884
Ever drank alcohol					
Yes	Ref	–			
No	0.58	0.25–1.37	0.214	0.23–1.45	0.246
Body Mass Index					
Underweight (<18.5)	Ref	–			
Normal (≥18.5–22.9)	1.47	0.51–4.25	0.478	0.51–4.22	0.474
Overweight (23–26.9)	0.88	0.28–2.78	0.831	0.18–4.35	0.878
Obese (>27)	1.57	0.54–4.54	0.408	0.70–3.52	0.276
h/o Hypertension					
Yes	1.45	0.72–2.95	0.300	0.91–2.31	0.113
No	Ref	–			
h/o Diabetes					
Yes	<b>2.52</b>	<b>1.25–5.09</b>	<b>0.010</b>	<b>1.23–5.17</b>	<b>0.011</b>
No	Ref	–			
h/o Heart Disease					
Yes	<b>17.53</b>	<b>5.80–53.01</b>	<b>&lt;0.001</b>	<b>6.26–49.05</b>	<b>&lt;0.001</b>
No	Ref	–			
Family h/o Hypertension					
Yes	<b>3.11</b>	<b>1.60–6.05</b>	<b>0.001</b>	<b>1.99–4.86</b>	<b>&lt;0.001</b>
No	Ref	–			
Family h/o Diabetes					
Yes	<b>2.37</b>	<b>1.21–4.62</b>	<b>0.011</b>	<b>1.48–3.78</b>	<b>&lt;0.001</b>
No	Ref	–			
Family h/o Heart Disease					
Yes	<b>4.92</b>	<b>2.46–9.87</b>	<b>&lt;0.001</b>	<b>2.88–8.40</b>	<b>&lt;0.001</b>
No	Ref	–			
Gravida categories					
0	Ref	–			
1–2	<b>0.22</b>	<b>0.07–0.75</b>	<b>0.015</b>	<b>0.06–0.78</b>	<b>0.018</b>
3–5	<b>0.21</b>	<b>0.07–0.62</b>	<b>0.005</b>	<b>0.08–0.53</b>	<b>0.001</b>
≥6	0.58	0.18–1.90	0.370	0.19–1.78	0.343
Parity categories					
0	Ref	–			
1–2	<b>0.22</b>	<b>0.08–0.61</b>	<b>0.004</b>	<b>0.07–0.70</b>	<b>0.010</b>
3–5	<b>0.38</b>	<b>0.15–0.97</b>	<b>0.042</b>	<b>0.22–0.64</b>	<b>&lt;0.001</b>
≥6	0.63	0.15–2.69	0.537	0.10–3.85	0.621
Age at menarche (in yrs)	<b>0.70</b>	<b>0.55–0.91</b>	<b>0.006</b>	<b>0.52–0.95</b>	<b>0.022</b>

h/o, History of.

#### 4.1. What is already known?

The results of studies on the relationship between parity and later life cardiovascular disease in women have been conflicting. Some studies have shown that both being nulliparous and multiparous was protective. Others have demonstrated a J-shaped relationship with primiparous women having the lowest risk, and still others show no association. This study is the first to be carried

out among a population of slum-dwelling women with almost universal breastfeeding.

#### 4.2. What this study adds?

This study found an association between parity and cardiovascular disease in a highly homogenous population of urban, low-income women, with high rates of breastfeeding. Added to the

**Table 4**  
Unadjusted and adjusted association for CHD by Parity among slum dwelling women in Mysore, India.

	Parity			
	0	1–2	3–5	≥6
No. of Subjects	44	252	283	28
No. of cases	7	10	19	3
Unadjusted model, no clustering	Ref	<b>0.22 (0.08–0.61)</b>	<b>0.38 (0.15–0.97)</b>	0.63 (0.15–2.69)
Unadjusted model, clustering		<b>0.07–0.70</b>	<b>0.22–0.64</b>	0.1–3.85
Model 1, no clustering	Ref	<b>0.23 (0.08–0.64)</b>	<b>0.38 (0.15–0.97)</b>	0.64 (0.15–2.71)
Model 1, clustering		<b>0.06–0.83</b>	<b>0.22–0.66</b>	0.10–3.95
Model 2, no clustering	Ref	<b>0.21 (0.07–0.60)</b>	<b>0.34 (0.13–0.88)</b>	0.57 (0.13–2.52)
Model 2, clustering	Ref	<b>0.05–0.90</b>	<b>0.18–0.65</b>	0.08–3.89
Model 3, no clustering	Ref	<b>0.23 (0.08–0.65)</b>	<b>0.38 (0.14–0.99)</b>	0.57 (0.13–2.52)
Model 3, clustering	Ref	<b>0.05–1.03*</b>	<b>0.17–0.85</b>	0.08–4.09
Model 4, no clustering	Ref	<b>0.25 (0.09–0.73)</b>	<b>0.37 (0.14–0.98)</b>	0.54 (0.12–2.42)
Model 4, clustering		0.05–1.29	<b>0.16–0.85</b>	0.07–4.16

Model 1: Age.

Model 2: Model 1 + sociodemographic factors index + lifestyle index.

Model 3: Model 2 + reproductive factors.

Model 4: Model 3 + mediating factors.

heterogeneity of previous findings, it suggests a relationship between reproductive factors and later life heart disease.

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### Role of the sponsor

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### Declaration of competing interest

None.

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