

# Paternal and Maternal Age and the Risk of Spontaneous Abortion: a Population-based Retrospective Cohort Study

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1. Paternal age were *independently associated* with increased risk of spontaneous abortion after taking consideration of maternal age.

2. Our study also call for attention on the increased risk of spontaneous abortion with *husband aged <25 years* if they are exposed to *low educational attainment, multiparity, and obesity*.

## BACKGROUND

Over the past few decades, women both in developed and developing countries have experienced parenthood postponement. The shift in reproductive behavior has drawn attention to the impacts of advanced parental age on reproductive health. Numerous studies have evaluated the independent effects of maternal age on spontaneous abortion (SAB), but the role of paternal age has rarely received attention.

## METHODS

The population-based retrospective cohort study was based on 13 927 067 females aged 20-49 years who had participated in the National Free Pre-pregnancy Check-ups Project and became pregnant during 2010-2018. Inverse probability weighting via propensity models was used to adjust for the imbalance by covariates. Logistic regression was applied to estimate ORs and 95% CIs of SAB associated with parental age. Exposure-response relationship of parental age and the risk of SAB by restricted cubic splines (RCS) was also estimated. Subgroup analyses according to the baseline characteristics were performed. The likelihood ratio tests were applied to test the compare models with and without an interaction term for parental age and each baseline characteristic.

## RESULTS

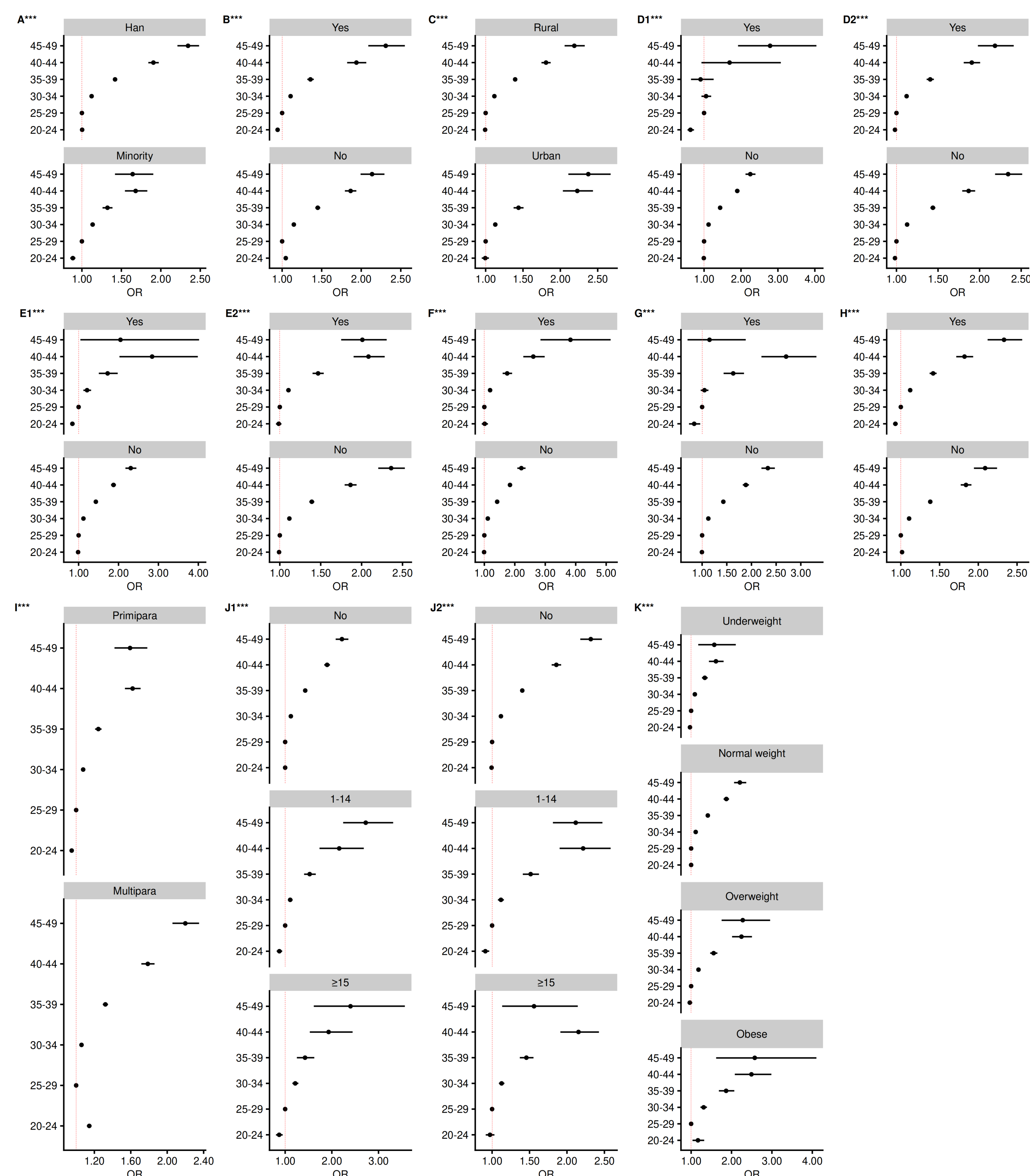
In comparison to participants with maternal age of 25-29, the IPW-adjusted ORs for SAB were 0.91 (95% CI: 0.90-0.92), 1.06 (1.05-1.07), 1.79 (1.75-1.83), 3.95 (3.85-4.05), and 6.50 (5.81-7.27) for participants with maternal age of 20-24, 30-34, 35-39, 40-44, and 45-49, respectively. And the corresponding ORs of paternal age were 0.99 (0.98-1.00), 1.12 (1.11-1.13), 1.42 (1.39-1.44), 1.89 (1.83-1.95), and 2.26 (2.14-2.38) (Table 1). The RCS results also showed a similar trend ( $P_{\text{nonlinear}} < 0.001$ ). Participants with advanced maternal age appeared to have a higher risk of SAB than participants with advanced paternal age. The results were consistent in subgroup analyses (Figure 1). In addition, younger paternal age was observed to associated with increased risk of SAB among participants with low educational attainment, multiparity, and obesity.

**Table 1. Association between parental age and the risk of SAB.**

	N (%)	OR (95% CI)		
		Age-adjusted	Fully-adjusted	IPW-adjusted
<b>Maternal age, years</b>				
20-24	76 470 (2.16)	1.00 (0.99-1.01)	1.04 (1.03-1.05)	0.91 (0.90-0.92)
25-29	123 092 (2.36)	1 (Reference)	1 (Reference)	1 (Reference)
30-34	55 786 (3.04)	1.12 (1.11-1.14)	1.03 (1.02-1.04)	1.06 (1.05-1.07)
35-39	27 118 (4.63)	1.50 (1.47-1.52)	1.35 (1.32-1.37)	1.79 (1.75-1.83)
40-44	10 746 (8.70)	2.60 (2.53-2.67)	2.43 (2.37-2.49)	3.95 (3.85-4.05)
45-49	1 503 (14.86)	4.34 (4.09-4.59)	4.34 (4.09-4.60)	6.50 (5.81-7.27)
$P_{\text{for trend}}$	0.014	0.021	0.033	0.018
<b>Paternal age, years</b>				
20-24	41 133 (2.10)	1.02 (1.01-1.04)	1.05 (1.04-1.06)	0.99 (0.98-1.00)
25-29	122 953 (2.26)	1 (Reference)	1 (Reference)	1 (Reference)
30-34	71 505 (2.75)	1.07 (1.06-1.08)	0.99 (0.98-1.00)	1.12 (1.11-1.13)
35-39	36 680 (3.89)	1.30 (1.28-1.32)	1.14 (1.12-1.16)	1.42 (1.39-1.44)
40-44	17 415 (5.81)	1.73 (1.70-1.77)	1.53 (1.49-1.56)	1.89 (1.83-1.95)
45-49	5 029 (8.45)	2.38 (2.30-2.46)	2.17 (2.10-2.25)	2.26 (2.14-2.38)
$P_{\text{for trend}}$	0.006	0.014	0.036	0.004

Notes: OR = Odds Ratio; CI = confidence interval; IPW = Inverse Probability Weighting.

## RESULTS CONTINUED



**Figure 1. Subgroup analysis of the relationship between paternal age and the risk of SAB.**

**Legend:** A = ethnicity; B = higher education; C = household registration; D = smoking; E = alcohol consumption; F = hypertension; G = diabetes mellitus; H = adverse outcomes in previous pregnancies; I = parity; J = secondhand smoking; K = pre-pregnancy BMI. “\*\*” indicated P for interaction < 0.05.

## CONCLUSIONS

Advanced parental age was independently associated with an increased risk of SAB, especially in couples with older mothers. Our findings emphasized the importance of parental age at preconception counseling and called for public health efforts to mitigate adverse pregnancy events related to advanced parental age.

## ADDITIONAL KEY INFORMATION

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