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Ambient temperature and fecundity in 2.4 million couples

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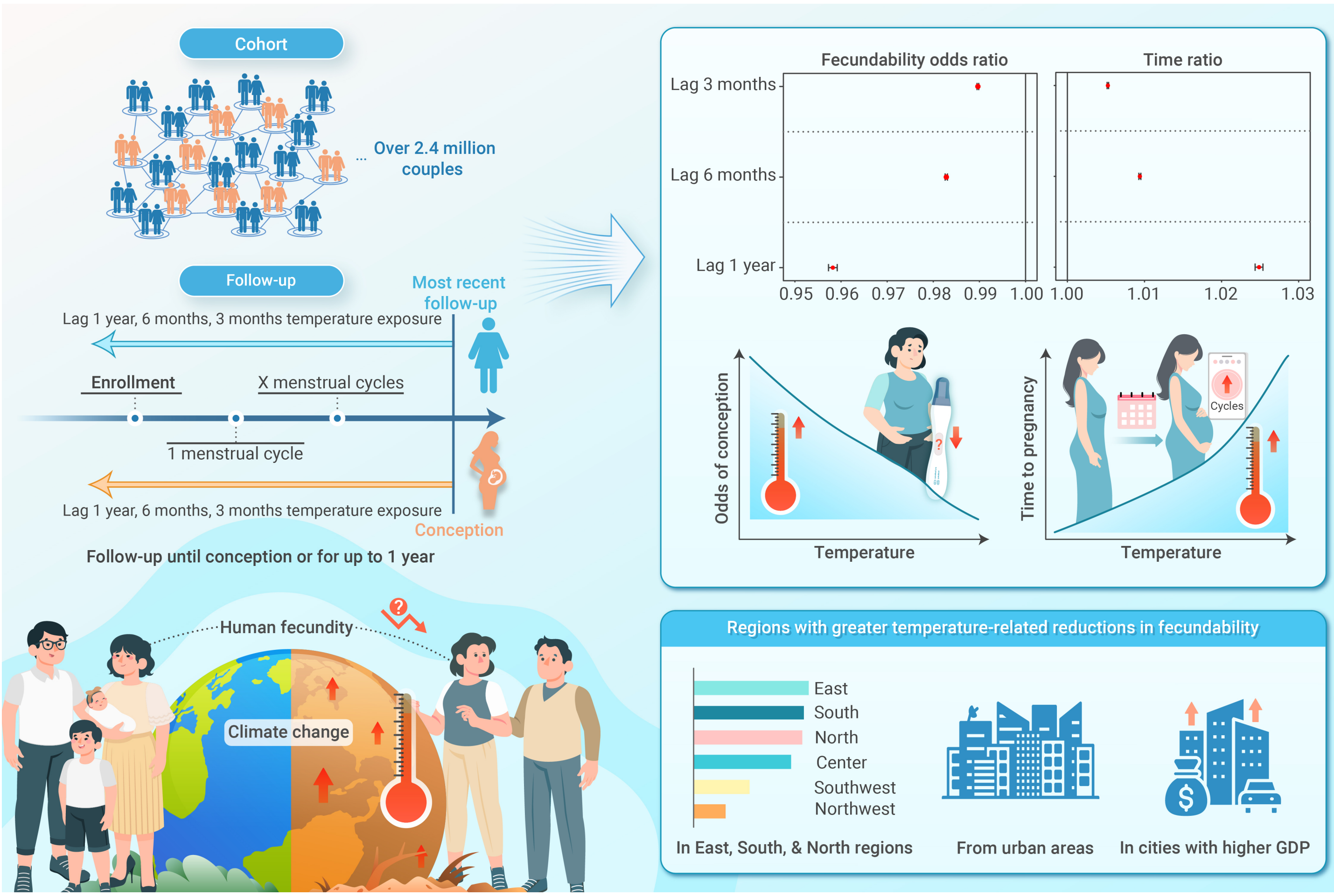
GRAPHICAL ABSTRACT



PUBLIC SUMMARY

- Exposure to higher temperatures were associated with reduced fecundity and longer time to pregnancy.
- Exposure-response relationships exhibited a monotonic manner.
- Decline in fecundity associated with rising temperatures was stronger in the East, South, and North regions.
- The associations were stronger in couples where the woman was overweight/obese or exposed to second-hand smoke.
- The associations were stronger in couples where the man was overweight/obese or consumed alcohol.

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Climate change may affect fertility; however, associations between ambient temperature and human fecundity remain understudied. We assessed the relationship between temperature and fecundity in 2,443,879 reproductive-age couples from 350 cities across China, with follow-up every 3 months until conception or for up to 1 year. We used Cox regression models to evaluate associations of 1-year, 6-month, and 3-month average temperature exposures preceding conception or censoring with fecundability odds ratios (FORs). Accelerated failure time and multivariate linear regression models were applied to examine associations between temperature and time to pregnancy (TTP). During the one-year follow-up, 2,038,378 (83.4%) couples conceived. Higher temperatures were associated with reduced fecundity and extended TTP, with monotonic exposure-response curves observed. Specifically, a 1°C increase in 1-year average temperature was associated with a 4.2% decrease in fecundity (FOR=0.958, 95% confidence interval [CI]: 0.957, 0.959). The corresponding absolute probability of pregnancy within 1 year decreased by 1.35% (absolute risk difference=–1.35%, 95% CI: –1.41%, –1.26%). Each 1°C increase in annual average temperature was associated with a 2.5% increase in median TTP for all couples (time ratio=1.025, 95% CI: 1.024, 1.025). Among couples who conceived within 1 year, TTP was prolonged by 1.60% (95% CI: 1.55%, 1.65%). Smaller FOR estimates, indicating reduced fecundity, were observed in the East, South, and North regions; in tropical and temperate monsoon zones; and among couples where either partner was overweight/obese, woman was attempting her first pregnancy or exposed to second-hand smoke, or man consumed alcohol. Increased temperatures may adversely impact fecundity by prolonging TTP, highlighting the need for heat mitigation strategies.

INTRODUCTION

Health challenges arising from population trends and climate change warrant urgent attention.[1,2] Human fertility is declining, with the global total fertility rate (TFR)—the average number of offspring per woman—declining from 4.84 in 1950 to 2.23 in 2021.[1] Notably, this decline has been even more pronounced in China, where the TFR dropping from 5.55 in 1950 to just 1.23 in 2021.[1] Reduced human fecundity can lead to social, economic, psychological, and physical suffering,[3,4] and may alter population structure, exacerbating the burden of an aging population on healthcare and social systems.[1] Furthermore, global temperatures have increased by 1.2°C compared with that of the preindustrial period (1850–1900).[2] In China, the annual average temperature has increased by 0.26°C per decade from 1951 to 2021.[5] Although multiple factors contribute to declining fertility, climate change is emerging as a potential determinant of reproductive health.[6] As climate change progresses, its impact on global health —including reproductive health—is expected to intensify.

Climate change affects human fertility through extreme weather, pollution, and wildfires.[6-8] However, few studies have specifically addressed the effects of ambient temperature on fertility. A study conducted on pregnancies recorded by the healthcare system in Hungary reported that exposure to temperatures above 25°C had a detrimental effect on conception rates (number of conceptions per week per 100,000 women aged 16–44 years) within a short term (up to 5 weeks after exposure).[9] Another study demonstrated that mean temperatures above 26.7 °C were associated with a significant decline in birth rates 8–10 months later in United States.[10] These existing studies were retrospective and primarily focused on the short-term effects of ambient temperature. However, the impact of relatively long-term exposure to ambient temperature on human fertility remains largely unexplored.

Previous evidence documented that higher temperatures during the 90 days before ovarian reserve testing and the 10–14 days before semen collection were associated with lower antral follicle counts and reduced sperm motility, respectively.[11,12] However, these fertility-related indicators reflect the conditions of only one partner, not the couple's overall fecundity. Time to pregnancy (TTP) —the number of calendar months or menstrual cycles required to conceive —can be used to evaluate couple's fecundity at the population level, with prolonged TTP serving as an indicator of reduced fecundability.[13]

In this study, we conducted a prospective cohort investigation to examine the effect of temperature exposure on fecundity in reproductive-age couples in China, as indicated by TTP, and to develop the corresponding exposure-response curves.

MATERIALS AND METHODS

Study population and design

This study draws on data from the National Free Preconception Health Examination Project (NFPHEP), which was launched by the Chinese National Health Commission and Ministry of Finance in 2010. The design, organization, and implementation of this project have been described previously.[14,15] Briefly, NFPHEP provides free preconception physical examinations, laboratory tests, risk assessments, consultations, and early pregnancy follow-ups to couples of reproductive age who intend to conceive. Demographic data, reproductive history, menstrual information, lifestyle factors, and residential addresses were collected through face-to-face interviews conducted by experienced local health professionals using standardized questionnaires.[16,17] Physical examinations and laboratory tests, including measurements of height, weight, blood pressure, and fasting venous blood sample collection for glucose testing in female partners, were also conducted. Follow-up was performed every 3 months via telephone interviews for up to 12 months after the preconception health examination. Hospital-based gynecologic type B ultrasound tests were performed to confirm conception.

From January 1, 2010 to December 31, 2015, 3,964,553 couples from 350 cities across 31 Chinese provincial-level administrative regions (Figure 1) participated in the NFPHEP. Female participants were aged 20–49 years and male participants were aged 22–60 years. Couples enrolled in the study confirmed that the women were not pregnant and were actively planning pregnancy. We excluded couples if either partner had medical conditions that could impair fertility or pose risks to pregnancy, including: self-reported physician-diagnosed infertility in either the female or male partner; uterine or adnexal structural abnormalities or reproductive organ developmental anomalies in the female partner identified via gynecological B-ultrasound; *Treponema pallidum* or cytomegalovirus infection in the female partner; varicocele, testicular loss, or epididymal abnormalities in the male partner identified via reproductive organ examination; or *Treponema pallidum* infection in the male partner. Additionally, we excluded couples if the female partner reported irregular menstrual cycles or had incomplete menstrual data, if pregnancy occurred in the first menstrual cycle after the preconception health examination, or if sociodemographic, lifestyle, or exposure data were missing (Figure S1).

The Institutional Review Board of the National Research Institute for Family Planning, Beijing, China approved the study (2009-02). All participants provided written informed consent.

Outcome definition

For women with regular menstrual cycles, TTP was calculated as: (date of last menstrual period [for pregnant couples] or date of most recent follow-up [for non-pregnant couples] – date of recruitment) / average menstrual cycle length + 1.[18] TTP was rounded to the nearest whole number. Menstrual regularity and the mean menstrual cycle length were derived from self-reported menstrual data over the past 6 months during the baseline interview. Couples were followed until pregnancy was reported or for up to 1 year. TTP was considered censored if the woman was lost to follow-up or did not conceive within 1 year. Further details on the collection of menstrual information are available in Text S1.

Meteorological parameters

Daily averages of ambient temperature and relative humidity were sourced from the China Meteorological Data Service Center. The residential addresses of the participants were obtained and subsequently geocoded into longitude and latitude and matched to the nearest meteorological monitoring station. Daily mean parameters were aggregated into annual mean (lag 1 year) preceding the endpoint date (conception or censor), representing relatively long-term exposure. Given the timeframe of spermatogenesis (approximately 3 months)[19] and follicular development (approximately 4 months for primary to secondary follicle development, and 3 months for secondary to preovulatory follicle),[11,20] we considered exposure periods of 6 months (lag 6 months) and 3 months (lag 3 months) preceding conception or censor.

We further obtained temperature and relative humidity data from the fifth-generation European Centre for Medium-Range Weather Forecasts Reanalysis (ERA5) atmospheric data, which offers a spatial resolution of 0.25° × 0.25° and hourly temporal resolution. Hourly data were extracted from the nearest grid cell in the ERA5 dataset based on participants' residential addresses and averaged over 1 year, 6 months, and 3 months preceding conception or censor. The ERA5 data have been compared with station observations and demonstrated good agreement. However, it has been noted that ERA5 may underestimate heat-related health risks, particularly in tropical regions.[21] Therefore, we used meteorological data from monitoring stations as the primary exposure data for our analysis, with ERA5 data employed for sensitivity analysis to validate our findings.

Statistical analyses

Discrete-time Cox regression models were employed to estimate fecundability odds ratios (FORs) and corresponding 95% confidence intervals (CIs) for 1°C increments in one-year, six-month, and three-month mean temperatures. TTP was treated as the time scale, and pregnancy was defined as the event. FORs represent the odds of conception for each cycle per 1°C increase in temperature exposure, conditional on not being pregnant in the previous cycle.[22] FORs <1 indicate reduced fecundity or longer TTP, whereas FORs >1 denote shorter TTP.

Initially, a crude model was constructed without adjusting for any covariates. Subsequently, a directed acyclic graph (DAG) guided the selection of a minimal sufficient adjustment set,[23] which included couples' age, body mass index (BMI), ethnicity, household registration, education, occupation, annual average gross domestic product (GDP) per capita at the city level in the survey year, latitude, month and year of first follow-up, relative humidity, and province (Figure S2). Considering the complexity of factors influencing fertility,[24,25] a fully adjusted model (main model) was further developed, incorporating additional variables such as couples' active smoking, exposure to second-hand smoke, alcohol use, preexisting diseases (hypertension and diabetes), woman's gravidity, menstrual cycle length, and age at menarche. Detailed information on covariates is provided in Text S2. Based on the FOR derived from the main model, we also calculated the absolute risk difference (ARD) and the absolute reduction in the number of pregnancies across exposure windows (see Text S3).[26,27]

Figure 1. Spatial distribution of study sites and regions of China.

Given the right-skewed distribution of TTP data, accelerated failure time (AFT) models with a Weibull distribution were employed to examine the association between temperature and TTP. The results were presented as time ratios (TRs), representing the fold change in median TTP per 1 °C increase in temperature. TRs > 1 indicate a prolonged TTP.[28,29] Parallel to the Cox regression analysis, three models were constructed for the AFT analysis: a crude model, a minimally adjusted model based on the DAG, and a fully adjusted model. Additionally, among couples who achieved pregnancy within 1 year, multivariate linear regression models were used to quantify the association between temperature and TTP. TTP was natural log-transformed to address data skewness, and the results were reported as percentage changes and 95% CIs in TTP for each 1°C increase in temperature.

To explore potential nonlinear relationships, temperature was modeled using restricted cubic splines with three knots in the Cox regression framework. The nonlinear associations were characterized as FORs at a given temperature relative to a referent exposure, chosen as the temperature corresponding to the highest point on the exposure-response curve. Similarly, nonlinear associations between temperature and TTP were assessed by incorporating restricted cubic splines with three knots in AFT models and multivariate linear regression models.

Several sensitivity analyses were conducted to test the robustness of our findings. First, ground-based meteorological measurements were replaced with data from the ERA5 dataset to assess consistency across different data sources. Second, a frailty Cox model including province as a random intercept following a gamma distribution was applied to account for potential clustering at the provincial level. Third, a generalized propensity score (GPS) weighting approach was employed to estimate the effects of ambient temperature,[30] with detailed methods described in Text S4.

To investigate potential effect modification in the associations between ambient temperature and fecundity, we conducted stratified analyses focusing on regional, temporal, and physiological factors. First, considering the geographic, climatic, and socioeconomic variability across China, analyses were stratified by geographic regions (East, South, North, Central, Southwest,

Table 1. Summary characteristics of the eligible couples from the National Free Preconception Health Examination Project between 2010 and 2015.

Characteristics *N* (%) / mean ± SD	Total (*N*=2,443,879)	Not pregnancy (*N*=405,501)	Pregnancy within one year (*N*=2,038,378, 83.4%)
Women			
Age (years)	26.20 ± 3.98	26.36 ± 4.44	26.17 ± 3.89
Fasting blood glucose (mmol/L)	4.91 ± 0.94	4.90 ± 1.02	4.91 ± 0.93
Age at menarche (years)	13.86 ± 1.20	13.81 ± 1.18	13.87 ± 1.20
Body mass index (kg/m^2)			
≤ 18.5	320,626 (13.1)	51,979 (12.8)	268,647 (13.2)
18.6–23.9	1,777,900 (72.7)	296,733 (73.2)	1,481,167 (72.7)
≥ 24	345,353 (14.1)	56,789 (14.0)	288,564 (14.2)
Ethnicity			
Han	2,233,591 (91.4)	349,919 (86.3)	1,883,672 (92.4)
Others	210,288 (8.6)	55,582 (13.7)	154,706 (7.6)
Education level			
Middle school or below	1,678,209 (68.7)	290,264 (71.6)	1,387,945 (68.1)
High school	422,894 (17.3)	63,723 (15.7)	359,171 (17.6)
College or above	342,776 (14.0)	51,514 (12.7)	291,262 (14.3)
Occupation*			
Farmer	1,887,875 (77.2)	312,533 (77.1)	1,575,342 (77.3)
Worker	180,509 (7.4)	26,733 (6.6)	153,776 (7.5)
Others	375,495 (15.4)	66,235 (16.3)	309,260 (15.2)
Gravidity			
0	1,292,586 (52.9)	204,971 (50.5)	1,087,615 (53.4)
≥ 1	1,151,293 (47.1)	200,530 (49.5)	950,763 (46.6)
Active smoking			
Yes	5,690 (0.2)	1,337 (0.3)	4,353 (0.2)
No	2,438,189 (99.8)	404,164 (99.7)	2,034,025 (99.8)
Passive smoking exposure			
Yes	272,879 (11.2)	46,390 (11.4)	226,489 (11.1)
No	2,171,000 (88.8)	359,111 (88.6)	1,811,889 (88.9)
Alcohol use			
Yes	66,651 (2.7)	11,875 (2.9)	54,776 (2.7)
No	2,377,228 (97.3)	393,626 (97.1)	1,983,602 (97.3)
Menstrual cycle length (days)			
21–26	91,340 (3.7)	14,514 (3.6)	76,826 (3.8)
27–29	1,401,642 (57.4)	237,203 (58.5)	1,164,439 (57.1)
30–35	950,897 (38.9)	153,784 (37.9)	797,113 (39.1)
Hypertension			
Yes	44,712 (1.8)	8,184 (2.0)	36,528 (1.8)
No	2,399,167 (98.2)	397,317 (98.0)	2,001,850 (98.2)
Men			
Age (years)	27.92 ± 4.38	28.34 ± 4.84	27.83 ± 4.28
Body mass index (kg/m^2)			
≤ 18.5	98,106 (4.0)	17,247 (4.3)	80,859 (4.0)

Table 1. *(Continued)*

Characteristics *N* (%) / mean ± SD	Total (*N*=2,443,879)	Not pregnancy (*N*=405,501)	Pregnancy within one year (*N*=2,038,378, 83.4%)
18.6–23.9	1,592,216 (65.2)	272,853 (67.3)	1,319,363 (64.7)
≥ 24	753,557 (30.8)	115,401 (28.5)	638,156 (31.3)
Ethnicity			
Han	2,240,877 (91.7)	351,132 (86.6)	1,889,745 (92.7)
Others	203,002 (8.3)	54,369 (13.4)	148,633 (7.3)
Education level			
Middle school or below	1,623,840 (66.4)	281,364 (69.4)	1,342,476 (65.9)
High school	461,122 (18.9)	70,012 (17.3)	391,110 (19.2)
College or above	358,917 (14.7)	54,125 (13.3)	304,792 (15.0)
Occupation*			
Farmer	1,849,331 (75.7)	306,999 (75.7)	1,542,332 (75.7)
Worker	245,904 (10.1)	38,231 (9.4)	207,673 (10.2)
Others	348,644 (14.3)	60,271 (14.9)	288,373 (14.1)
Active smoking			
Yes	684,734 (28.0)	120,385 (29.7)	564,349 (27.7)
No	1,759,145 (72.0)	285,116 (70.3)	1,474,029 (72.3)
Passive smoking exposure			
Yes	595,190 (24.4)	98,497 (24.3)	496,693 (24.4)
No	1,848,689 (75.6)	307,004 (75.7)	1,541,685 (75.6)
Alcohol use			
Yes	719,142 (29.4)	118,656 (29.3)	600,486 (29.5)
No	1,724,737 (70.6)	286,845 (70.7)	1,437,892 (70.5)
Hypertension			
Yes	123,402 (5.0)	20,880 (5.1)	102,522 (5.0)
No	2,320,477 (95.0)	384,621 (94.9)	1,935,856 (95.0)

Abbreviation: SD, standard deviation. *Worker indicates industrial or construction workers, and other occupation indicates non-labor workers.

and Northwest China; Figure 1), climatic zones (alpine, tropical monsoon, temperate continental, temperate monsoon, and subtropical monsoon; Figure S3), and socioeconomic development indicators, including rural and urban residence and quartiles of city-level annual GDP per capita. Second, temporal variation was assessed by stratifying according to the season in which couples initiated conception attempts. Third, we explored potential effect modification by individual-level demographic and behavioral factors that may influence fecundability[31-37] or alter susceptibility to environmental exposures. For female partners, these included age (<35 vs. ≥35 years), BMI (<24 vs. ≥24 kg/m^2), educational attainment (middle school or below vs. high school or above), gravidity (0 vs. ≥1), active smoking (yes vs. no), passive smoking exposure (yes vs. no), and alcohol use (yes vs. no). Corresponding stratifications were applied to male partners based on the same factors, excluding gravidity. A multiplicative interaction term between annual mean temperature and each individual-level factor was introduced into the model separately. If the Wald test *p*-value for the interaction term was <0.05, we proceeded to fit separate models within each stratum of the effect modifier to estimate stratum-specific associations. Statistical differences between stratum-specific estimates were tested using 2-sample *z*-tests with the following formula:

$$z = \frac{\beta_1 - \beta_2}{\sqrt{SE_1^2 + SE_2^2}}$$

where β_1 and β_2 represent the stratum-specific regression coefficients, and SE_1 and SE_2 are the corresponding standard errors.[38] To account for multiple comparisons and reduce the likelihood of false positives, the Benjamini–Hochberg correction was applied, and adjusted *p*-values were reported.

Statistical analyses were conducted using R software (version 4.1.2) with the *survival*, *survminer*, and *rms* packages. All statistical tests were two-sided, with statistical significance defined as a *p*-value < 0.05.

RESULTS

Descriptive data

After applying the exclusion criteria (Figure S1), the analysis included 2,443,879 couples from 350 cities in China. Participants who were excluded from the analyses had similar characteristics to those included (Table S1). Of the included couples, the median time to pregnancy was five cycles. Most participants were of Han ethnicity and had an educational level of high school or below. The mean (± standard deviation [SD]) ages of the women and their male partners were 26.20 (± 3.98) years and 27.92 (± 4.38) years, respectively. Men were more likely to be overweight or obese than women (30.8% vs. 14.1%) (Table 1). Within the 1-year follow-up period, 2,038,378 (83.4%) couples conceived.

The means (± SD) of ambient temperature during the periods of 1 year, 6 months, and 3 months preceding conception or censor were 15.8 (± 3.7), 15.7 (± 6.7), and 16.1 (± 8.5) °C, respectively (Table 2). Annual mean temperatures varied significantly across geographic regions (range: 10.2–21.7 °C) and climatic zones (range: 8.2–20.3 °C) (Table S2).

Table 2. Summary statistics for average temperature during different exposure windows (°C).

Exposure window	Mean ± SD	Min	P25	Medium	P75	Max
Lag 1 year	15.8 ± 3.7	-5.1	14.1	15.8	17.8	26.3
Lag 6 months	15.7 ± 6.7	-20.4	10.6	16.2	21.4	29.4
Lag 3 months	16.1 ± 8.5	-27.6	9.5	17.3	23.6	32.7

Abbreviation: SD, standard deviation; P25, the 25th percentile; P75, the 75th percentile.

Table 3. Fecundability odds ratios (95% confidence intervals) associated with 1°C increase in 1-year, 6-month, and 3-month average ambient temperature (*N*=2,443,879).

Exposure windows	Fecundability odds ratio estimates		
	The crude model	The minimal sufficient adjustment model[a]	The main model[b]
Lag 1 year	0.975 (0.974, 0.976)	0.959 (0.958, 0.960)	0.958 (0.957, 0.959)
Lag 6 months	0.990 (0.990, 0.991)	0.983 (0.983, 0.983)	0.983 (0.983, 0.983)
Lag 3 months	0.994 (0.994, 0.994)	0.990 (0.989, 0.990)	0.990 (0.989, 0.990)

[a]Adjusted for couples' age, BMI, ethnicity, household registration, education, occupation, latitude, annual average gross domestic product per capita at the city level, month and year of first follow-up, relative humidity, and province.

[b]Adjusted for couples' age, BMI, ethnicity, household registration, education, occupation, active smoking, exposure to second-hand smoke, alcohol use, disease state (hypertension and diabetes (woman only)), woman's gravidity, menstrual cycle length, age at menarche, latitude, annual average gross domestic product per capita at the city level, month and year of first follow-up, relative humidity, and province.

Associations of ambient temperature with fecundability odds ratios

Associations between temperature and FORs were consistent across the three models (Table 3). In the main model, a 1°C increase in average temperature over 1 year, 6 months, and 3 months was associated with a 4.2% (FOR=0.958, 95% CI: 0.957, 0.959), 1.7% (FOR=0.983, 95% CI: 0.983, 0.983), and 1.0% (FOR=0.990, 95% CI: 0.989, 0.990) decrease in fecundity, respectively. When using temperature data extracted from the ERA5 dataset, the estimates for FOR associated with temperature were similar to those based on monitoring station data (Table S3). Applying frailty Cox models that incorporated province as a random intercept term yielded FOR estimates consistent with those from the main models that treated province as a fixed-effect covariate (Table S4). In the GPS weighting approach, the mean AC ranged from 0.019 to 0.079 across different temperature exposure windows, indicating that covariate balance was achieved. Although the estimated effects were slightly attenuated, the overall findings remained consistent and robust (Table S5).

The absolute probability of conception within 1 year decreased by 1.35% (ARD=−1.35%, 95% CI: −1.41%, −1.26%), 0.45% (ARD=−0.45%, 95% CI: −0.47%, −0.42%), and 0.28% (ARD=−0.28%, 95% CI: −0.30%, −0.26%) per 1°C increase in average temperature over 1 year, 6 months, and 3 months, respectively. This corresponds to an estimated additional 33.0 (95% CI: 30.8, 34.5), 11.0 (95% CI: 10.3, 11.5), and 6.8 (95% CI: 6.4, 7.3) thousand couples nationwide who could not achieve conception within 1 year, respectively (Table S6). Additionally, the FORs exhibited a monotonic downward trend with increasing mean temperature across the three exposure windows (Figure 2).

Associations of ambient temperature with time to pregnancy

Among all couples, ambient temperature exposure was significantly associated with a longer TTP, indicating reduced fecundity. Specifically, each 1°C increase in average temperature over 1 year, 6 months, and 3 months was associated with a 2.5% (TR=1.025, 95% CI: 1.024, 1.025), 0.9% (TR=1.009, 95% CI: 1.009, 1.010), and 0.5% (TR=1.005, 95% CI: 1.005, 1.005) increase in median TTP, respectively (Table 4). The TRs showed monotonic increasing trends with higher temperatures across all three exposure periods (Figure S4). These associations remained robust when temperature exposure was assessed using the ERA5 dataset (Table S7). Similarly, results from the GPS weighting approach remained consistent with our main findings, although the effect sizes were slightly attenuated (Table S8).

For couples achieving pregnancy within 1 year, TTP was prolonged by 1.60% (95% CI: 1.55%, 1.65%), 0.73% (95% CI: 0.71%, 0.74%), and 0.47% (95% CI: 0.46%, 0.48%) per 1°C increase in mean ambient temperature over 1 year, 6 months, and 3 months, respectively (Table 5). A consistent percentage increase in TTP with increasing temperatures was also observed in this population (Figure S5). The results from the main model demonstrated minimal variations when substituting temperature and relative humidity data from weather stations with those from the ERA5 dataset (Table S9).

Associations of annual mean temperature with fecundity based on regions

Associations between annual mean ambient temperature and FORs varied significantly across geographic regions (Table S10), with the greatest effect estimates in the East (FOR=0.949, 95% CI: 0.947, 0.951), followed by the South (FOR=0.951, 95% CI: 0.949, 0.954), North (FOR=0.952, 95% CI: 0.948, 0.956), Central (FOR=0.957, 95% CI: 0.954, 0.960), Southwest (FOR=0.975, 95% CI: 0.973, 0.977), and Northwest (FOR=0.986, 95% CI: 0.984, 0.988) regions. The results for TTP were typically consistent with those for FOR, showing the most pronounced prolongations in the South (TR=1.027, 95% CI: 1.026, 1.028) and East (TR=1.026, 95% CI: 1.025, 1.027), followed by the North (TR=1.024, 95% CI: 1.022, 1.025), Central (TR=1.017, 95% CI: 1.015, 1.018), Southwest (TR=1.103, 95% CI: 1.012, 1.014), and Northwest (TR=1.009, 95% CI: 1.008, 1.010) regions (Table S11).

The associations between annual mean temperature and fecundity differed across climatic zones. The strongest associations were observed in the tropical (FOR=0.941, 95% CI: 0.936, 0.946) and temperate (FOR=0.945, 95% CI: 0.943, 0.946) monsoon zones, followed by the subtropical monsoon zone (FOR=0.963, 95% CI: 0.962, 0.965), alpine zone (FOR=0.979, 95% CI: 0.972, 0.986), and temperate continental zone (FOR=0.997, 95% CI: 0.994, 1.000) (Table S12). The corresponding TRs exhibited a consistent pattern across climatic zones (Table S13).

Associations between annual temperature and FOR were stronger in couples from urban areas (women: FOR=0.950, 95% CI: 0.946, 0.954; men: FOR=0.950, 95% CI: 0.947, 0.953) than those from rural areas (FOR=0.959, 95% CI: 0.958, 0.960) (Table S14). A 1°C increase in annual mean temperature was associated with a greater decline in fecundability in cities with higher GDP per capita, with the strongest effect observed in the highest quartile group (FOR=0.943, 95% CI: 0.941, 0.945) (Table S15).

Associations of annual mean temperature with fecundity based on seasons

Temperature-related reductions in fecundability varied by season when couples initiated conception attempts. Specifically, the strongest association was observed among couples who attempted to conceive in the summer

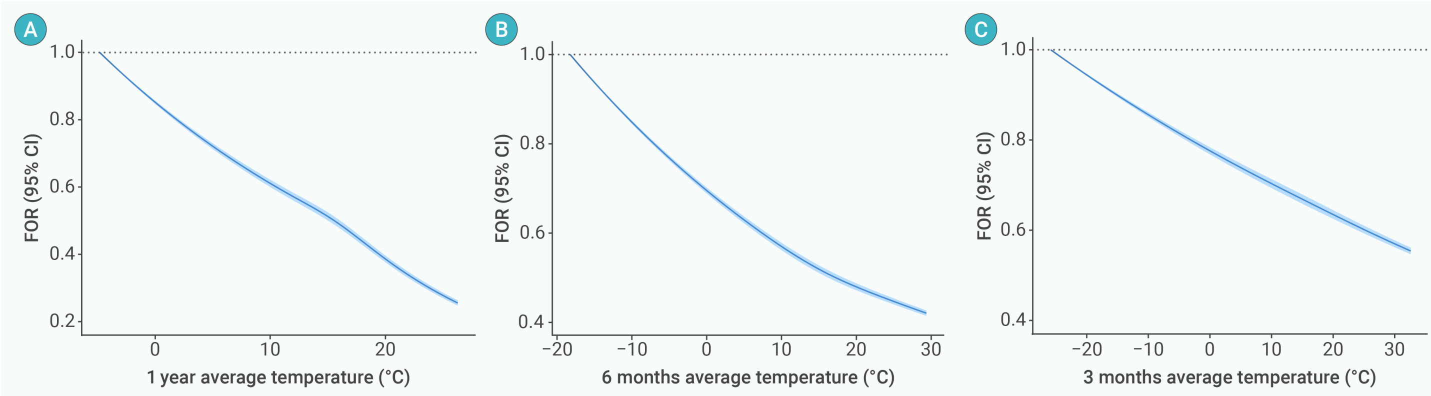

Figure 2. Exposure-response curves for 1-year (A), 6-month (B), and 3-month (C) average ambient temperature and fecundability odds ratios (*N*=2,443,879).

Table 4. Time ratios (95% confidence intervals) associated with 1°C increase in 1-year, 6-month, and 3-month average ambient temperature (*N*=2,443,879).

Exposure windows	Time ratios		
	The crude model	The minimal sufficient adjustment model[a]	The main model[b]
Lag 1 year	1.015 (1.014, 1.015)	1.024 (1.024, 1.025)	1.025 (1.024, 1.025)
Lag 6 months	1.005 (1.005, 1.005)	1.009 (1.009, 1.010)	1.009 (1.009, 1.010)
Lag 3 months	1.003 (1.003, 1.003)	1.005 (1.005, 1.005)	1.005 (1.005, 1.005)

[a]Adjusted for couples' age, BMI, ethnicity, household registration, education, occupation, latitude, annual average gross domestic product per capita at the city level, month and year of first follow-up, relative humidity, and province.
[b]Adjusted for couples' age, BMI, ethnicity, household registration, education, occupation, active smoking, exposure to second-hand smoke, alcohol use, disease state (hypertension and diabetes (woman only)), woman's gravidity, menstrual cycle length, age at menarche, latitude, annual average gross domestic product per capita at the city level, month and year of first follow-up, relative humidity, and province.

Table 5. Percentage changes (95% confidence intervals) in time to pregnancy associated with 1°C increase in 1-year, 6-month, and 3-month average ambient temperature among couples achieving pregnancy within 1 year (*N*=2,038,378).

Exposure windows	Percentage changes in time to pregnancy (%)		
	The crude model	The minimal sufficient adjustment model[a]	The main model[b]
Lag 1 year	1.01 (0.97, 1.05)	1.56 (1.51, 1.61)	1.60 (1.55, 1.65)
Lag 6 months	0.38 (0.37, 0.39)	0.73 (0.72, 0.75)	0.73 (0.71, 0.74)
Lag 3 months	0.17 (0.17, 0.18)	0.47 (0.46, 0.48)	0.47 (0.46, 0.48)

[a]Adjusted for couples' age, BMI, ethnicity, household registration, education, occupation, latitude, annual average gross domestic product per capita at the city level, month and year of first follow-up, relative humidity, and province.
[b]Adjusted for couples' age, BMI, ethnicity, household registration, education, occupation, active smoking, exposure to second-hand smoke, alcohol use, disease state (hypertension and diabetes (woman only)), woman's gravidity, menstrual cycle length, age at menarche, latitude, annual average gross domestic product per capita at the city level, month and year of first follow-up, relative humidity, and province.

(FOR=0.946, 95% CI: 0.944, 0.948), followed by autumn (FOR=0.950, 95% CI: 0.948, 0.952) and spring (FOR=0.956, 95% CI: 0.954, 0.958). The weakest association was observed among those who attempted in the winter (FOR=0.973, 95% CI: 0.971, 0.975) (Table S16).

Associations of annual mean temperature with fecundity based on couples' characteristics

The *p*-values for multiplicative interactions between annual mean temperature and education, female partners' active smoking and alcohol use, and male partners' age were greater than 0.05; hence, stratified analyses were not conducted for these variables. Significant multiplicative interactions were observed between temperature and couples' BMI, passive smoking exposure, female partners' age and gravidity, as well as male partners' active smoking and alcohol use (p-values for interaction <0.05) (Table S17). In stratified analyses, temperature-related reductions in fecundity were more pronounced in couples who were overweight or obese (women: FOR=0.955, 95% CI: 0.952, 0.957 vs. FOR=0.958, 95% CI: 0.957, 0.959; men: FOR=0.955, 95% CI: 0.953, 0.957 vs. FOR=0.959, 95% CI: 0.958, 0.960) than those who were not. Associations between temperature and FOR were higher in women exposed to second-hand smoke (FOR=0.951, 95% CI: 0.948, 0.953) than those unexposed (FOR=0.959, 95% CI: 0.958, 0.960), in men who did not actively smoke (FOR=0.956, 95% CI: 0.955, 0.957) than smokers (FOR=0.962, 95% CI: 0.960, 0.964), and in men who consumed alcohol (FOR=0.953, 95% CI: 0.951, 0.955) than non-drinkers (FOR=0.960, 95% CI: 0.959, 0.961). The association was higher for women trying to conceive for the first time (FOR=0.953, 95% CI: 0.951, 0.954) than others (FOR=0.961, 95% CI: 0.959, 0.962). However, no statistically significant differences were observed between women aged ≥35 years and those younger (adjusted *p*-value for inter-group comparisons= 0.763) or between men exposed and unexposed to second-hand smoke (adjusted *p*-value for inter-group comparisons=0.482).

DISCUSSION

In this cohort study, we found that higher temperatures were associated with reduced fecundity and longer TTP, with clear monotonic exposure-response curves. The decline in fecundability associated with increasing temperatures was more significant in the East, South, and North regions of China, as well as in the tropical and temperate monsoon zones. The effects were also stronger in couples where the woman was overweight or obese, attempting her first pregnancy, or exposed to second-hand smoke, or where the man was overweight, obese, or consumed alcohol.

Our study shows that higher temperatures over 1 year, 6 months, and 3 months are linked to prolonged TTP and reduced fecundity. Although limited research has directly connected environmental temperature with human fecundity, several studies have observed similar trends. Hajdu et al. found that in Hungary, exposure to high temperatures (daily mean temperature > 25°C) reduced conceptions within 5 weeks, with the strongest effect occurring 2–4 weeks post-exposure.[9] Similarly, Gudziunaite et al. reported a decline in successful conceptions in Vienna following same-week exposure to high temperatures.[39] Additionally, Barreca et al. observed that each day with temperatures exceeding 26.7°C in the United States was linked to a decline in birth rates approximately 8–10 months later.[10] However, these studies mainly focused on short-term temperature exposure and used population-level indicators, such as conception and birth rates. To our knowledge, our study is the first nationwide analysis in China to examine the relationship between relatively long-term exposure to ambient temperature and couples' fecundity.

Although the biological mechanisms underlying the reduced fecundity associated with higher temperatures remain unclear, several explanations are possible. Previous human studies have documented relationships between higher temperatures and lower ovarian reserve[11] and semen quality,[19,40] suggesting that elevated temperatures may impair fertility by harming gamete development. Animal studies also support this hypothesis; for example, high temperatures in dairy cows have been linked to impaired oocyte maturation, decreased developmental capacity, and reduced fecundity.[41,42] In male mice, elevated temperatures increased apoptosis of germ and Leydig cells, reduced Sertoli cell efficiency, and resulted in deficient sperm output.[43,44] Moreover, high temperatures were associated with poorer early embryonic development success and a higher risk of pregnancy loss in dairy cows.[45,46] Besides biological mechanisms, temperature might affect reproductive outcomes by influencing sexual activity patterns.[10] Although most sexual activity occurs indoors, where direct exposure to outdoor temperatures is limited, stressful temperatures—especially during the day—may cause thermal discomfort and fatigue, potentially reducing nighttime sexual activity and coital frequency.[39]

We found that the impacts of temperature on fecundity varied depending on the duration of exposure. The negative effects became progressively more pronounced with longer exposure periods. Previous studies have also identified cumulative effects of heat.[47] Prolonged exposure to high temperatures may place continuous stress on physiological systems.[48] Chronic stress decreases fertility by damaging oocyte maturation and development, and reducing semen quality.[49,50] We hypothesize that the cumulative effect of heat exposure may impair long-term development potential of gametes. Shorter exposure windows (e.g., 3 months) may not capture these cumulative effects, especially if they occur during the colder months, missing the residual effects of summer heat. The season in which couples begin attempting to conceive may also influence their susceptibility to temperature-related impacts, suggesting that environmental conditions prior to conception may affect reproductive potential.

The impact of elevated temperatures on pregnancy likelihood was more pronounced in East, South, and North China—regions with higher economic status and urbanization. This finding suggests that socioeconomic factors may increase vulnerability to heat-related reproductive risks. The observed stronger associations between higher temperatures and reduced fecundability in areas with higher GDP per capita further support this hypothesis. Regions with higher economic status and urbanization are prone to the heat island effect because of their denser populations, increased energy consumption, and more complex built environments (such as heat-retaining impervious surfaces that inhibit nighttime cooling).[51] Additionally, economic development is associated with decreased fertility,[52] which may be associated with delayed pregnancies.[53] Other climatic factors may also play a role. The East and South regions are characterized by high humidity during periods of extreme heat, which may amplify the adverse health effects associated with high temperatures.[54] Moreover, the temperature-related decline in fecundability varied across climatic zones, which may reflect both variations in ambient temperature and differences in population-level heat adaptability. The tropical monsoon zone, known for its comparatively hotter climate than other zones (as shown in Table S2), shows the strongest negative association.[55,56] Besides, the association was more pronounced in the temperate monsoon zone, which may be attributed to the relatively lower heat adaptation capacity of populations in this region.[57]

Overweight or obese individuals may be more sensitive to high temperature, owing to different metabolism and thermoregulation efficiency, making them less physiologically adaptable to temperature.[58] This study found that women's exposure to second-hand smoke and men's alcohol consumption may cause greater reductions in temperature-related fecundity. Exposure to tobacco smoke can alter hormone output and affect ovarian function,[59] while alcohol consumption deteriorates sperm maturity and damages DNA integrity.[34] However, in this study, male smoking did not appear to exacerbate temperature-related declines in fecundity, despite the percentage of couples conceiving within 1 year being lower in the smoking group (82.4% vs. 83.8% in non-smokers). This unexpected observation may be explained by a "ceiling effect" of smoking. Smoking is a well-established risk factor for reduced sperm quality and fertility.[33,60] For smokers —whose sperm quality may already be compromised to a certain extent —the incremental impact of heat exposure may be less pronounced or masked, whereas non-smokers, starting with relatively better baseline sperm quality, may exhibit more noticeable adverse effects from heat. Future studies should focus on exploring the combined effects of smoking and environmental factors on fertility. Regardless, promoting healthy lifestyles and maintaining healthy BMI may mitigate fecundity decline and help cope with challenges posed by climate change. We observed that attempting to conceive for the first time may experience more physiological stress and uncertainty, making them more vulnerable to environmental stressors.

These findings have important public health implications for the development of heat mitigation strategies and environmental policies aimed at preserving reproductive health, particularly in regions experiencing sustained temperature increases owing to climate change. Although the temperature-related reduction in fecundity may appear modest at the individual level—a 1°C increase in annual mean temperature was associated with a 1.35% decrease in conception probability within 1 year —may have substantial public health consequences. Based on our data, such a shift could result in approximately 33,000 additional couples in China failing to achieve pregnancy within 1 year. Prolonged TTP causes psychological stress and increases reliance on assisted reproductive technologies, placing additional demands on reproductive health services. Importantly, the exposure-response curves suggest no threshold for the relationship between temperature and fecundity, indicating that fertility declines continuously with increasing temperatures. Without timely and effective interventions, climate change could increasingly burden fertility.

Our study has several strengths. It is longitudinal, which allows us to establish temporality. With more than 2.4 million couples, this nationwide cohort study enhances the generalizability of the results and ensures a sufficient sample size to examine associations among subpopulations. Additionally, we employed the TTP metric to assess couples' overall fecundity and adjusted for key confounders that influence male and female fertility. This study is the first to explore the effects of ambient temperature on TTP and establish an exposure-response relationship in China.

However, our study has limitations. First, we relied on ambient temperature data, without considering indoor temperature or activity patterns, which could lead to misclassification bias. Second, although we accounted for several potential confounders, there may be unmeasured factors, such as physical activity, family history of infertility, income level, or use of air conditioning, that could influence the results. Third, recall and reporting bias may affect self-reported data on factors like menstrual information, smoking, and alcohol consumption. Fourth, the study did not collect data on the duration of pregnancy attempts before enrollment, which could lead to an underestimation of the true TTP and an overestimation of the proportion of pregnancies achieved within 1 year. Consequently, the associations observed between ambient temperature exposure and fecundity outcomes may be conservative estimates of the true effects. However, a retrospective subsurvey using NFPHEP demonstrated that most participants were early in their conception attempts at recruitment, which may help to mitigate concerns about misclassification of TTP or FOR.[61] Finally, NFPHEP was initially launched in rural areas and later expanded to urban regions. As a result, the majority of participants in our study were from rural areas, which may limit the generalizability of the findings to urban couples with higher SES to some extent. However, stratified analyses based on rural/urban area suggest that we may have underestimated the overall effects across the entire population. Future studies with more balanced urban-rural representation are needed to fully understand the broader implications of socioeconomic and environmental factors on reproductive health.

CONCLUSION

Exposure to higher temperatures may negatively impact human fecundity by prolonging TTP in China. Given the significant consequences for public health, future research should aim to replicate these findings and identify physiological mechanisms behind these effects.

REFERENCES

1. GBD 2021 Fertility and Forecasting Collaborators. (2024). Global fertility in 204 countries and territories, 1950-2021, with forecasts to 2100: A comprehensive demographic analysis for the Global Burden of Disease Study 2021. *Lancet* **403**:2057–2099. DOI:10.1016/S0140-6736(24)00550-6
2. Romanello M., McGushin A., Di Napoli C., et al. (2021). The 2021 report of the Lancet Countdown on health and climate change: Code red for a healthy future. *Lancet* **398**:1619–1662. DOI:10.1016/s0140-6736(21)01787-6
3. Temitope L. (2022). A qualitative synthesis of the impact of infertility on the mental health of African women. *Afr. J. Reprod. Health* **26**:49–57. DOI:10.29063/ajrh2022/v26i12.6
4. Öztürk R., Bloom T. L., Li Y., et al. (2021). Stress, stigma, violence experiences and social support of US infertile women. *J. Reprod. Infant. Psychol.* **39**:205–217. DOI:10.1080/02646838.2020.1754373
5. China meteorological administration. (2022). Chapter 1: Atmosphere. Yang F., Li J. (ed). Blue Book on Climate Change in China (2022) (Beijing: Science Press), pp: 11-44. ISBN: 978-7-03-072789-3
6. Segal T. R. and Giudice L. C. (2022). Systematic review of climate change effects on reproductive health. *Fertil. Steril.* **118**:215–223. DOI:10.1016/j.fertnstert.2022.06.005
7. Girardi G. and Bremer A. A. (2022). Effects of climate and environmental changes on women's reproductive health. *J. Womens Health (Larchmt)* **31**:755–757. DOI:10.1089/jwh.2021.0631
8. Chalupka S. M., Latter A. and Trombley J. (2023). Climate and environmental change: A generation at risk. *MCN Am. J. Matern. Child Nurs.* **48**:181–187. DOI:10.1097/nmc.0000000000000924
9. Hajdu T. and Hajdu G. (2021). Temperature, climate change, and human conception rates: Evidence from Hungary. *J. Popul. Econ.* **35**:1751–1776. DOI:10.1007/s00148-020-00814-1
10. Barreca A., Deschenes O. and Guldi M. (2018). Maybe next month. *Temperature shocks and dynamic adjustments in birth rates. Demography* **55**:1269–1293. DOI:10.1007/s13524-018-0690-7
11. Gaskins A. J., Minguez-Alarcon L., VoPham T., et al. (2021). Impact of ambient temperature on ovarian reserve. *Fertil. Steril.* **116**:1052–1060. DOI:10.1016/j.fertnstert.2021.05.091
12. Zhang X., Fan Z., Wang Q., et al. (2023). Association between ambient temperature and semen quality among sperm donation volunteers in South China. *Environ. Int.* **173**:107809. DOI:10.1016/j.envint.2023.107809
13. Joffe M. (1997). Time to pregnancy: A measure of reproductive function in either sex. *Asclepios Project. Occup. Environ. Med.* **54**:289–295. DOI:10.1136/oem.54.5.289
14. Zhang S., Wang Q. and Shen H. (2015). Design of the national free proception health examination project in China. *Zhonghua Yi Xue Za Zhi* **95**:162–165. DOI:10.3760/cma.j.issn.0376-2491.2015.03.002
15. Shen Y., Jiang L., Xie X., et al. (2024). Long-term exposure to fine particulate matter and fasting blood glucose and diabetes in 20 million Chinese women of reproductive age. *Diabetes Care* **47**:1400–1407. DOI:10.2337/dc23-2153
16. Zhao J., Xuan Y., Zhang Y., et al. (2023). Assessment of prior infection with hepatitis B virus and fecundability in couples planning pregnancy. *JAMA Netw. Open* **6**:e2330870. DOI:10.1001/jamanetworkopen.2023.30870
17. Yang Y., Guo T., Fu J., et al. (2022). Association of preconception thyrotropin levels with fecundability and risk of spontaneous abortion in China. *JAMA Netw. Open* **5**:e2228892. DOI:10.1001/jamanetworkopen.2022.28892
18. Hong X., Zhao J., Huang K., et al. (2019). Preconception blood pressure and time to pregnancy among couples attempting to conceive their first pregnancy. *Am. J. Obstet. Gynecol.* **221**:470 e471-470 e410. DOI:10.1016/j.ajog.2019.05.038
19. Zhou Y., Meng T., Wu L., et al. (2020). Association between ambient temperature and semen quality: A longitudinal study of 10 802 men in China. *Environ. Int.* **135**:105364. DOI:10.1016/j.envint.2019.105364
20. Pang L., Jiang M., Sui X., et al. (2024). Association of PM2.5 mass and its components with ovarian reserve in a northern peninsular province, China: The critical exposure period and components. *J. Hazard. Mater.* **462**:132735. DOI:10.1016/j.jhazmat.2023.132735
21. Mistry M. N., Schneider R., Masselot P., et al. (2022). Comparison of weather station and climate reanalysis data for modelling temperature-related mortality. *Sci. Rep.* **12**:5178. DOI:10.1038/s41598-022-09049-4
22. Velez M. P., Arbuckle T. E. and Fraser W. D. (2015). Maternal exposure to perfluorinated chemicals and reduced fecundity: The MIREC study. *Hum. Reprod.* **30**:701–709. DOI:10.1093/humrep/deu350
23. Textor J., van der Zander B., Gilthorpe M. S., et al. (2016). Robust causal inference using directed acyclic graphs: The R package 'dagitty'. *Int. J. Epidemiol.* **45**:1887–1894. DOI:10.1093/ije/dyw341
24. Sharma R., Biedenharn K. R., Fedor J. M., et al. (2013). Lifestyle factors and reproductive health: Taking control of your fertility. *Reprod. Biol. Endocrinol.* **11**:66. DOI:10.1186/1477-7827-11-66
25. Cao Y., Zhao X., Dou Z., et al. (2024). The correlation between menstrual characteristics and fertility in women of reproductive age: A systematic review and meta-analysis. *Fertil. Steril.* **122**:918–927. DOI:10.1016/j.fertnstert.2024.06.016
26. Zhong V. W., Van Horn L., Cornelis M. C., et al. (2019). Associations of dietary cholesterol or egg consumption with incident cardiovascular disease and mortality. *JAMA* **321**:1081–1095. DOI:10.1001/jama.2019.1572
27. Zhong V. W., Van Horn L., Greenland P., et al. (2020). Associations of processed meat, unprocessed red meat, poultry, or fish intake with incident cardiovascular disease and all-cause mortality. *JAMA Intern. Med.* **180**:503–512. DOI:10.1001/jamainternmed.2019.6969
28. Tong M., Lu H., Xu H., et al. (2024). Reduced human fecundity attributable to ambient fine particles in low- and middle-income countries. *Environ. Int.* **189**:108784. DOI:10.1016/j.envint.2024.108784
29. Patel K., Kay R. and Rowell L. (2006). Comparing proportional hazards and accelerated failure time models: an application in influenza. *Pharm. Stat.* **5**:213–224. DOI:10.1002/pst.213
30. Wu X., Braun D., Schwartz J., et al. (2020). Evaluating the impact of long-term exposure to fine particulate matter on mortality among the elderly. *Sci. Adv.* **6**:eaba5692. DOI:10.1126/sciadv.aba5692
31. Broekmans F. J., Soules M. R. and Fauser B. C. (2009). Ovarian aging: Mechanisms and clinical consequences. *Endocr. Rev.* **30**:465–493. DOI:10.1210/er.2009-0006
32. Broughton D. E. and Moley K. H. (2017). Obesity and female infertility: Potential mediators of obesity's impact. *Fertil. Steril.* **107**:840–847. DOI:10.1016/j.fertnstert.2017.01.017
33. Practice Committee of the American Society for Reproductive Medicine. Electronic address a. a. o. (2024). Tobacco or marijuana use and infertility: A committee opinion. *Fertil. Steril.* **121**:589–603. DOI:10.1016/j.fertnstert.2023.12.029
34. Amor H., Hammadeh M. E., Mohd I., et al. (2022). Impact of heavy alcohol consumption and cigarette smoking on sperm DNA integrity. *Andrologia* **54**:e14434. DOI:10.1111/and.14434
35. Bitler M. and Schmidt L. (2006). Health disparities and infertility: Impacts of state-level insurance mandates. *Fertil. Steril.* **85**:858–865. DOI:10.1016/j.fertnstert.2005.11.038
36. Xu H., Feng G., Yang R., et al. (2023). OvaRePred: Online tool for predicting the age of fertility milestones. *The Innovation* **4**:100490. DOI:10.1016/j.xinn.2023.100490
37. Xu H., Feng G., Yang R., et al. (2025). Reaffirming the role of ovarian reserve in fertility assessment: Insights from OvaRePred. *Innov. Med.* **3**:100135. DOI:10.59717/j.xinn-med.2025.100135
38. Chen R., Jiang Y., Hu J., et al. (2022). Hourly air pollutants and acute coronary syndrome onset in 1.29 million patients. *Circulation* **145**:1749-1760. DOI:10.1161/CIRCULATIONAHA.121.057179
39. Gudziunaite S. and Moshammer H. (2022). Temporal patterns of weekly births and conceptions predicted by meteorology, seasonal variation, and lunar phases. *Wien. Klin. Wochenschr.* **134**:538–545. DOI:10.1007/s00508-022-02038-7
40. Santi D., Magnani E., Michelangeli M., et al. (2018). Seasonal variation of semen parameters correlates with environmental temperature and air pollution: A big data analysis over 6 years. *Environ. Pollut.* **235**:806–813. DOI:10.1016/j.envpol.2018.01.021
41. Sammad A., Umer S., Shi R., et al. (2020). Dairy cow reproduction under the influence of heat stress. *J. Anim. Physiol. Anim. Nutr. (Berl)* **104**:978–986. DOI:10.1111/jpn.13257
42. Roth Z. (2017). Effect of heat stress on reproduction in dairy cows: Insights into the cellular and molecular responses of the oocyte. *Annu. Rev. Anim. Biosci.* **5**:151–170. DOI:10.1146/annurev-animal-022516-022849
43. Wechalekar H., Setchell B. P., Pilkington K. R., et al. (2016). Effects of whole-body heat on male germ cell development and sperm motility in the laboratory mouse. *Reprod. Fertil. Dev.* **28**:545–555. DOI:10.1071/rd13395
44. Costa G. M. J., Lacerda S., Figueiredo A. F. A., et al. (2018). Higher environmental temperatures promote acceleration of spermatogenesis in vivo in mice (Mus

musculus). *J. Therm. Biol.* 77:14–23. DOI:10.1016/j.jtherbio.2018.07.010
45. Pavani K., Carvalhais I., Faheem M., et al. (2015). Reproductive performance of holstein dairy cows grazing in dry-summer subtropical climatic conditions: Effect of heat stress and heat shock on meiotic competence and in vitro fertilization. *Asian-Australas J. Anim. Sci.* 28:334–342. DOI:10.5713/ajas.14.0480
46. Santolaria P., López-Gatius F., García-Ispierto I., et al. (2010). Effects of cumulative stressful and acute variation episodes of farm climate conditions on late embryo/early fetal loss in high producing dairy cows. *Int. J. Biometeorol.* 54:93–98. DOI:10.1007/s00484-009-0258-8
47. Wang L., Di J., Wang Q., et al. (2024). Heat exposure induced risks of preterm birth mediated by maternal hypertension. *Nat. Med.* 30:1974–1981. DOI:10.1038/s41591-024-03002-w
48. Greaney J. L., Kenney W. L. and Alexander L. M. (2016). Sympathetic regulation during thermal stress in human aging and disease. *Auton. Neurosci.* 196:81–90. DOI:10.1016/j.autneu.2015.11.002
49. Casillas F., Flores-Gonzalez A., Juarez-Rojas L., et al. (2023). Chronic stress decreases fertility parameters in female rats. *Syst. Biol. Reprod. Med.* 69:234–244. DOI:10.1080/19396368.2023.2171822
50. Iamsaard S., Tongpan S., Yannasithinon S., et al. (2021). Effect of chronic stress on expression and secretion of seminal vesicle proteins in adult rats. *Andrologia* 53:e13800. DOI:10.1111/and.13800
51. Harlan S. L. and Ruddell D. M. (2011). Climate change and health in cities: Impacts of heat and air pollution and potential co-benefits from mitigation and adaptation. *Curr. Opin. Environ. Sustain.* 3:126–134. DOI:10.1016/j.cosust.2011.01.001
52. Lacalle-Calderon M., Perez-Trujillo M. and Neira I. (2017). Fertility and economic development: Quantile regression evidence on the inverse J-shaped pattern. *Eur. J. Popul.* 33:1–31. DOI:10.1007/s10680-016-9382-4
53. Mills M., Rindfuss R. R., McDonald P., et al. (2011). Why do people postpone parenthood. *Reasons and social policy incentives. Hum. Reprod. Update* 17:848–860. DOI:10.1093/humupd/dmr026
54. Liu J., Varghese B. M., Hansen A., et al. (2022). Heat exposure and cardiovascular health outcomes: A systematic review and meta-analysis. *Lancet Planet. Health* 6:e484–e495. DOI:10.1016/s2542-5196(22)00117-6
55. Liu J., Varghese B. M., Hansen A., et al. (2025). Increasing burden of poor mental health attributable to high temperature in Australia. *Nat. Clim. Change* 15:489–496. DOI:10.1038/s41558-025-02309-x
56. Qi J., Wang Y., Wang L., et al. (2023). The modification effect of ozone pollution on the associations between heat wave and cardiovascular mortality. *Innov. Med.* 1:100043. DOI:10.59717/j.xinn-med.2023.100043
57. Chen R., Yin P., Wang L., et al. (2018). Association between ambient temperature and mortality risk and burden: Time series study in 272 main Chinese cities. *BMJ* 363:k4306. DOI:10.1136/bmj.k4306
58. Qiu J., Liang Z., Yi J., et al. (2023). Extreme temperature exposure increases the risk of preterm birth in women with abnormal pre-pregnancy body mass index: A cohort study in a southern province of China. *Front. Public Health* 11:1156880. DOI:10.3389/fpubh.2023.1156880
59. Camlin N. J., McLaughlin E. A. and Holt J. E. (2014). Through the smoke: Use of in vivo and in vitro cigarette smoking models to elucidate its effect on female fertility. *Toxicol. Appl. Pharmacol.* 281:266–275. DOI:10.1016/j.taap.2014.10.010
60. Barratt C. L. R., Bjorndahl L., De Jonge C. J., et al. (2017). The diagnosis of male infertility: An analysis of the evidence to support the development of global WHO guidance-challenges and future research opportunities. *Hum. Reprod. Update* 23:660–680. DOI:10.1093/humupd/dmx021
61. Zhang Q., Wang Y. Y., Zhang Y., et al. (2017). The influence of age at menarche, menstrual cycle length and bleeding duration on time to pregnancy: A large prospective cohort study among rural Chinese women. *BJOG* 124:1654–1662. DOI:10.1111/1471-0528.14469

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AUTHOR CONTRIBUTIONS

JC, XM, HK, and YH initiated the study. JC, YS, and JD analyzed the data and drafted the manuscript. YN, YZ[1], and CH contributed to data analyses. YS, JD, SS, HL, QW, HS, YZ[2], and DY collected the data. YN, MB, XM, HK, and YH thoroughly helped improved sentence structure and word choice of this manuscript. All authors contributed to the interpretation of results and critically revised the draft ([1] Yixiang Zhu; [2] Yiping Zhang).

DECLARATION OF INTERESTS

Haidong Kan is an Editorial Board member of The Innovation Medicine. He was blinded from reviewing or making final decisions on the manuscript. The article was subject to the journal's standard procedures, with peer review handled independently of this Editorial Board member and their research groups. The other authors declare no competing interests.

ETHICAL STATEMENT AND PATIENT CONSENT

The Institutional Review Board of National Research Institute for Family Planning, Beijing, China approved the study (2009-02). All enrolled participants provided written informed consent.

DATA AND CODE AVAILABILITY

The datasets used in this study are not publicly available due to privacy protection.

SUPPLEMENTAL INFORMATION

It can be found online at https://doi.org/10.59717/j.xinn-med.2025.100139