Supplementary Table S1. Maternal characteristics of twin pregnancies in China, 2010–2020, by urban-rural residence

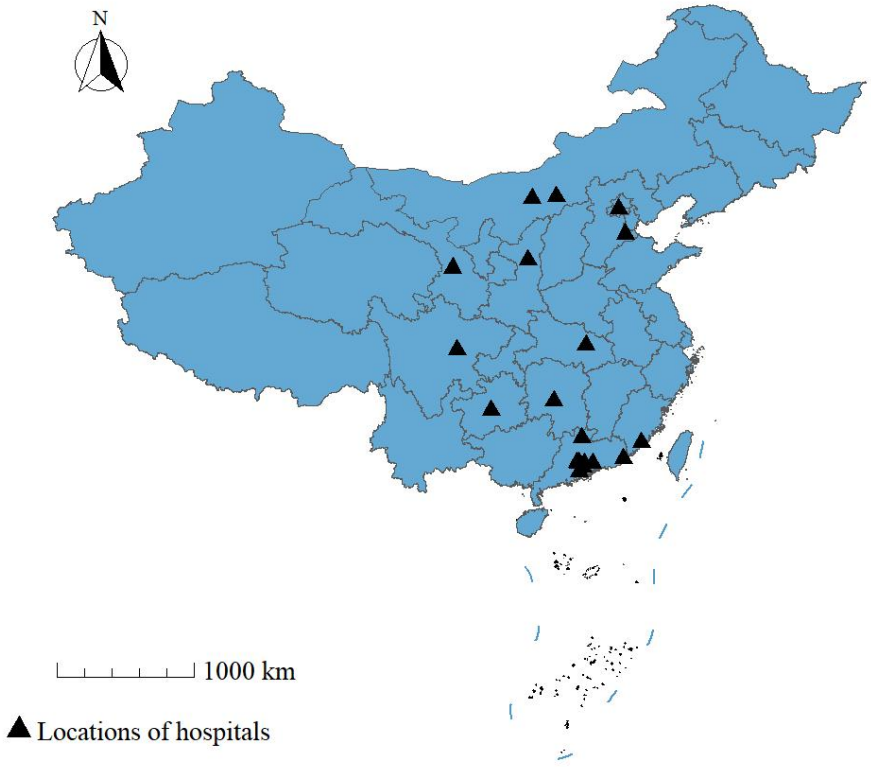
Characteristics *n* (%) / mean (SD)	Total *n* = 8,334	Rural *n* = 2,807	Urban *n* = 5,527	*P*
NEC				1.000
No	8107 (97.3)	2731 (97.3)	5376 (97.3)	
Yes	227 (2.7)	76 (2.7)	151 (2.7)	
Infant sex				0.632
Male-female	2977 (35.7)	985 (35.1)	1992 (36.0)	
Male-male	3006 (36.1)	1015 (36.2)	1991 (36.0)	
Female-female	2351 (28.2)	807 (28.7)	1544 (27.9)	
Season of conception				0.699
Cold season	4070 (48.8)	1362 (48.5)	2708 (49.0)	
Warm season	4264 (51.2)	1445 (51.5)	2819 (51.0)	
Parity				<0.001
Nulliparous	5421 (65.2)	1678 (59.8)	3743 (67.9)	
Multiparous	2899 (34.8)	1126 (40.2)	1773 (32.1)	
Delivery mode				
Vaginal	879 (10.6)	350 (12.5)	529 (9.6)	<0.001
Cesarean	7428 (89.4)	2449 (87.5)	4979 (90.4)	
Ambient temperature (℃)	19.1 (5.23)	18.5 (5.07)	19.5 (5.28)	<0.001
Maternal age (Continuous, years)	31.1 (4.55)	30.3 (4.71)	31.6 (4.41)	<0.001
Gestation week (weeks)	35.54 (2.41)	35.21 (2.61)	35.71 (2.29)	<0.001
Heatwaves				<0.001
No	796 (9.6)	326 (11.6)	470 (8.5)	
Yes	7538 (90.4)	2481 (88.4)	5057 (91.5)	
Types of conception				
Natural pregnancy	3324 (40.1)	1183 (42.4)	2141 (38.9)	0.002
Assisted reproduction	4971 (59.9)	1608 (57.6)	3363 (61.1)	
MDA8 O_3(ug/m^3)	88.9 (14.28)	87.9 (12.92)	89.4 (14.91)	<0.001
$PM_{2.5}$(ug/m^3)	37.5 (12.74)	36.0 (13.69)	38.3 (12.16)	<0.001

Note. SD, standard deviation; NEC, necrotizing enterocolitis; $PM_{2.5}$, fine particulate matter ≤ 2.5 μm in diameter; MDA8 O_3, daily 8h maximum ozone concentrations. A chi-square test was applied to compare the differences in categorical variables between groups with and without NEC; a *t*-test was applied to compare the differences in continuous variables between groups with and without NEC. The ambient temperature values in the table represent the average temperatures across the entire pregnancy period, covering both cold and warm seasons; therefore, the final values exhibit a relatively narrow range of variation

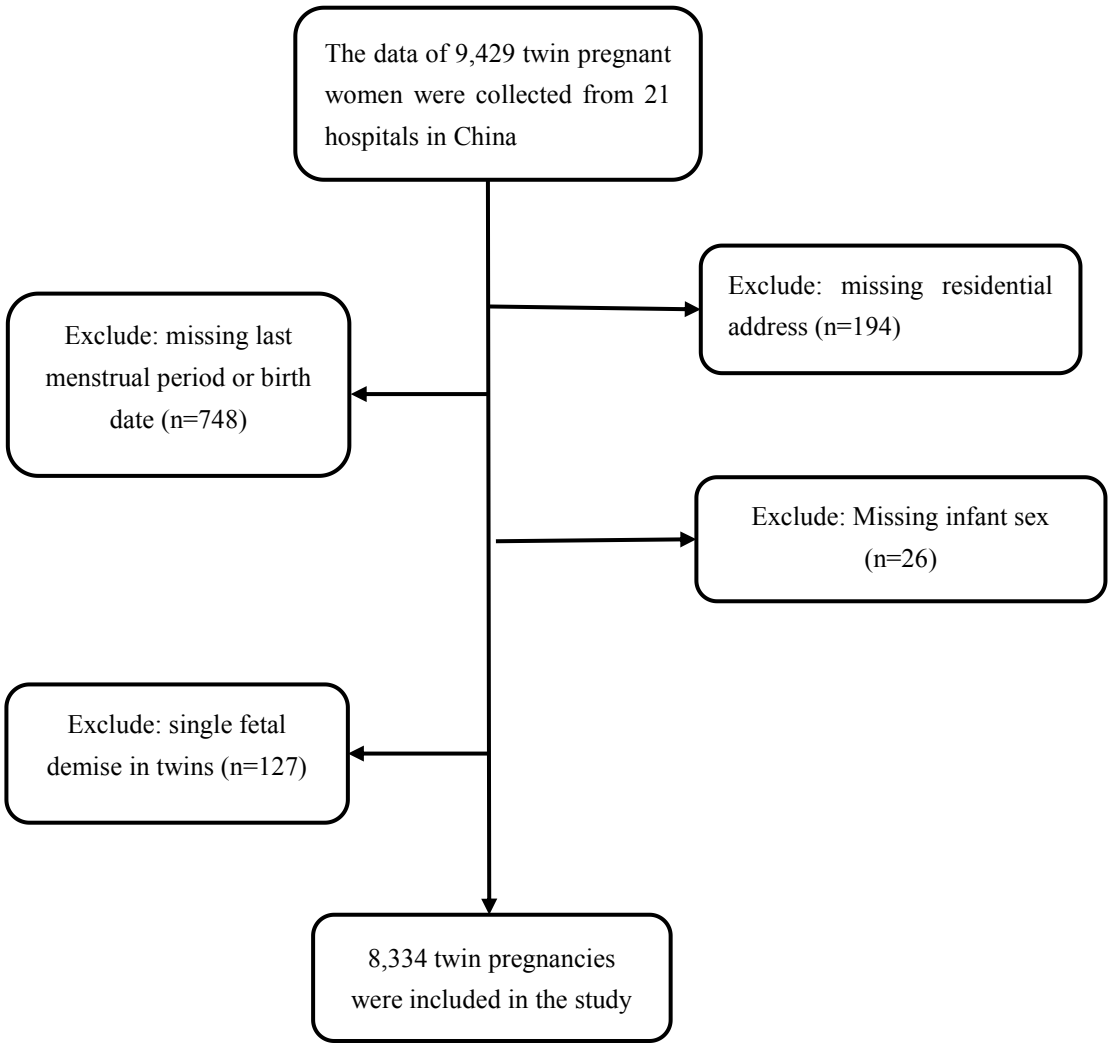
Supplementary Table S2. Correlation coefficients for TM, $PM_{2.5}$, MDA8 O3 and RH during the entire pregnancy

	TM	$PM_{2.5}$	MDA8 O_3
TM	1.00		
$PM_{2.5}$	-0.42*	1.00	
O_3	0.19*	-0.04*	1.00

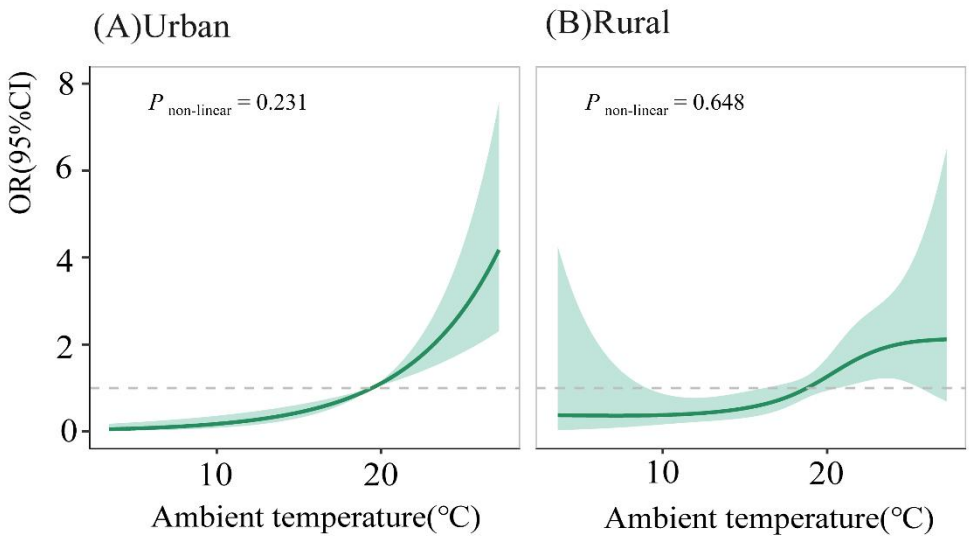
Note. TM, ambient temperature; $PM_{2.5}$, fine particulate matter ≤2.5μm in diameter; MDA8 O_3, daily 8- h maximum ozone concentrations. *P < 0.001.



Supplementary Figure S1. The geographic locations of 21 Grade-A tertiary hospitals in China. GS(2020)4619.



Supplementary Figure S2. Participant screening flowchart from 21 hospitals in China.



Supplementary Figure S3. The exposure-response association curves between Prenatal TM exposure during the entire pregnancy and the risk of NEC, stratified by urban and rural areas. Models were adjusted for maternal age, parity, gestational age, seasons of conception, sex of twin fetuses, year of conception, maternal ethnicity, type of conception, modes of delivery, $PM_{2.5}$, and MDA8 O_3. *OR*, odds ratio; *CI*, confidence interval; TM, ambient temperature; NEC, necrotizing enterocolitis; $PM_{2.5}$, fine particulate matter ≤ 2.5 μm in diameter; MDA8 O_3, daily 8- h maximum ozone concentrations.

Supplementary Table S3. PAFs of NEC attributable to prenatal exposure to TM and heatwaves

	PAF (%, 95% *CI*)	
	Ambient temperature [a]	Heatwaves [b]
Entire pregnancy	22.35 (-2.82, 42.08)	31.27 (25.98, 37.00)
First trimester	21.33 (-7.11, 42.86)	28.04 (13.68, 40.02)
Second trimester	31.69 (3.21, 52,36)	28.64 (12.05, 42.10)
Third Trimester	15.21 (-15.19, 38.28)	

Note. NEC, necrotizing enterocolitis; TM, ambient temperature; PAF, population attributable fraction; $PM_{2.5}$, fine particulate matter ≤ 2.5 μm in diameter; MDA8 O_3, daily 8- h maximum ozone concentration.CI, confidence interval; a: Models were adjusted for maternal age, parity, gestational age, seasons of conception, sex of twin fetuses, year of conception, maternal ethnicity, type of conception, modes of delivery, $PM_{2.5}$, and MDA8 O_3. *P* value for intergroup comparisons in stratified analyses. b: Models were adjusted for maternal age, parity, gestational age, seasons of conception, sex of twin fetuses, year of conception, maternal ethnicity, type of conception, modes of delivery, and MDA8 O_3. The heatwaves in the third trimester had no statistically significant effect on NEC, so the PAF value of NEC caused by the heatwaves in the third trimester was not calculated

Supplementary Table S4. Sensitivity analysis on the associations of maternal exposure to specific centile of TM and heatwaves with NEC

		Entire pregnancy		First trimester		Second trimester		Third trimester	
		TM(°C)	OR(95%CI)	TM(°C)	OR(95%CI)	TM(°C)	OR(95%CI)	TM(°C)	OR(95%CI)
Percentile of TM									
Model1	Reference temperature	20.7		13,3		19.6		18.4	
	90th percentile	24.8	2.09(1.71, 2.55)	27.5	1.27(1.01, 1.60)	27.4	1.80(1.44, 2.25)	27.9	1.54(1.24, 1.92)
	95th percentile	25.4	2.42(1.88, 3.13)	28.0	1.31(0.98, 1.73)	28.0	1.85(1.41, 2.42)	28.3	1.72(1.32, 2.24)
Model2	Reference temperature	19.8		18.6		19.8		20.9	
	90th percentile	24.8	2.68(1.93, 3.72)	27.5	2.41(1.63, 3.55)	27.4	3.30(2.18, 4.99)	27.9	2.06(1.43, 2.98)
	95th percentile	25.4	3.03(2.06, 4.46)	28.0	2.59(1.66, 4.04)	28.0	3.56(2.24, 5.67)	28.3	2.25(1.49, 3.38)
Model3	Reference temperature	20.5		18.6		20.8		23.4	
	90th percentile	24.9	2.88(1.97, 4.22)	27.6	2.45(1.52, 3.93)	27.5	3.62(2.22, 5.90)	28.0	1.70(1.11, 2.59)
	95th percentile	25.4	3.37(2.17, 5.23)	28.1	2.56(1.50, 4.36)	28.0	4.05(2.36, 6.94)	28.4	1.82(1.14, 2.92)
Heatwaves									
Model4			1.16(0.72, 1.87)		1.17(0.90, 1.52)		1.62(1.24, 2.12)		0.73(0.55,0.98)
Model5			1.98(1.14, 3.43)		1.81(1.26, 2.59)		1.81(1.19, 2.75)		0.94(0.65,1.36)
Model6			1.94(1.05, 3.60)		1.82(1.22, 2.72)		1.71(1.07, 2.74)		0.85(0.56, 1.28)

Note. TM, ambient temperature; NEC, necrotizing enterocolitis; OR, odds ratio; CI, confidence interval;

Model1 and Model4 were crude model; Model2 were adjusted for maternal age, parity, gestational age, seasons of conception, sex of twin fetuses, year of conception, maternal ethnicity, type of conception, modes of delivery, $PM_{2.5}$, and MDA8 O_3; Model3 were adjusted for maternal age, parity, gestational age, seasons of conception, sex of twin fetuses, year of conception, maternal ethnicity, type of conception, modes of delivery, BMI, $PM_{2.5}$, and MDA8 O_3; Model5 were adjusted for maternal age, parity, gestational age, seasons of conception, sex of twin fetuses, year of conception, maternal ethnicity, type of conception, modes of delivery, and MDA8 O_3. Model6 were adjusted for maternal age, parity, gestational age, seasons of conception, sex of twin fetuses, year of conception, maternal ethnicity, type of conception, modes of delivery, BMI and MDA8 O_3. $PM_{2.5}$, fine particulate matter ≤ 2.5 μm in diameter; MDA8 O_3, daily 8- h maximum ozone concentration.