BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Ten-year time trends in preterm birth during a sociodemographic transition period: a retrospective cohort study in Shenzhen, China

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-037266
Article Type:	Original research
Date Submitted by the Author:	26-Jan-2020

Complete List of Authors:	Zou, Lingyun; Shenzhen City Baoan District Womens and Childrens Hospital, Center for Big Data Research in Health Zhang, Lian; Shenzhen City Baoan District Womens and Childrens Hospital, Department of Neonatology Ma, Rui; Shenzhen City Baoan District Womens and Childrens Hospital, Center for Big Data Research in Health Luo, Yali; Shenzhen City Baoan District Womens and Childrens Hospital, Department of Prevention & Health Care Wang, Jun; Shenzhen City Baoan District Womens and Childrens Hospital, Center for Big Data Research in Health Zhou, Yanxia; Shenzhen City Baoan District Womens and Childrens Hospital, Centre for Big Data Research in Health Sun, Haiyang; Shenzhen City Baoan District Womens and Childrens Hospital, Centre for Big Data Research in Health Ren, Xi; Shenzhen City Baoan District Womens and Childrens Hospital, Centre for Big Data Research in Health Xu, Quan; Shenzhen City Baoan District Womens and Childrens Hospital, Department of Prevention & Health Care

Keywords:	EPIDEMIOLOGY, PUBLIC HEALTH, Maternal medicine < OBSTETRICS, Child protection < PAEDIATRICS

SCHOLARONE™
Manuscripts

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Ten-year time trends in preterm birth during a sociodemographic transition period: a retrospective cohort study in Shenzhen, China

Rui Ma[1], Yali Luo[2], Jun Wang[3], Yanxia Zhou[4], Haiyang Sun[5], Xi Ren[6], Quan Xu[7], Lian Zhang[1], Lingyun Zou[1]

Author affiliations

Rui Ma: Center for Big Data Research in Health, Bao'an Women's and Children's Hospital, Jinan University, Shenzhen, China.
Yali Luo: Department of Prevention & Health Care, Bao'an Women's and Children's Hospital, Jinan University, Shenzhen, China.
Jun Wang: Center for Big Data Research in Health, Bao'an Women's and Children's Hospital, Jinan University, Shenzhen, China.
Yanxia Zhou: Center for Big Data Research in Health, Bao'an Women's and Children's Hospital, Jinan University, Shenzhen, China.
Haiyang Sun: Center for Big Data Research in Health, Bao'an Women's and Children's Hospital, Jinan University, Shenzhen, China.
Xi Ren: Center for Big Data Research in Health, Bao'an Women's and Children's Hospital, Jinan University, Shenzhen, China.
Quan Xu: Department of Prevention & Health Care, Bao'an Women's and Children's Hospital, Jinan University, Shenzhen, China.
Lian Zhang: Department of Neonatology, Bao'an Women's and Children's Hospital, Jinan University, Shenzhen, China.
Lingyun Zou: Center for Big Data Research in Health, Bao'an Women's and Children's Hospital, Jinan University, Shenzhen, China.

Correspondence to

Dr Lingyun Zou, Center for Big Data Research in Health, Bao'an Women's and Children's Hospital, Jinan University, Shenzhen, 518102, China; +86 18825262859; lingyun.zou@gmail.com

Wordcount: 3587

Abstract

Objectives To investigate time trends of preterm birth and estimate the contributions of risk factors to the changes in preterm birth rates over a decade (2009-2018) of transitional period in Shenzhen, China.

Design Retrospective cohort study between 2009 and 2018.

Setting All births in Bao'an during January 2009 and December 2018 registered in the Shenzhen Birth Registry Database.

Participants 478,044 live births were included with sociodemographic and medical records for both women and infants.

Outcome measures The incidence rate of preterm birth stratified by different maternal and infant characteristics. Multiple logistic regression was used to identify significant risk factors associated with preterm birth. The population attributable risk fraction of each factor was calculated to estimate its contribution to variations of preterm birth rate over the ten years.

Results A total of 27,829 preterm births from 478,044 live births (5.82%) was recorded and the preterm birth rate increased from 5.65% in 2009 to 6.18% in 2018. Risk factors including maternal age (0.03% increase) and multiple pregnancy (0.28% increase) drove the rise of preterm birth rate whereas changes in maternal educational attainment (0.22% reduction), parity (0.06% reduction) and prenatal care utilization (0.45% reduction) had contributed to the decline in preterm birth rate.

Conclusions An uptrend of preterm birth rate was observed in an area under rapid sociodemographic transitions during 2009-2018 and the changes were associated with these sociodemographic transitions. Continued investments in girls' education and prenatal care have the potential of reducing preterm birth rate.

Strengths and limitations of this study

- The study provides unique information about the time trends in preterm birth over the last decade in a setting of rapid sociodemographic transitions with a large proportion of migrant workers.
- Population attribution risk fraction was used to quantify the contributions of changes in risk factors to the variations of preterm birth rate.
- We had no information about family income and maternal employment and their effects on preterm birth trends were unable to be analysed in this study.
- A limited number of risk factors that drove the growth of preterm birth rate have been examined in this study.

Introduction

Defined as birth prior to 37 completed weeks' gestation, preterm birth is a syndrome with many causes and multiple phenotypes [1-2]. Globally, approximately 15 million neonates were born preterm in 2014 and over one million children die each year due to preterm birth complications, contributing to approximately 16% of all deaths and 35% of newborn deaths in 2019 [3-4]. Despite decades of substantial research, the increasing prevalence of preterm birth remained in many countries worldwide, from 9.8% in 2000 to 10.6% in 2014 [5]. Even fortunate survivors may suffer from lifetime disabilities, including neurodevelopmental and physical impairments, as well as behavioral effects, which impose heavy family and societal burden [6]. The economic burden associated with preterm birth complications was at least $26.2 billion in the United States in 2005 and $587.1 million in Canada in 2014 [7, 8]. Addressing risk factors of preterm birth and the cause of the incremental incidence are critical to inform public health policies aiming at reducing the global burden of preterm births and achieving the Global Strategy for Women's, Children's, and Adolescents' Health under the Sustainable Development Goal [9].

Sociodemographic transitions have been shown associated with time trends in preterm birth, especially in areas during the industrialization period. A cohort study from Bangladesh unveiled that 27% of the decline in preterm birth rate could be attributed to the decrease in parity and expansion of maternal education during 1990-2014 [10]. Maternal age at delivery could explain the secular trends of preterm birth in Japan from 1979 to 2014 based on national birth data [11]. During the Chilean sociodemographic transition period 1991-2012, the increase in advanced maternal age (35 or older) was evaluated to increase the risk of preterm birth significantly [12]. Economic inequalities were also found in relation to preterm births in four Brazilian birth cohort studies between 1982 and 2011 [13]. A study on births in the UK between 2004-2016 confirmed that socioeconomic indicators were associated with the risk of preterm birth independently with strong significance [14].

China accounted for 7.8% (1.17 million) of preterm births worldwide with the second largest number of preterm neonates [5]. From 2000 to 2014, the estimated preterm birth rate in China had risen from 6.35% to 6.94% [5]. As the first Special Economic Zone located in the Pearl River Delta of South China, Shenzhen has undergone rapid urbanization and attracted millions of migrant labourers since the beginning of the 1980s [15]. Bao'an is a typical epitome of this urbanization as the largest district in Shenzhen with more than 3.26 million year-end permanent population in 2018 and around 82% are migrants from other parts of China [16]. Between 2012 and 2018, the de jure population of Bao'an has quickly expanded from 2.68 million to 3.26 million and the gross domestic product per capita has grown from $8556 in 2008 to $15981 in 2017 [16-18]. In addition, the proportion of labourers in the tertiary sector of the economy increased from 15.7% in 2012 to 22.6% in 2017 [16-17].

However, limited studies on long-term time trends in preterm birth are available in areas under drastic sociodemographic transitions in China during recent decades. Transitions in society and their contributions to the changes in preterm birth rate are still unclear. The present study was based on all births in Bao'an during 2009-2018 registered in the Shenzhen Birth Registry Database. We sought to assess the temporal trends of preterm birth and associated risk factors among a large proportion of migrant population. We further estimated quantitative contributions of these factors to the changes in preterm birth rates over the last decade.

Methods

Study design and data collection

This cohort study was based on data of all births in Bao'an during 1 January 2009 and 31 December 2018 extracted from the Shenzhen Birth Registry Database, which has served as a system for birth registration and maternal, infant health management since 2000 [19]. Demographic and clinical records of both mothers and newborns were available for the identification of preterm birth and risk factors. Only live births were included in this study and ineligible data were excluded to ensure the coherence and continuity of preterm birth rate calculation based on prior related research: (1) Stillbirths or births with unknown results; (2) Births with missing gestational age or gestational age < 22 weeks or > 46 weeks; (3) Births with missing maternal age or maternal age < 13 years or > 50 years. The flowchart of data selection was shown in the supplementary file: Figure 1 [5, 20].

Patient and public involvement

This study used routinely collected administrative health data and no patients were involved in the conception, design and conduct of the research. Results will be disseminated via open access publication.

Ethics approval

This study was approved by the medical ethics committee of Bao'an Women's and Children's Hospital, Jinan University. Data collected in the study were anonymous and no individually identifiable information was available for the analysis.

Definition and measurements

Preterm birth was defined by WHO as all births before 37 completed weeks of gestation or fewer than 259 days since the first day of a woman's last menstrual period [3, 21]. Based on gestational age, it was further grouped as extremely preterm (<28 weeks), very preterm (28 - <32 weeks) and late preterm (32 - <37 weeks). Preterm birth rate was calculated using the number of live births in a specific preterm category divided by all live births multiplied by 100 in a specific time period [21].

Potential risk factors related to preterm birth were selected and analysed based on the literature review [10-14]. Variables including gestational age, maternal age, maternal education, parity, number of prenatal care visits, maternal chronic conditions, gestational hypertension, infant gender and time of delivery were included into our analysis. Numeric variables including gestational age and maternal age were categorized into ordinal subgroups. We classified maternal education into 3 categories for a more balanced population and clear data interpretation: primary school and below, secondary and high school, college and above [22]. The number of prenatal care visits was transformed into prenatal care utilization rate, by calculating the ratio between the actual number of visits and the recommended number of visits. The ratio was then classified into three groups: inadequate (< 50%), intermediate and appropriate (50-110%), adequate plus (≥ 110%) [23]. To analyse the effect of the universal two-child policy, we classified births into two groups based on time of delivery: births taking place before or within nine months after the implementation of the universal two-child policy in October 2015 (June 2016) and births taking place nine months after the policy [24].

Statistical analysis

Chi-Square test was used to evaluate statistical differences in frequencies of preterm birth between each maternal and infant group in this study [25]. Annual preterm birth rates for each risk factor subcategory were calculated to present the temporal trends stratified by different characteristics over the decade. Yearly percent compositions of each risk factor were calculated to show the changes in sociodemographic indicators. The sensitive analysis was performed to examine changes in linear trends of annual preterm birth rates by calculating risk ratios, with the year 2009 as a reference [26]. A multivariable binomial logistic regression model was applied to estimate adjusted odds ratios (AORs) and 95% confidence intervals (95% CI) of covariates [27]. Possible independent variables were selected based on univariate analyses ($p<0.05$) and their probable associations with preterm birth judged by prior domain knowledge [28].

To examine the contribution of risk factors to preterm birth incidence in the entire study population over the decade, we measured the population attributable risk fraction with formula (1) where AFp_i is the population attributable risk fraction for risk factor i, PF_j is the proportion of the total population and RR_j is the risk ratio for the exposure category j ($j = 1, 2, ..., m$) of risk factor i ($i = 1, 2, ..., n$). RR_j was approximated by using OR_i

to avoid overlap from different risk factors [29, 30]. AFp was then calculated with formula (2) to measure the total population attributable risk fraction across all risk factors.

$$AFp_i = \frac{\sum_1^m PF_j * (RR_j - 1)}{1 + \sum_1^m PF_j * (RR_j - 1)} \quad (1)$$

$$AFp = 1 - \prod_i^n (1 - AFp_i) \quad (2)$$

We evaluated sociodemographic changes after the universal two-child policy and their contributions to the variations of preterm birth rate with approaches: (1) calculate PF for each selected factor in two time periods, (2) identify the risk of preterm birth for these factors with odds ratios (ORs) in a logistical regression among births after the policy, (3) estimate AFp for each factor before and after the policy (AFp_{before} was calculated by PF_{before} and OR_{after} whereas AFp_{after} was calculated by PF_{after} and OR_{after}), (4) calculate the total contribution to the changes in preterm birth rate between two periods by multiplying AFp with the preterm birth rate after the policy and subtract the result for before the policy with formula (3) [20, 31].

$$Increased\ Rate = AFp_{after} * Rate_{after} - AFp_{before} * Rate_{after} \quad (3)$$

All the analyses were conducted using Python software (version 3.6.6; Python Software Foundation). Alpha levels of 0.001, 0.01 and 0.05 indicated statistical significance for a two-tailed test separately [32]. Missing values of several variables were included in the descriptive analysis but removed from the logistic regression analyses.

Results

Preterm birth rates in Bao'an, Shenzhen

A total of 480,845 births in Bao'an, Shenzhen was identified in the Shenzhen Birth Registry Database during 2009 and 2018. 478,044 (99.42%) live births were included in the final study population after excluding 2801 (0.58%) ineligible birth records: 2561 (0.53%) stillbirths or births with unknown results, 182 (0.04%) live births with maternal age under 13 years or over 50 years, 58 (0.01%) live births with missing gestational age, gestational age lower than 22 weeks or higher than 46 weeks. There were 27,829 (5.82%) preterm births in Bao'an from 2009 to 2018 with 312 (0.07%) extremely preterm births (<28 weeks), 2686 (0.56%) very preterm births (28-<32 weeks) and 24831 (5.19%) late preterm births (32-<37 weeks) respectively. Preterm birth rates among different exposure categories for each maternal and infant group are presented in **Table 1**.

Table 1
Descriptive Statistics of Preterm Births in Bao'an, Shenzhen, 2009–2018

	Live births	Term births		Preterm births		P value[d]
	N	N	%	N	%	
All live births	478044	450215	94.18	27829	5.82	
Maternal age (year)						<0.001
≤20	23055	21209	91.99	1846	8.01	
21-35	416608	393874	94.54	22734	5.46	
≥36	38381	35132	91.53	3249	8.47	
Maternal education						<0.001
Primary school and below	16687	15693	94.04	994	5.96	
Secondary and high school	351920	330947	94.04	20973	5.96	
College and above	109437	103575	94.64	5862	5.36	
Parity						<0.001
0	223429	209789	93.90	13640	6.10	
≥1	253680	239604	94.45	14076	5.55	

Missing	935	-	-	-	-	
Multiple pregnancy						<0.001
No	467871	444638	95.03	23233	4.97	
Yes	10173	5577	54.82	4596	45.18	
Prenatal care utilization rate[a]						<0.001
< 50%	121974	114194	93.62	7780	6.38	
50% - < 110%	277690	264111	95.11	13579	4.89	
≥ 110%	78283	71829	91.76	6454	8.24	
Missing	97	-	-	-	-	
Maternal chronic conditions[b]						0.139
No	471057	443664	94.18	27393	5.82	
Yes	6987	6551	93.76	436	6.24	
Gestational hypertension						<0.001
No	477826	450023	94.18	27803	5.82	
Yes	218	192	88.07	26	11.93	
Preeclampsia or eclampsia						<0.001
No	477552	449890	94.21	27662	5.79	
Yes	492	325	66.06	167	33.94	
Two-child policy[c]						<0.001
No	346225	326548	94.32	19677	5.68	
Yes	131819	123667	93.82	8152	6.18	
Infant Gender						<0.001
Female	219629	207946	94.68	11683	5.32	
Male	258396	242257	93.75	16139	6.25	
Missing	19	-	-	-	-	

- a. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
- b. chronic conditions include hypertension, hepatopathy, nephropathy, heart disease, diabetes, and anemia.
- c. The universal two-child policy effect time is defined as the delivery time before 1 July 2016, nine months after the policy was announced in October 2015.
- d. Preterm birth frequencies among subcategories of each variable were compared with the Chi-Square test.

Temporal trends in preterm birth rate

The annual preterm birth rates for the uncategorized study population and each exposure category of the selected risk factors during 2009-2018 were shown in **Figure 1 (supplementary file: Table 1)**. The overall preterm birth rate fluctuated between 5.54% and 5.80% during 2009-2015 and surpassed 6.0% in 2016 with reaching the highest in 2017 (6.36%) (**Figure.1-a**). Annual changes in late preterm was more obvious than in extremely preterm and very preterm (**Figure.1-b**). Generally, the rising trends in preterm birth were observed in all exposure subcategories of risk factors including maternal age (**Figure.1-c**), maternal education (**Figure.1-d**), parity (**Figure.1-e**), multiple pregnancy (**Figure.1-f**) and infant gender (**Figure.1-h**), except for adequate plus prenatal care utilization group (**Figure.1-g**). Births with younger (≤ 20) or older maternal age (≥ 36 years), lower education level, nulliparity, multiple pregnancy, inadequate prenatal care utilization and male gender had a higher risk of preterm birth. The result of sensitivity analysis (**supplementary file: Table 2**) indicated that statistically significant changes in annual preterm birth rates occurred only in years 2016, 2017 and 2018 compared with the year 2009. The preterm birth trends for chronic maternal condition, gestational hypertension, preeclampsia or eclampsia were not measured as their small proportions in positive results.

Risk factors for preterm birth

Statistically significant risk factors of preterm birth including maternal age, education level, parity, multiple pregnancy, prenatal care utilization, gestational hypertension, preeclampsia or eclampsia, two-child policy and infant gender. Corresponding adjusted odds ratios presented in **Table 2** indicated that births with multiple pregnancy had higher risk of preterm than the reference group (adjusted odds ratio [AOR] 15.2, 95% CI: 14.54, 15.82; p<0.001). Also, the population attributable risk fraction of each risk factor in **Table 2** suggested that only 57.1% of preterm births can be explained by these factors. Multiple pregnancy, maternal education, prenatal care utilization and infant gender had larger impacts on preterm birth than gestational hypertension and preeclampsia or eclampsia in our study. The universal two-child policy had driven the risk of preterm birth upward slightly with an adjusted odds ratio of 1.06 (95% CI: 1.03, 1.10; p<0.001).

Table 2

Multivariable Logistic Regression of Risk Factors for Preterm Birth in Bao'an, Shenzhen, 2009–2018[a]

	β[d]	AOR (95% CI)[e,f]	AFp(%)[g]
Overall			57.09
Maternal age (year)			6.24
≤ 20	0.4361	1.55(1.47,1.63)***	
21-35	-	Reference	
≥ 36	0.4027	1.50(1.43,1.56)***	
Maternal education			16.57
Primary school and below	0.1865	1.21(1.12,1.30)***	
Secondary and high school	0.2340	1.26(1.22,1.31)***	
College and above	-	Reference	
Parity			4.08
0	-	Reference	
≥ 1	-0.0879	0.92(0.89,0.94)***	
Multiple pregnancy			23.18
No	-	Reference	
Yes	2.7192	15.17(14.54,15.82)***	
Prenatal care utilization rate[b]			14.76
< 50%	0.2780	1.32(1.28,1.36)***	
50% - < 110%	-	Reference	
≥ 110%	0.4466	1.56(1.51,1.62)***	
Gestational hypertension			0.04
No	-	Reference	
Yes	0.5768	1.78(1.15,2.76)*	
Preeclampsia or eclampsia			0.62
No	-	Reference	
Yes	1.9762	7.22(5.90,8.82)***	
Two-child policy[c]			1.63
No	-	Reference	
Yes	0.0628	1.06(1.03,1.10)***	
Infant Gender			10.63
Female	-	Reference	
Male	0.1991	1.22(1.19,1.25)***	

- a. 476997 live births were included after removing 1047 records due to missing values in any risk factor.

- b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
- c. The universal two-child policy is defined as the delivery time before 1 July 2016, nine months after the policy was announced in October 2015.
- d. β, coefficients of risk factors in the multivariable binomial logistic regression model.
- e. AOR, adjusted odds ratio; CI, confidence interval.
- f. *, *P*<0.05; **, *P*<0.01; ***, *P*<0.001.
- g. AFp, Attributable risk fraction for the population.

Temporal trends in the distribution of sociodemographic factors

The distributions of sociodemographic factors including maternal age, education, parity, prenatal care utilization and infant gender were shown in **Figure 2** (**supplementary file: Table 3**). Prenatal care utilization has improved with a drastic increase in the proportion of adequate plus utilization group from 5.4% in 2009 to 44.8% in 2018 (**Figure.2-e**). Improvement in maternal educational attainment was presented in **Figure.2-c**, showing that the proportion of women with education level Primary School and Below decreased from 17.59% in 2009 to 1.20% in 2018. However, the advanced maternal age group and multiparity group expanded during the period (**Figure.2-b, d**). The male-to-female sex ratio in Bao'an, Shenzhen stayed around 117:100 over the decade in our study (**Figure.2-f**).

Contributions of transitions in sociodemographic factors to variations of preterm birth rate

The preterm birth rate increased from 5.66% during 1 January 2009 and 30 June 2016 to 6.18% between 1July 2016 and 31 December 2018, with 88% of the increase attributed to late preterm birth. We compared preterm birth rates subcategorized by sociodemographic factors including maternal age, maternal education, parity, multiple pregnancy, prenatal care utilization and infant gender, as well as the percent compositions of these factors in **Table 3**. Except for the adequate plus group of prenatal care utilization, preterm birth rates increased in all the categories after the policy. Contributions of sociodemographic factors to the variations of preterm birth rate between two periods were visualized with population attribution risk fraction in **Figure 3 (supplementary file: Table 4)**. Maternal age and multiple pregnancy were drivers behind the increment of preterm birth rate whereas maternal education, parity, prenatal care utilization and infant gender had contributed to the rate reduction. Particularly, maternal education level increased, especially in the group College and Above, from 18.03% to 35.76% and an attributed 0.22% of the reduction of preterm birth rate was evaluated. Births with inadequate prenatal care utilization (<50%) decreased obviously from 32.16% to 7.69%, which contributed to a 0.45% decrease of preterm birth rate. Even with a small composition change, from 1.99% to 2.49%, multiple pregnancy had contributed to over half of the increase (0.28%/0.52%) in preterm birth rate. The proportion of younger maternal age dropped from 5.59% to 2.75% while advanced maternal age (≥36) grew from 6.86% to 11.07%, contributing a 0.03% increase of preterm birth rate. Multiparous births expanded from 50.43% to 60.33% and had made a 0.06% decrease of preterm birth rate. The infant gender ratio kept stable during two periods and its contribution to the change of preterm birth rate was very small.

Table 3

Preterm Birth Rate and Distribution of Risk Factors in Bao'an, Shenzhen, 2009 - 2018[a]

	Preterm birth rate (%)		Distribution percentage (%)[c]	
	2009.01-2016.06	2016.07-2018.12	2009.01-2016.06	2016.07-2018.12
All live birth	5.66	6.18	72.40	27.60
Gestational age(week)				
< 28	0.05	0.11	0.84	1.78
28 -< 32	0.56	0.56	9.86	9.05
32 -< 37	5.05	5.51	89.30	89.17

Maternal age(year)				
≤ 20	7.84	8.49	5.59	2.75
21-35	5.32	5.77	87.55	86.18
≥ 36	8.23	8.79	6.86	11.07
Maternal education				
Primary school and below	5.74	7.76	4.38	1.16
Secondary and high school	5.78	6.47	77.59	63.08
College and above	5.15	5.62	18.03	35.76
Parity				
0	5.94	6.64	49.57	39.67
≥1	5.39	5.88	50.43	60.33
Multiple pregnancy				
No	4.91	5.06	98.01	97.51
Yes	42.69	50.17	1.99	2.49
Prenatal care utilization rate[b]				
< 50%	6.11	8.86	32.16	7.69
50% -< 110%	4.79	5.16	58.11	58.40
≥ 110%	9.44	7.34	9.73	33.91
Infant Gender				
Female	5.21	5.55	45.75	46.45
Male	6.04	6.73	54.25	53.55

- a. 476997 live births were included after removing 1047 records due to missing values in any risk factor.
- b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
- c. The distribution percentage for each category is the number of cases divided by the total number of preterm births.

Discussion

To date, the persistency of increasing preterm birth rate remains a challenging public health issue facing the world and limited studies have focused on the temporal trends of preterm birth during a sociodemographic transition period in recent decades. In this retrospective cohort study, a statistical analysis of 478,044 birth records demonstrated the drivers of the time trends in preterm birth among a mixed population under the sociodemographic transition background in Shenzhen. The findings of this study highlight the importance of safeguarding the health and well-being of women to reduce preterm birth, especially through improving maternal education and prenatal care service coverage.

During the sociodemographic transition period between 2009 and 2018, the overall preterm birth rate of 5.82% in Bao'an was at a relatively lower level compared with the global preterm birth rate ranging from 5% in northern European countries to 18% in African countries [6]. It is also lower than the weighted national incidence of 6.7% in China during 2015-2016 [33]. However, compared with the whole Shenzhen preterm birth rate of 5.7% during 2003-2012, it was slightly higher during 2009-2018 [20]. Consistent with the global trend of the rising preterm birth rate reported by many countries in recent years, the prevalence of preterm birth in Bao'an increased from 5.65% in 2009 to 6.18% in 2018 under the sociodemographic transition background [5, 34]. In our analysis of risk factors and their contributions to the changes in preterm birth rates, more than half of the increase between two periods (before and after implementation of the universal two-child policy) could be explained by the increment in the proportion of multiple pregnancy, which was a strong risk factor for preterm birth with a 7 to10 time higher risk than singletons [35-36]. Concerns have been raised in many studies about the increasing trend of multiple pregnancy reported both in China and worldwide, which was associated with the global rising of advanced maternal age, infertility treatments and obstetric interventions performed before 37 gestational weeks, especially in 34-36 weeks [38-41]. However, this study was limited in information about subtypes of preterm birth, infertility treatment and obstetric interventions, which restricted our further analysis about the hidden drivers of increment in multiple pregnancy and their effects on preterm birth.

In contrast with multiple pregnancy, the improvements in maternal education and prenatal care utilization have contributed to the reduction of preterm birth rate, which coincided with the overall socio-economic developments in China with the launch of laws and policies including 9-Year Compulsory Education for All and National Commitment to Maternal and Child Survival and Health [42, 43]. Particularly, the proportion of pregnant women with inadequate prenatal care utilization narrowed down obviously after implementation of the universal two-child policy and contributed to a 0.45% decline in preterm birth rate. The positive effect of prenatal care on preterm birth during 2009-2018 was estimated to be larger than the period 2003-2012 in the whole Shenzhen birth population [20]. As suggested by the Born Too Soon Group, further studies are needed to clarify the association between the timing and quality of prenatal care visits and preterm birth [44]. Additionally, 0.22% of reduction in preterm birth rate could be explained by the expansion of maternal educational attainment during 2009-2018. However, the effect of maternal education found in this study is contrary to the result in the Shenzhen preterm birth research during 2003-2012, which demonstrated that the education improvement had contributed to 0.2% of rise in preterm birth rate [20]. It should be noted that the proportion of multiparous births increased continuously over the decade, and a near 10% increment after the implementation of the universal two-child policy, which has brought a small reduction in preterm birth rate. The percentage of multiparity in this study was around 15.28% higher than the Shenzhen birth population during 2003-2012 and also higher than the national level [20, 24]. The male-to-female sex ratio in Bao'an during 2009-2018 remained abnormal compared with the natural sex ratio at birth, which indicated that the more balanced sex ratio as one of the expected benefits of the universal two-child policy has not been achieved yet [45, 46].

The present study is unique in reporting the new information about time trends in preterm birth under a rapid sociodemographic transition setting over 10 years. Both contributions of sociodemographic factors to preterm birth and to the incidence changes were calculated for a more comprehensive and quantitative understanding of their pathogenesis of temporal trends in preterm birth. Percent compositions of sociodemographic factors in each year have been presented to give a better landscape of the socio-economic transition in this area. Few missing information on prenatal care utilization and parity unlikely impacted hugely on the results. However, data about maternal socioeconomic status and employment, as well as phenotypes of preterm birth including spontaneous preterm and iatrogenic preterm were not available. As a result, analysis about whether income and employment factors mediated the time trends of specific preterm birth was not available. Meanwhile, among the risk factors analysed in this study, only sociodemographic transitions in maternal age and multiple pregnancy have been identified as contributors to the rising preterm birth rate in Bao'an, Shenzhen during 2009-2018, which indicated that about half the change is unexplained. Other important factors including non-medically indicated labour, induction and cesarean section deliveries, assisted reproductive technologies need to be analysed in future studies.

Conclusions

In conclusion, the present study provides unique information about the temporal trends in preterm birth among a mixed population under the rapid sociodemographic transition setting in China during the last decade. The observed increment in preterm birth rate was significantly associated with the expansion of multiple pregnancy. Fortunately, maternal educational attainment and prenatal care utilization have improved obviously during the period and positive contributions to the decline in preterm birth incidence have been made. The study findings highlight that the investment in girls' education, quality reproductive and maternal healthcare may render significant reductions in the rate of babies born too soon and economic burden of preterm birth. More studies need to be conducted to discover the hidden risk factors that drive the increase of preterm birth rate and finally to reduce the prevalence of preterm birth and its global burden.

Acknowledgments

We would like to thank the staff who provided us with limited but accredited access to the Shenzhen Birth Registry Database and suggestions on the use of this database.

References

1. Romero R, Dey SK, Fisher SJ. Preterm labor: one syndrome, many causes. *Science* 2014;345(6198):760-765.
2. Maghsoudlou S, Yu ZM, Beyene J, *et al*. Phenotypic Classification of Preterm Birth Among Nulliparous Women: A Population-Based Cohort Study. *J Obstet Gynaecol Can* 2019;41(10):1423-1432 e1429.
3. Lawn JE, Kinney MV, Belizan JM, *et al*. Born too soon: accelerating actions for prevention and care of 15 million newborns born too soon. *Reprod Health* 2013;10 Suppl 1:S6.
4. United Nations Inter-agency Group for Child Mortality Estimation (UNIGME). Levels & Trends in Child Mortality: Report 2019, Estimates developed by the United Nations Inter-agency Group for Child Mortality Estimation. United Nations Children's Fund, New York, 2019.
5. Chawanpaiboon S, Vogel JP, Moller AB, *et al*. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *Lancet Glob Health* 2019; 7(1):e37-e46.
6. Blencowe H, Cousens S, Chou D, *et al*. Born too soon: the global epidemiology of 15 million preterm births. *Reprod Health* 2013;10 Suppl 1:S2.
7. Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes; Behrman RE, Butler AS. Preterm Birth: Causes, Consequences, and Prevention. *National Academies Press (US)* 2007.
8. Johnston KM, Gooch K, Korol E, *et al*. The economic burden of prematurity in Canada. *BMC Pediatr* 2014;14:93.
9. Boerma T. Countdown to 2030: tracking progress towards universal coverage for reproductive, maternal, newborn, and child health. *Lancet* 2018;391(10129):1538-1548.
10. Rahman A, Rahman M, Pervin J, *et al*. Time trends and sociodemographic determinants of preterm births in pregnancy cohorts in Matlab, Bangladesh, 1990-2014. *BMJ Glob Health* 2019;4(4):e001462.
11. Sakata S, Konishi S, Ng CFS, *et al*. Preterm birth rates in Japan from 1979 to 2014: Analysis of national vital statistics. *J Obstet Gynaecol Res* 2018;44(3):390-396.
12. Lopez Orellana P. Increase in Preterm Birth during Demographic Transition in Chile from 1991 to 2012. *Biomed Res Int* 2015;2015:845968.
13. Sadovsky ADI, Matijasevich A, Santos IS, *et al*. Socioeconomic inequality in preterm birth in four Brazilian birth cohort studies. *J Pediatr (Rio J)* 2018;94(1):15-22.
14. Wilding S, Ziauddeen N, Roderick P, *et al*. Are socioeconomic inequalities in the incidence of small-for-gestational-age birth narrowing? Findings from a population-based cohort in the South of England. *BMJ Open* 2019;9(7):e026998.
15. Yang M, Dijst M, Helbich M. Mental Health among Migrants in Shenzhen, China: Does it Matter Whether the Migrant Population is Identified by Hukou or Birthplace? *Int J Environ Res Public Health*. 2018;15(12):2671.
16. Shenzhen Statistics Bureau. Shenzhen Statistical Yearbook 2019. Date accessed: December 30, 2019. Available online: http://www.sz.gov.cn/attachment/0/405/405056/6616865.pdf.
17. Shenzhen Bao'an Statistics Bureau. Shenzhen Bao'an Statistical Yearbook 2017. Date accessed: November 30, 2018. Available online: http://sso.sz.gov.cn/pub/baqzfzx2017/tjj/ywgz_136262/tjsj_137617/tjnj_137621/201811/P020181130433800362927.pdf.
18. Shenzhen Bao'an Statistics Bureau. Shenzhen Bao'an Statistical Yearbook 2012. Date accessed: February 24, 2014. Available online:

http://sso.sz.gov.cn/pub/baqzfzx2017/tjj/ywgz_136262/tjsj_137617/tjnj_137621/201404/P020140429367563038549.pdf.
19. Liang Z, Lin Y, Ma Y, et al. The association between ambient temperature and preterm birth in Shenzhen, China: a distributed lag non-linear time series analysis. *Environ Health* 2016;15(1):84.
20. Li C, Liang Z, Bloom MS, *et al*. Temporal trends of preterm birth in Shenzhen, China: a retrospective study. *Reprod Health* 2018;15(1):47.
21. WHO. Recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. Modifications recommended by FIGO as amended October 14, 1976. *Acta Obstet Gynecol Scand* 1977;56(3):247-253.
22. Tang K, Wang H, Tan SH, *et al*. Association between maternal education and breast feeding practices in China: a population-based cross-sectional study. *BMJ Open* 2019;9(8):e028485.
23. Osterman MJK, Martin JA. Timing and Adequacy of Prenatal Care in the United States, 2016. *Natl Vital Stat Rep* 2018;67(3):1-14.
24. Li HT, Xue M, Hellerstein S, et al. Association of China's universal two child policy with changes in births and birth related health factors: national, descriptive comparative study. *BMJ* 2019;366:l4680.
25. McHugh ML. The chi-square test of independence. *Biochem Med (Zagreb*) 2013, 23(2):143-149.
26. Thabane L, Mbuagbaw L, Zhang S, *et al*. A tutorial on sensitivity analyses in clinical trials: the what, why, when and how. *BMC Med Res Methodol* 2013;13:92.
27. Sperandei S. Understanding logistic regression analysis. *Biochem Med (Zagreb)* 2014;24(1):12-18.
28. Goldenberg RL, Culhane JF, Iams JD, *et al*. Epidemiology and causes of preterm birth. *Lancet* 2008;371(9606):75-84.
29. Auger N, Le TU, Park AL, *et al*. Association between maternal comorbidity and preterm birth by severity and clinical subtype: retrospective cohort study. *BMC Pregnancy Childbirth* 2011;11:67.
30. VanderWeele TJ, Lantos JD, Lauderdale DS. Rising preterm birth rates, 1989-2004: changing demographics or changing obstetric practice? *Soc Sci Med* 2012;74(2):196-201.
31. Chang HH, Larson J, Blencowe H, *et al*. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. *Lancet* 2013;381(9862):223-234.
32. Greenland S, Senn SJ, Rothman KJ, *et al*. Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations. *Eur J Epidemiol* 2016;31(4):337-350.
33. Chen C, Zhang J, Xia H, *et al*. Epidemiology of preterm birth in China in 2015 and 2016: a nationwide survey. *The Lancet* 2018;392:S73.
34. Chang HH, Larson J, Blencowe H, et al. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. *Lancet* 2013;381(9862):223-234.
35. Dodd JM, Grivell RM, CM OB, *et al*. Prenatal administration of progestogens for preventing spontaneous preterm birth in women with a multiple pregnancy. *Cochrane Database Syst Rev* 2019;2019(11).
36. Blondel B, Macfarlane A, Gissler M, *et al*. General obstetrics: Preterm birth and multiple pregnancy in European countries participating in the PERISTAT project. *BJOG* 2006;113(5):528-535.
37. Deng C, Dai L, Yi L, *et al*. Temporal trends in the birth rates and perinatal mortality of twins: A population-based study in China. *PLoS One* 2019;14(1):e0209962.
38. Pison G, Monden C, Smits J. Twinning Rates in Developed Countries: Trends and Explanations. *Population and Development Review* 2015;41(4):629-649.
39. Richards JL, Kramer MS, Deb-Rinker P, Rouleau J, Mortensen L, Gissler M, Morken NH, Skjaerven R, Cnattingius S, Johansson S *et al*. Temporal Trends in Late Preterm and Early Term Birth Rates in 6 High-Income Countries in North America and Europe and Association With Clinician-Initiated Obstetric Interventions. *JAMA* 2016;316(4):410-419.
40. Fox H, Callander E, Lindsay D, Topp S. Evidence of overuse? Patterns of obstetric interventions during labour and birth among Australian mothers. *BMC Pregnancy and Childbirth* 2019;19(1):226.
41. Zhong N. Achieving Lower Preterm Birth Rates in China via Reductions in Iatrogenic Preterm Births. *Am J Public Health* 2019;109(11):1489-1490.
42. He C, Liu L, Chu Y, *et al*. National and subnational all-cause and cause-specific child mortality in China, 1996-2015: a systematic analysis with implications for the Sustainable Development Goals. *Lancet Glob Health* 2017;5(2):e186-e197.
43. Guo Y, Bai J, Na H. The history of China's maternal and child health care development. *Semin Fetal Neonatal Med* 2015;20(5):309-314.

44. Requejo J, Merialdi M, Althabe F, *et al*. Born too soon: care during pregnancy and childbirth to reduce preterm deliveries and improve health outcomes of the preterm baby. *Reprod Health* 2013;10 Suppl 1:S4.
45. Shah PS, Knowledge Synthesis Group on Determinants of LBWPTb. Parity and low birth weight and preterm birth: a systematic review and meta-analyses. *Acta Obstet Gynecol Scand* 2010;89(7):862-875.
46. Zeng Y, Hesketh T. The effects of China's universal two-child policy. *Lancet* 2016; 388(10054): 1930-1938.

Footnotes

Contributors: LYZ, LZ and RM developed the study concept and design. RM, YLL and QX collected data. RM cleaned the data and performed data analysis. RM and LYZ drafted the manuscript. LYZ, LZ, YLL, JW, YXZ, HYS, XR provided oversight and expert advice for the research and the written paper. All authors revised and approved the final paper.

Funding: This study is supported by the National Natural Science Foundation of China (grant number: 31771468)

Disclaimer: The funding sources had no involvement in any aspect of this study.

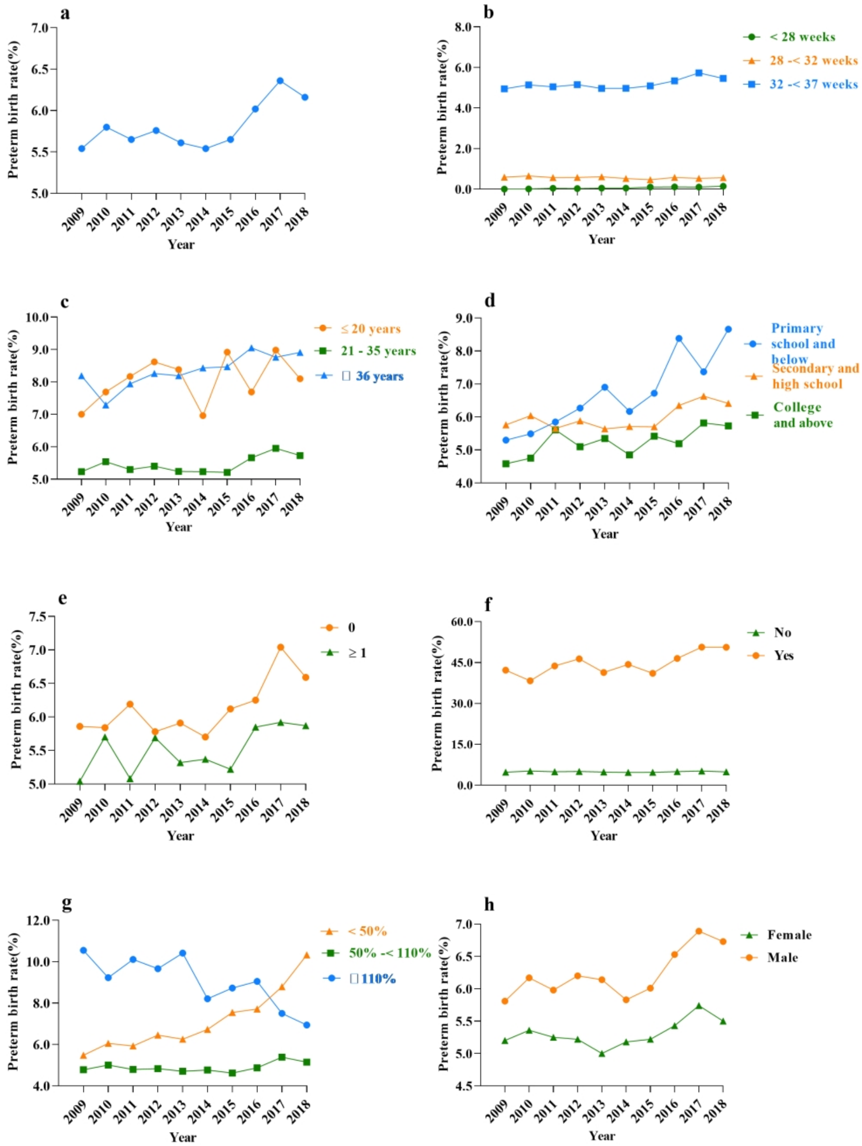
Competing interests: None declared.

Patient consent for publication: Not required.

Ethics approval: This study was approved by the medical ethics committee of Bao'an Women's and Children's Hospital, Jinan University, Shenzhen, China (number LLSC-2019-07-01). All data used in this study have been completely anonymized before accession and were analysed anonymously.

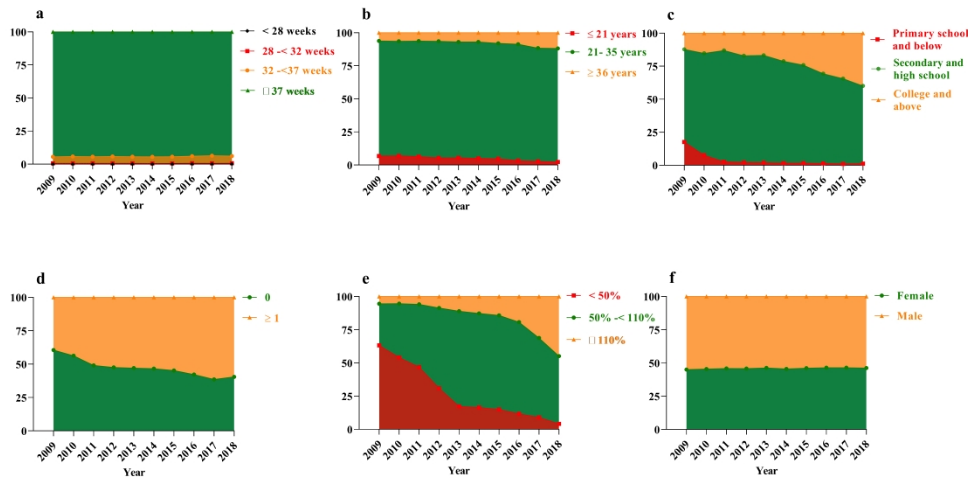
Provenance and peer review: Not commissioned; externally peer reviewed.

Data sharing statement: Data are available upon reasonable request to the corresponding author.



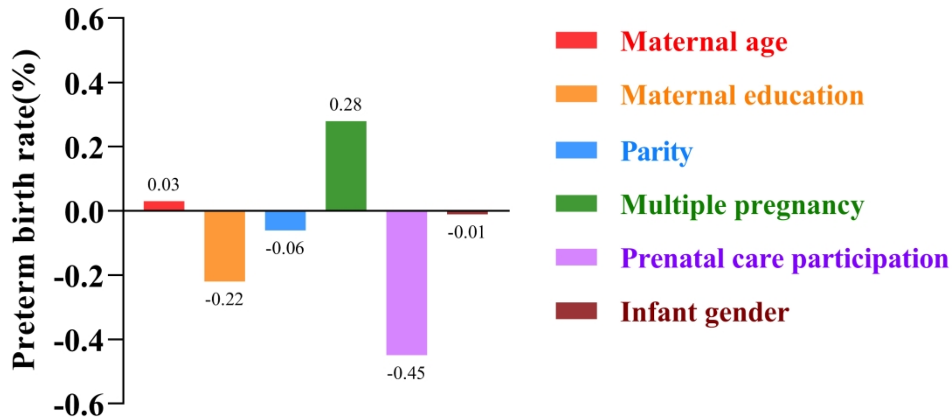
Temporal Trends in Preterm Birth Rate Subcategorized by Risk Factors in Bao'an, Shenzhen, 2009-2018.
a. Overall b. Gestational age c. Maternal age d. Maternal education e. Parity f. Multiple pregnancy
g. Prenatal care utilization h. Infant gender

213x281mm (300 x 300 DPI)



Temporal Trends in the Distribution of Sociodemographic Factors in Bao'an, Shenzhen, 2009-2018.
a. Gestational age b. Maternal age c. Maternal education d. Parity e. Prenatal care utilization f. Infant gender

301x156mm (600 x 600 DPI)



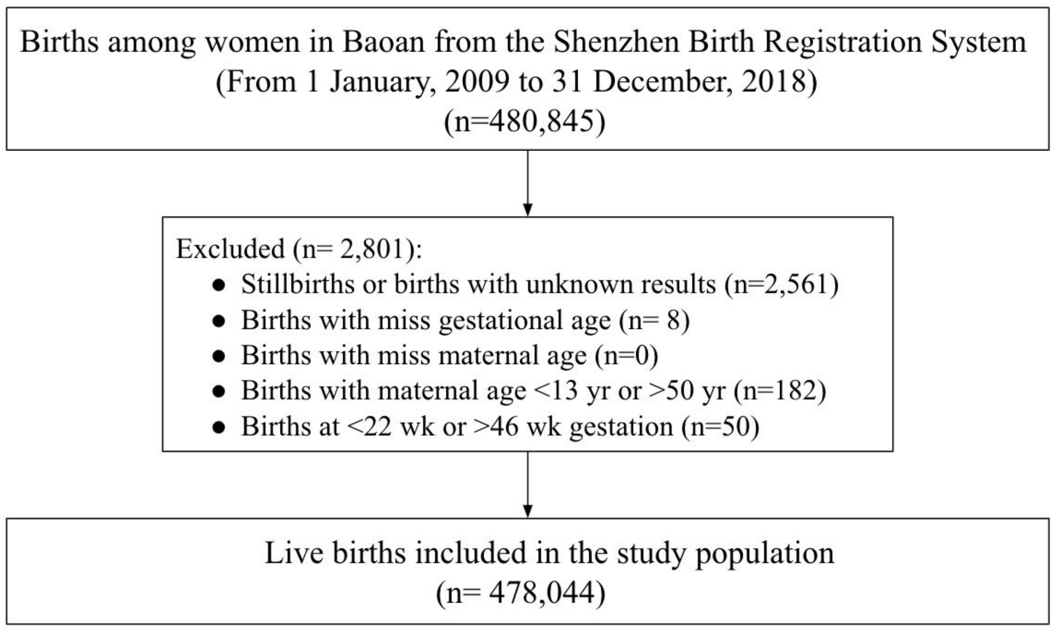
Analysis of Sociodemographic Factors Contributing to the Variations of Preterm Birth Rate in Bao'an, Shenzhen, 2009-2018

131x60mm (600 x 600 DPI)

Supplementary Materials

Ten-year time trends in preterm birth during a sociodemographic transition period: a retrospective cohort study in Shenzhen, China

Supplementary Figure 1. Flowchart of Study Population



Supplementary Table 1. Temporal Trends in Preterm Birth Rate (%) in Baoan, Shenzhen, 2009 - 2018

	Year									
	2009	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Overall Preterm Birth Rate	5.54	5.80	5.65	5.76	5.61	5.54	5.65	6.02	6.36	6.16
Gestational age(week)										
< 28	0.00	0.01	0.04	0.03	0.05	0.05	0.10	0.11	0.10	0.14
28 -< 32	0.59	0.65	0.57	0.58	0.61	0.52	0.46	0.58	0.53	0.56
32 -< 37	4.94	5.14	5.04	5.15	4.96	4.97	5.09	5.34	5.73	5.46
Maternal age(year)										
≤ 20	7.00	7.69	8.17	8.62	8.38	6.96	8.92	7.69	8.98	8.10
21-35	5.23	5.54	5.30	5.40	5.24	5.23	5.21	5.66	5.95	5.73
≥ 36	8.19	7.29	7.94	8.26	8.19	8.43	8.47	9.05	8.76	8.91
Maternal education										
Primary school and below	5.30	5.49	5.85	6.27	6.90	6.17	6.72	8.38	7.37	8.66
Secondary and high school	5.76	6.04	5.65	5.88	5.64	5.71	5.70	6.35	6.63	6.41
College and above	4.58	4.75	5.61	5.10	5.35	4.85	5.42	5.19	5.82	5.73
Parity										
0	5.86	5.84	6.19	5.78	5.91	5.7	6.12	6.25	7.04	6.59
≥ 1	5.04	5.7	5.08	5.69	5.32	5.37	5.22	5.85	5.92	5.87
Multiple pregnancy										
No	4.84	5.23	4.96	5.06	4.87	4.71	4.80	5.00	5.23	4.94
Yes	42.24	38.32	43.78	46.37	41.40	44.32	41.06	46.51	50.68	50.65
Prenatal care utilization rate[a]										
< 50%	5.48	6.06	5.93	6.46	6.26	6.73	7.55	7.72	8.79	10.33
50% - < 110%	4.78	5.01	4.8	4.84	4.71	4.77	4.62	4.88	5.39	5.15
≥ 110%	10.55	9.23	10.11	9.66	10.42	8.21	8.73	9.05	7.5	6.94
Infant gender										
Female	5.20	5.36	5.25	5.22	5.00	5.18	5.22	5.43	5.74	5.50
Male	5.81	6.17	5.98	6.20	6.14	5.83	6.01	6.53	6.89	6.73

a. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.

Supplementary Table 2. Sensitivity Analysis of Temporal Trends for Overall Preterm Birth Rates in Baoan, Shenzhen, 2009 - 2018

Year	Preterm birth rate(%)	Risk Ratio(95%CI)	P Value
2009	5.54	Reference	
2010	5.80	1.003(0.999,1.006)	0.104
2011	5.65	1.001(0.998,1.004)	0.493
2012	5.76	1.002(0.999,1.006)	0.148
2013	5.61	1.001(0.998,1.004)	0.626
2014	5.54	1.000(0.997,1.003)	0.986
2015	5.65	1.001(0.998,1.004)	0.494
2016	6.02	1.005(1.002,1.008)	0.002
2017	6.36	1.009(1.005,1.012)	0.000
2018	6.16	1.007(1.003,1.010)	0.000

Supplementary Table 3. Temporal Trends in the Distribution Percentage (%) of Sociodemographic Factors in Baoan, Shenzhen, 2009 - 2018[a]

	Year									
	2009	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
All live births	38590	41912	46617	54957	46861	50063	45872	51328	52823	49021
Gestational age(week)										
< 28	0.00	0.01	0.04	0.03	0.05	0.05	0.10	0.11	0.10	0.14
28 -< 32	0.59	0.65	0.57	0.58	0.61	0.52	0.46	0.58	0.53	0.56
32 -< 37	4.94	5.14	5.04	5.15	4.96	4.97	5.09	5.34	5.73	5.46
≥ 37	94.46	94.20	94.35	94.24	94.39	94.46	94.35	93.98	93.64	93.84
Maternal age(year)										
≤ 20	6.81	6.92	6.41	5.36	5.48	5.05	4.72	3.37	2.80	2.29
21-35	86.99	86.63	87.32	88.21	87.60	88.03	87.23	87.91	85.61	85.81
≥ 36	6.20	6.45	6.27	6.43	6.93	6.92	8.05	8.72	11.58	11.90
Maternal education										
Primary school and below	17.59	7.60	2.64	2.12	1.92	1.62	1.62	1.37	1.08	1.20
Secondary and high school	70.19	77.18	84.35	80.87	81.39	77.18	74.22	68.01	64.57	58.91
College and above	12.22	15.22	13.01	17.01	16.69	21.20	24.16	30.62	34.35	39.88
Parity										
0	60.54	56.25	49.06	47.50	47.05	46.66	45.18	42.19	38.51	40.47
≥ 1	39.46	43.75	50.94	52.50	52.95	53.34	54.82	57.81	61.49	59.53
Multiple pregnancy										
No	98.13	98.26	98.24	98.30	97.95	97.91	97.66	97.54	97.51	97.33
Yes	1.87	1.74	1.76	1.70	2.05	2.09	2.34	2.46	2.49	2.67
Prenatal care utilization rate[b]										
< 50%	63.24	54.13	46.82	30.96	17.33	16.44	15.05	11.72	9.05	4.11
50% - <110%	31.33	40.49	47.30	60.38	71.64	70.88	70.70	68.97	59.72	51.05
≥ 110%	5.43	5.38	5.88	8.67	11.02	12.68	14.24	19.32	31.24	44.84
Infant Gender										
Female	45.02	45.44	45.90	45.77	46.26	45.58	46.14	46.46	46.43	46.17
Male	54.98	54.56	54.10	54.23	53.74	54.42	53.86	53.54	53.57	53.83

a. The distribution percentage (%) for each category is the number of cases divided by the total number of preterm births.
b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.

Supplementary Table 4. Analysis of Sociodemographic Factors Contributing to Variations of Preterm Birth Rate in Baoan, Shenzhen, 2009-2018[a]

	Distribution percentage(%)[c]		AOR[d]	AFp(%)[e]		Preterm Birth Rate Change(%)[f]
	2009.01-2016.06	2016.07-2018.12		2009.01-2016.06	2016.07-2018.12	
Maternal age(year)				6.02	6.48	0.03
≤20	5.59	2.75	1.54			
21-35	87.55	86.18	Reference			
≥36	6.86	11.07	1.49			
Maternal education				17.91	14.30	-0.22
Primary school and below	4.38	1.16	1.44			
Secondary and high school	77.59	63.08	1.26			
College and above	18.03	35.76	Reference			
Parity				4.83	3.90	-0.06
0	49.57	39.67	1.10			
≥ 1	50.43	60.33	Reference			
Multiple pregnancy				25.65	30.15	0.28
No	98.01	97.51	Reference			
Yes	1.99	2.49	18.34			
Prenatal care utilization rate[b]				22.30	15.06	-0.45
< 50%	32.16	7.69	1.79			
50% - <110%	58.11	58.40	Reference			
≥ 110%	9.73	33.91	1.34			
Infant Gender				12.68	12.54	-0.01
Female	45.75	46.45	Reference			
Male	54.25	53.55	1.27			

a. 476997 live births were included after removing 1047 records due to missing values in any risk factor.
b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
c. The distribution percentage for each category is the number of cases divided by the total number of preterm births.
d. AOR: adjusted odds ratio
e. AFp: Attributable risk fraction for the population.
f. Preterm birth rate change is calculated by multiplying AFp with the preterm birth rate after the policy and subtract the result for before the policy.

Supplementary Table 5. Comparisons of Preterm Birth Rates and Risk Factor Distribution Percentages in Baoan, Shenzhen, 2003-2018[a]

	Distribution percentage(%)[c]		Preterm birth rate(%)	
	2003-2012[c]	**2009-2018**	**2003-2012[c]**	**2009-2018**
Gestational age(week)				
<28 weeks	10.27	1.12	0.58	0.07
28-<32 weeks	12.79	9.65	0.72	0.56
32-<37 weeks	76.94	89.23	4.34	5.19
Maternal age(year)				
≤20	5.88	4.82	6.97	8.01
21-35	88.79	87.15	5.40	5.46
≥36	5.33	8.03	8.34	8.47
Maternal education				
Less than high school	43.27	34.59	5.71	5.82
High school and college	35.98	55.17	5.82	5.93
Bachelor	19.04	8.89	5.21	5.29
Postgraduate	1.71	1.35	5.35	4.69
Parity				
0	62.08	46.83	5.77	6.10
≥ 1	37.92	53.17	5.42	5.55
Prenatal care utilization rate[b]				
< 50%	45.88	25.52	7.14	6.38
50% - <110%	39.88	58.10	5.28	4.89
≥ 110%	14.23	16.38	1.86	8.24
Infant Gender				
Female	45.72	45.95	5.26	5.32
Male	54.28	54.05	5.97	6.25

a. Li C, Liang Z, Bloom MS, et al. Temporal trends of preterm birth in Shenzhen, China: a retrospective study. *Reprod Health* 2018;15(1):47.
b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
c. The distribution percentage for each category is the number of cases divided by the total number of preterm births.

STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	4
		(*b*) For matched studies, give matching criteria and the number of controls per case	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, explain how matching of cases and controls was addressed	
		(*e*) Describe any sensitivity analyses	4
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	5-8

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Ten-year time trends in preterm birth during a sociodemographic transition period: a retrospective cohort study in Shenzhen, China

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-037266.R1
Article Type:	Original research
Date Submitted by the Author:	19-Jun-2020

Complete List of Authors:	Ma, Rui; Shenzhen City Baoan District Womens and Childrens Hospital, Center for Big Data Research in Health Luo, Yali; Shenzhen City Baoan District Womens and Childrens Hospital, Department of Prevention & Health Care Wang, Jun; Shenzhen City Baoan District Womens and Childrens Hospital, Center for Big Data Research in Health Zhou, Yanxia; Shenzhen City Baoan District Womens and Childrens Hospital, Centre for Big Data Research in Health Sun, Haiyang; Shenzhen City Baoan District Womens and Childrens Hospital, Centre for Big Data Research in Health Ren, Xi; Shenzhen City Baoan District Womens and Childrens Hospital, Centre for Big Data Research in Health Xu, Quan; Shenzhen City Baoan District Womens and Childrens Hospital, Department of Prevention & Health Care Zhang, Lian; Shenzhen City Baoan District Womens and Childrens Hospital, Department of Neonatology Zou, Lingyun; Shenzhen City Baoan District Womens and Childrens Hospital, Center for Big Data Research in Health

Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health, Epidemiology
Keywords:	EPIDEMIOLOGY, PUBLIC HEALTH, Maternal medicine < OBSTETRICS, Child protection < PAEDIATRICS

Ten-year time trends in preterm birth during a sociodemographic transition period: a retrospective cohort study in Shenzhen, China

Rui Ma[1], Yali Luo[2], Jun Wang[1], Yanxia Zhou[1], Haiyang Sun[1], Xi Ren[1], Quan Xu[2], Lian Zhang[3*], Lingyun Zou[1*]

Author affiliations
[1] Center for Big Data Research in Health, Shenzhen Baoan Women's and Children's Hospital, Jinan University, Shenzhen, China
[2] Department of Prevention & Health Care, Shenzhen Baoan Women's and Children's Hospital, Jinan University, Shenzhen, China
[3] Department of Neonatology, Shenzhen Baoan Women's and Children's Hospital, Jinan University, Shenzhen, China

***Correspondence to**
Dr Lingyun Zou, Center for Big Data Research in Health, Shenzhen Baoan Women's and Children's Hospital, Jinan University, Shenzhen, 518102, China; +86 755 23202015; lingyun.zou@gmail.com

Dr Lian Zhang, Department of Neonatology, Shenzhen Baoan Women's and Children's Hospital, Jinan University, Shenzhen, 518102, China; +86 755 23202015; zhliande@qq.com

Wordcount: 4222

Abstract

Objectives To investigate time trends of preterm birth and estimate the contributions of risk factors to the changes in preterm birth rates over a decade (2009-2018) of transitional period in Shenzhen, China.

Design Retrospective cohort study between 2009 and 2018.

Setting All births in Baoan during January 2009 and December 2018 registered in the Shenzhen Birth Registry Database.

Participants 478,044 live births were included with sociodemographic and medical records for both women and infants.

Outcome measures The incidence rate of preterm birth stratified by different maternal and infant characteristics. Multiple logistic regression was used to identify significant risk factors associated with preterm birth. The population attributable risk fraction of each factor was calculated to estimate its contribution to variations of preterm birth rate over the ten years.

Results A total of 27,829 preterm births from 478,044 live births (5.82%) was recorded and the preterm birth rate increased from 5.65% in 2009 to 6.18% in 2018. Medically induced preterm birth rate increased from 2.03% in 2009 to 3.38% in 2018 while spontaneous preterm labor rate decreased from 3.34% to 2.68% over the decade years. Risk factors including maternal age (0.03% increase) and multiple pregnancy (0.28% increase) drove the rise of preterm birth rate whereas changes in maternal educational attainment (0.22% reduction), parity (0.06% reduction) and prenatal care utilization (0.45% reduction) had contributed to the decline in preterm birth rate.

Conclusions An uptrend of preterm birth rate was observed in an area under rapid sociodemographic transitions during 2009-2018 and the changes were associated with these sociodemographic transitions. Continued investments in girls' education and prenatal care have the potential of reducing preterm birth rate.

Strengths and limitations of this study

- The study provides unique information about the time trends in preterm birth over the last decade in a setting of rapid sociodemographic transitions with a large proportion of migrant workers.
- Population attribution risk fraction was used to quantify the contributions of changes in risk factors to the variations of preterm birth rate. Overall preterm births were classified into subtypes including spontaneous preterm births and iatrogenic preterm births.
- We had no information about family income and maternal employment and their effects on preterm birth trends were unable to be analysed in this study.
- A limited number of risk factors that drove the growth of preterm birth rate have been examined in this study.

Introduction

Defined as birth prior to 37 completed weeks' gestation, preterm birth is a syndrome with many causes and multiple phenotypes [1-2]. Globally, approximately 15 million neonates were born preterm in 2014 and over one million children die each year due to preterm birth complications, contributing to approximately 16% of all deaths and 35% of newborn deaths in 2019 [3-4]. Despite decades of substantial research, the increasing prevalence of preterm birth remained in many countries worldwide, from 9.8% in 2000 to 10.6% in 2014 [5]. Even fortunate survivors may suffer from lifetime disabilities, including neurodevelopmental and physical impairments, as well as behavioral effects, which impose heavy family and societal burden [6]. The economic burden associated with preterm birth complications was at least $26.2 billion in the United States in 2005 and $587.1 million in Canada in 2014 [7, 8]. Addressing risk factors of preterm birth and the cause of the incremental incidence are critical to inform public health policies aiming at reducing the global burden of preterm births and achieving the Global Strategy for Women's, Children's, and Adolescents' Health under the Sustainable Development Goal [9].

Sociodemographic transitions have been shown associated with time trends in preterm birth, especially in areas during the industrialization period. A cohort study from Bangladesh unveiled that 27% of the decline in preterm birth rate could be attributed to the decrease in parity and expansion of maternal education during 1990-2014 [10]. Maternal age at delivery could explain the secular trends of preterm birth in Japan from 1979 to 2014 based on national birth data [11]. During the Chilean sociodemographic transition period 1991-2012, the increase in advanced maternal age (35 or older) was evaluated to increase the risk of preterm birth significantly [12]. Economic inequalities were also found in relation to preterm births in four Brazilian birth cohort studies between 1982 and 2011 [13]. A population-based cohort study on births in Newcastle upon Tyne, North of England over four decades confirmed the widened preterm birth gap between the most and least deprived socioeconomic groups [14].

China accounted for 7.8% (1.17 million) of preterm births worldwide with the second largest number of preterm neonates [5]. From 2000 to 2014, the estimated preterm birth rate in China had risen from 6.35% to 6.94% [5]. As the first Special Economic Zone located in the Pearl River Delta of South China, Shenzhen has undergone rapid urbanization and attracted millions of migrant labourers since the beginning of the 1980s [15]. Baoan is a typical epitome of this urbanization as the largest district in Shenzhen with more than 3.26 million year-end permanent population in 2018 and around 82% are migrants from other parts of China [16]. Between 2012 and 2018, the de jure population of Baoan has quickly expanded from 2.68 million to 3.26 million and the gross domestic product per capita has grown from $8556 in 2008 to $15981 in 2017 [16-18]. In addition, the proportion of labourers in the tertiary sector of the economy increased from 15.7% in 2012 to 22.6% in 2017 [16-17].

However, limited studies on long-term time trends in preterm birth are available in areas under drastic sociodemographic transitions in China during recent decades. Transitions in society and their contributions to the changes in preterm birth rate are still unclear. The present study was based on all births in Baoan during 2009-2018 registered in the Shenzhen Birth Registry Database. We sought to assess the temporal trends of preterm birth and associated risk factors among a large proportion of migrant population. We further estimated quantitative contributions of these factors to the changes in preterm birth rates over the last decade.

Methods

Study design and data collection

This cohort study was based on data of all births in Baoan during 1 January 2009 and 31 December 2018 extracted from the Shenzhen Birth Registry Database, which has served as a system for birth registration and maternal, infant health management since 2000 [19]. Demographic and clinical records of both mothers and newborns were available for the identification of preterm birth and risk factors. Only live births were included in this study and ineligible data were excluded to ensure the coherence and continuity of preterm birth rate calculation based on prior related research: (1) Stillbirths or births with unknown results; (2) Births with missing gestational age or gestational age < 22 weeks or > 46 weeks; (3) Births with missing maternal age or maternal age < 13 years or > 50 years. The flowchart of data selection was shown in the supplementary file: Figure 1 [5, 20].

Patient and public involvement

This study used routinely collected administrative health data and no patients were involved in the conception, design and conduct of the research. Results will be disseminated via open access publication.

Ethics approval

This study was approved by the medical ethics committee of Baoan Women's and Children's Hospital, Jinan University. Data collected in the study were anonymous and no individually identifiable information was available for the analysis.

Definition and measurements

Preterm birth was defined by WHO as all births before 37 completed weeks of gestation or fewer than 259 days since the first day of a woman's last menstrual period [3, 21]. Based on gestational age, it was further grouped as extremely preterm (<28 weeks), very preterm (28 - <32 weeks) and late preterm (32 - <37 weeks). Preterm birth rate was calculated using the number of live births in a specific preterm category divided by all live births multiplied by 100 in a specific time period [21].

Based on delivery mode and surgical indications recorded in the database, we categorized preterm birth into three subtypes: two spontaneous preterm birth subtypes including preterm premature rupture of membranes (PROM-PTB) and preterm labor (S-PTB), and the third subtype medically induced preterm birth (MI-PTB). Preterm premature rupture of membranes (PROM-PTB) was defined as preterm birth with premature rupture of membranes; preterm labor (S-PTB) was defined as non-PROM with vaginal deliveries; medically induced preterm birth (MI-PTB) was defined as preterm birth with either induction of labor or cesarean section delivery but without PROM [20].

Potential risk factors related to preterm birth were selected and analysed based on the literature review [10-14]. Variables including gestational age, maternal age, maternal education, maternal ethnicity , immigrant, smoking, drinking, parity, delivery mode, fertility treatment, gestational age of first prenatal care visit, number of prenatal care visits, gestational hypertension, gestational diabetes, preeclampsia or eclampsia, infant gender and date of delivery were included into our analysis. Numeric variables including gestational age, maternal age, gestational age of first prenatal care visit were categorized into ordinal subgroups. We classified maternal education into 3 categories for a more balanced population and clear data interpretation: primary school and below, secondary and high school, college and above [22]. Prenatal care utilization is recommended by the Law of the People's Republic of China on Maternal and Infant Health Care with initiating antenatal care during the first trimester of pregnancy and making five or more antenatal care visits [23]. Three first visit trimester groups were generated based on gestational age of first prenatal care visit [24]. The number of prenatal care visits was transformed into prenatal care utilization rate, by calculating the ratio between the actual number of visits and the recommended number of visits. The ratio was then classified into three groups: inadequate (< 50%), intermediate and appropriate (50-110%), adequate plus (≥ 110%) [24]. To analyse the effect of the universal two-child policy, we classified births into two groups based on time of delivery: births taking place before or within nine months after the implementation of the universal two-child policy in October 2015 (June 2016) and births taking place nine months after the policy [25].

Statistical analysis

Chi-Square test was used to evaluate statistical differences in frequencies of both overall and subtypes of preterm birth between each maternal and infant group in this study [26]. Annual overall preterm birth rates for each risk factor subcategory were calculated to present the temporal trends stratified by different characteristics over the decade. Yearly percent compositions of each risk factor were calculated to show the changes in sociodemographic indicators. The sensitive analysis was performed to examine changes in linear trends of annual overall preterm birth rates by calculating risk ratios, with the year 2009 as a reference [27]. Multivariable binomial logistic regression models were applied to estimate adjusted odds ratios (AORs) and 95% confidence intervals (95% CI) of covariates for overall preterm birth and subtype-specific preterm birth [28]. Possible independent variables were selected based on univariate analyses (p<0.05) and their probable associations with preterm birth judged by prior domain knowledge [29].

To examine the contribution of risk factors to preterm birth incidence in the entire study population over the decade, we measured the population attributable risk fraction with formula (1) where AFp_i is the population attributable risk fraction for risk factor i, PF_j is the proportion of the total population and RR_j is the risk ratio for the exposure category j ($j = 1, 2, ..., m$) of risk factor i ($i = 1, 2, ..., n$). RR_j was approximated by using OR_i to avoid overlap from different risk factors [30, 31]. AFp was then calculated with formula (2) to measure the total population attributable risk fraction across all risk factors.

$$AFp_i = \frac{\sum_1^m PF_j * (RR_j - 1)}{1 + \sum_1^m PF_j * (RR_j - 1)} \quad (1)$$

$$AFp = 1 - \prod_i^n (1 - AFp_i) \quad (2)$$

We evaluated sociodemographic changes after the universal two-child policy and their contributions to the variations of preterm birth rate with approaches: (1) calculate PF for each selected factor in two time periods, (2) identify the risk of preterm birth for these factors with odds ratios (ORs) in a logistical regression among births after the policy, (3) estimate AFp for each factor before and after the policy (AFp_{before} was calculated by PF_{before} and OR_{after} whereas AFp_{after} was calculated by PF_{after} and OR_{after}), (4) calculate the total contribution to the changes in preterm birth rate between two periods by multiplying AFp with the preterm birth rate after the policy and subtract the result for before the policy with formula (3) [20, 32].

$$Increased\ Rate = AFp_{after} * Rate_{after} - AFp_{before} * Rate_{after} \quad (3)$$

All the analyses were conducted using Python software (version 3.6.6; Python Software Foundation). Alpha levels of 0.001, 0.01 and 0.05 indicated statistical significance for a two-tailed test separately [33]. Missing values of several variables were included in the descriptive analysis but removed from the logistic regression analyses.

Results

Preterm birth rates in Baoan, Shenzhen

A total of 480,845 births in Baoan, Shenzhen was identified in the Shenzhen Birth Registry Database during 2009 and 2018. 478,044 (99.42%) live births were included in the final study population after excluding 2801 (0.58%) ineligible birth records: 2561 (0.53%) stillbirths or births with unknown results, 182 (0.04%) live births with maternal age under 13 years or over 50 years, 58 (0.01%) live births with missing gestational age, gestational age lower than 22 weeks or higher than 46 weeks. There were 27,829 (5.82%) preterm births in Baoan from 2009 to 2018 with 312 (0.07%) extremely preterm births (<28 weeks), 2686 (0.56%) very preterm births (28-<32 weeks) and 24831 (5.19%) late preterm births (32-<37 weeks) respectively. Rates of PROM-PTB, S-PTB and MI-PTB were 0.08%, 3.13% and 2.61%, accounting for 1.42%, 53.84% and 44.75% of the overall preterm births respectively. Overall preterm birth rates and subtype-specific preterm birth rates among different exposure categories for each maternal and infant group are presented in **Table 1**.

Table 1 Descriptive Statistics of Preterm Birth Subtypes in Baoan, Shenzhen, 2009–2018

	Live births	Preterm births	P value[e]	PROM-PTB	P value[e]	S-PTB	P value[e]	MI-PTB	P value[e]
	N(%[c])	N(%[d]) [e]		N(%[d]) [e]		N(%[d]) [e]		N(%[d]) [e]	
All live births	478044	27829(5.82)		394(0.08)		14982(3.13)		12453(2.61)	
Maternal age (year)									
≤20	23055(4.82)	1846(8.01)		14(0.06)		1473(6.39)		359(1.56)	
21-35	416608(87.15)	22734(5.46)	<0.001	327(0.08)	<0.001	12392(2.97)	<0.001	10015(2.40)	<0.001
≥36	38381(8.03)	3249(8.47)		53(0.14)		1117(2.91)		2079(5.42)	
Maternal education									
Primary school and below	16687(3.49)	994(5.96)		25(0.15)		562(3.37)		407(2.44)	
Secondary and high school	351920(73.62)	20973(5.96)	<0.001	263(0.07)	<0.001	11806(3.35)	<0.001	8904(2.53)	<0.001
College and above	109437(22.89)	5862(5.36)		106(0.10)		2614(2.39)		3142(2.87)	
Maternal ethnicity									
Non-Han	25851(5.41)	1589(6.15)	0.222	17(0.07)	0.396	896(3.47)	0.002	676(2.61)	0.933
Han	452193(94.59)	26240(5.80)		377(0.08)		14084(3.12)		11777(2.60)	
Immigrant									
No	53014(11.09)	3234(6.10)	0.004	64(0.12)	0.001	1304(2.46)	<0.001	1866(3.52)	<0.001
Yes	425031(88.91)	24595(5.79)		330(0.08)		12678(3.22)		10587(2.49)	
Smoking									
No	477964(99.98)	27825(5.82)	0.094	394(0.08)	-	14980(3.13)	0.518	12450(2.60)	0.770
Yes	80(0.02)	4(5.00)		0(0.00)		1(1.25)		3(3.75)	
Drinking									
No	477954(99.89)	27826(5.82)	0.433	394(0.08)	-	14980(3.13)	0.846	12452(2.61)	0.576
Yes	90(0.02)	3(3.33)		0(0.00)		2(2.22)		1(1.11)	
Parity									
0	223429(46.74)	13640(6.10)		232(0.10)		7785(3.48)		5623(2.52)	
≥1	253680(53.07)	14076(5.55)	<0.001	159(0.06)	<0.001	7129(2.81)	<0.001	6788(2.68)	<0.001
Missing	935(0.20)	-		935		-		-	
Multiple pregnancy									
No	467871(97.87)	23233(4.97)	<0.001	339(0.07)	<0.001	14033(3.00)	<0.001	8861(1.89)	<0.001
Yes	10173(2.13)	4596(45.18)		55(0.54)		949(9.33)		3592(35.31)	
Delivery mode									
Vaginal delivery	313532(65.59)	14983(4.78)	<0.001	1(0.00)	<0.001	14982(4.78)	-	0(0.00)	-
Labour induction/ Caesarean section	164512(34.41)	12846(7.81)		393(0.24)		0(0.00)		12453(7.57)	
Fertility treatment									
No	476667(99.71)	27463(5.76)	<0.001	386(0.08)	<0.001	14939(3.13)	<0.957	12138(2.55)	<0.001
Yes	1377(0.29)	366(26.58)		8(0.58)		43(3.12)		315(22.88)	
First visit trimester									

First trimester	350437(73.31)	19860(5.67)		288(0.08)		10383(2.96)		9189(2.62)	
Second trimester	66110(13.83)	4080(6.17)	<0.001	61(0.09)	0.138	2040(3.09)	<0.001	1979(2.99)	<0.001
Third trimester	61497(12.86)	3889(6.32)		45(0.07)		2559(4.16)		1285(2.09)	
Prenatal care utilization rate[a]									
< 50%	121974(25.52)	7780(6.38)		97(0.08)		4941(4.05)		2742(2.25)	
50% - < 110%	277690(58.09)	13579(4.89)	<0.001	183(0.07)	<0.001	7304(2.63)	<0.001	6092(2.19)	<0.001
≥ 110%	78283(16.38)	6454(8.24)		114(0.15)		2728(3.48)		3612(4.61)	
Missing	97(0.02)	-	-	-		-		-	
Gestational hypertension									
No	477826(99.95)	27803(5.82)	<0.001	394(0.08)	-	14979(3.13)	<0.195	12430(2.60)	<0.001
Yes	218(0.05)	26(11.93)		0(0.00)		3(1.38)		23(10.55)	
Gestational diabetes									
No	477682(99.92)	27804(5.82)	0.441	389(0.08)	<0.001	14981(3.14)	0.002	12434(2.60)	0.003
Yes	362(0.08)	25(6.91)		5(1.38)		1(0.28)		19(5.25)	
Preeclampsia or eclampsia									
No	477552(99.90)	27662(5.79)	<0.001	394(0.08)	-	14969(3.13)	0.619	12299(2.58)	<0.001
Yes	492(0.10)	167(33.94)		0(0.00)		13(2.64)		154(31.30)	
Two-child policy[b]									
No	346225(72.43)	19677(5.68)	<0.001	264(0.08)	<0.001	11237(3.25)	<0.001	8176(2.36)	<0.001
Yes	131819(27.57)	8152(6.18)		130(0.10)		3745(2.84)		4277(3.24)	
Infant Gender									
Female	219629(45.94)	11683(5.32)		167(0.08)		6130(2.79)		5386(2.45)	
Male	258396(54.05)	16139(6.25)	<0.001	227(0.09)	0.019	8847(3.42)	<0.001	7065(2.73)	<0.001
Missing	19(0.01)	-	-	19		-		-	

a. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
b. The universal two-child policy effect time is defined as the delivery time before 1 July 2016, nine months after the policy was announced in October 2015
c. Distributions of maternal characteristics among the whole study population were calculated by the number of women in each subcategory divided by the total number of women, 478044.
d. Overall and subtype preterm birth rates were calculated by the number of preterm births divided by the number of women in each subcategory.
e. Preterm birth frequencies among subcategories of each variable were compared with the Chi-Square test.

Temporal trends in preterm birth rate

The annual overall preterm birth rates for the uncategorized study population and each exposure category of the selected risk factors during 2009-2018 were shown in **Figure 1 (supplementary file: Table 1)**. The overall preterm birth rate fluctuated between 5.54% and 5.80% during 2009-2015 and surpassed 6.0% in 2016 with reaching the highest in 2017 (6.36%) (**Figure 1-a**). Spontaneous preterm birth rates decreased, with approximately 0.07% decline in PROM-PTB and 0.66% decline in S-PTB. However, MI-PTB rate had increased year by year from 2.03% in 2009 to 3.38% in 2018 (**Figure 1-a**). Annual changes in late preterm was more obvious than in extremely preterm and very preterm (**Figure 1-b**). Generally, the rising trends in preterm birth were observed in all exposure subcategories of risk factors including maternal age (**Figure 1-c**), maternal education (**Figure 1-d**), immigration (**Figure 1-e**), parity (**Figure 1-f**), multiple pregnancy (**Figure 1-g**), fertility treatment (**Figure 1-i**), first visit trimester (**Figure 1-j**), infant gender (**Figure 1-l**), except for vaginal delivery mode (**Figure 1-h**) and adequate plus prenatal care utilization group (**Figure 1-k**) . Births with younger (≤ 20) or older maternal age (≥ 36 years), lower education level, nulliparity, multiple pregnancy, labor induction or cesarean section, fertility treatment, late first prenatal care visit, inadequate prenatal care utilization and male gender had a higher risk of overall preterm birth. The result of sensitivity analysis (**supplementary file: Table 2**) indicated that statistically significant changes in annual preterm birth rates occurred only in years 2016, 2017 and 2018 compared with the year 2009. The overall preterm birth trends for smoking, drinking, gestational hypertension, gestational diabetes, preeclampsia or eclampsia were not measured as their small proportions in positive results.

Risk factors for preterm birth

Based on the results of Chi-Square test of possible maternal characteristics in Table 1, statistically significant risk factors of both overall preterm birth and subtypes of preterm birth including maternal age, education level, immigrant, parity, multiple pregnancy, fertility treatment, first prenatal care visit trimester, prenatal care utilization, two-child policy and infant gender were further analyzed through Multivariable Logistic Regression. Gestational hypertension, diabetes and preeclampsia or eclampsia were not included in the Regression model as their small positive proportion in subgroups of preterm birth even with significant associations with preterm birth in Table 1. Corresponding adjusted odds ratios for each characteristic were presented in **Table 2.** Maternal age, maternal education, parity, multiple pregnancy, prenatal care utilization and infant gender still showed significant associations with both overall preterm birth and subtypes of preterm birth. For example, women with multiple pregnancy had a higher risk of preterm than the reference group (adjusted odds ratio [AOR] 15.20, 95% CI: 14.56, 15.89; $p<0.001$) with the highest risk of MI-PTB (adjusted odds ratio [AOR] 25.55, 95% CI: 24.36, 26.82; $p<0.001$) and lower risks of PROM-PTB (adjusted odds ratio [AOR] 5.68, 95% CI: 4.17, 7.74; $p<0.001$) and S-PTB (adjusted odds ratio [AOR] 3.50, 95% CI: 3.26, 3.75; $p<0.001$). Births with maternal fertility treatment had much higher risk of preterm birth rate, especially PROM-PTB rate and MI-PTB rate (Table 1), but the strong association was reduced adjusted by other risk factors in our multivariable Logistic Regression analysis (Table 2).

Table 2
Multivariable Logistic Regression of Risk Factors for Overall Preterm Birth and Subtypes of preterm Birth in Baoan, Shenzhen, 2009–2018[a]

	Overall PTB		PROM-PTB		S-PTB		MI-PTB	
	β^d	AOR[e] (95% CI)[f]	β^d	AOR[e] (95% CI)[f]	β^d	AOR[e] (95% CI)[f]	β^d	AOR[e] (95% CI)[f]
Maternal age (year)								
≤ 20	0.435	1.55(1.47,1.63)*	-0.305	0.74(0.43,1.27)	0.647	1.91(1.80,2.03)*	-0.227	0.80(0.71,0.89)*
21-35	-	Reference	-	Reference	-	Reference	-	Reference
≥ 36	0.416	1.52(1.45,1.58)*	0.550	1.73(1.27,2.37)*	0.008	1.01(0.95,1.07)	0.717	2.05(1.94,2.16)*
Maternal education								
Primary school and below	0.169	1.18(1.02,1.28)*	0.802	2.23(1.98,3.56)$	0.267	1.31(1.18,1.44)*	0.017	1.02(0.91,1.14)
Secondary and high school	0.216	1.24(1.02,1.29)*	0.114	1.12(0.86,1.46)	0.314	1.37(1.30,1.44)*	0.083	1.09(1.03,1.14)#
College and above	-	Reference	-	Reference	-	Reference	-	Reference
Immigrant								
No	-	Reference	-	Reference	-	Reference	-	Reference
Yes	0.067	1.07(1.02,1,12)#	-0.173	0.82(0.63,1.14)	0.124	1.13(1.06,1.21)*	0.028	1.03(0.97,1.09)
Parity								
0	-	Reference	-	Reference	-	Reference	-	Reference
≥ 1	-0.088	0.92(0.89,0.94)*	-0.566	0.57(0.46,0.71)*	-0.181	0.83(0.81,0.87)*	0.067	1.07(1.03,1.11)#
Multiple pregnancy								
No	-	Reference	-	Reference	-	Reference	-	Reference
Yes	2.723	15.20 (14.56,15.89)*	1.737	5.68 (4.17,7.74)*	1.252	3.50 (3.26,3.75)*	3.241	25.55 (24.36,26.82)*
Fertility treatment								
No	-	Reference	-	Reference	-	Reference	-	Reference

Yes	-0.011	0.99(0.86,1.14)	0.388	1.47(0.70,3.10)	-0.748	0.47(0.35,0.65)[*]	0.155	1.17(1.00,1.36)[$]
First visit trimester								
First trimester	-	Reference	-	Reference	-	Reference	-	Reference
Second trimester	0.043	1.04(1.00,1.08)[$]	0.248	1.28(0.96,1.71)	-0.095	0.91(0.86,0.96)[*]	0.204	1.23(1.16,1.30)[*]
Third trimester	0.015	1.02(0.97,1.06)	-0.051	0.95(0.63,1.43)	-0.033	1.03(0.98,1.09)	-0.047	0.95(0.88,1.03)
Prenatal care utilization rate[b]								
< 50%	-0.187	0.83(0.79,0.87)[*]	-0.355	0.70(0.49,1.01)	-0.006	0.99(0.93,1.06)	-0.385	0.68(0.63,0.73)[*]
50% - < 110%	-0.456	0.63(0.61,0.66)[*]	-0.545	0.58(0.45,2.37)[*]	-0.365	0.69(0.66,0.73)[*]	-0.492	0.61(0.58,0.64)[*]
≥ 110%	-	Reference	-	Reference	-	Reference	-	Reference
Two-child policy[c]								
No	-	Reference	-	Reference	-	Reference	-	Reference
Yes	0.065	1.07(1.04,1.10)[*]	0.186	1.20(0.95,1.52)	-0.027	0.97(0.93,1.01)	0.161	1.17(1.12,1.23)[*]
Infant Gender								
Female	-	Reference	-	Reference	-	Reference	-	Reference
Male	0.198	1.22(1.19,1.25)[*]	0.165	1.18(0.96,1.44)	0.224	1.25(1.21,1.29)[*]	0.143	1.15(1.11,1.20)[*]

a. 476997 live births were included after removing 1047 records due to missing values in any risk factor.
b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
c. The universal two-child policy is defined as the delivery time before 1 July 2016, nine months after the policy was announced in October 2015.
d. β, coefficients of risk factors in the multivariable binomial logistic regression model.
e. AOR, adjusted odds ratio; CI, confidence interval.
f. [$]: P<0.05; [#]: P<0.01; [*]: P<0.001.

Temporal trends in the distribution of sociodemographic factors

The distributions of sociodemographic factors including maternal age, education, immigration, parity, multiple pregnancy, delivery mode, first prenatal care visit trimester, prenatal care utilization and infant gender were shown in **Figure 2** (**supplementary file: Table 3**). Preterm births and the increase of preterm birth rate mainly took place in the late preterm group (gestational age 32-<37 weeks) (**Figure 2-a**). Improvement in maternal educational attainment was presented in **Figure 2-c**, showing that the proportion of women with education level Primary School and Below decreased from 17.59% in 2009 to 1.20% in 2018. However, the advanced maternal age group and multiparity group expanded during the period (**Figure 2-b, e**). Percentage of immigrants contracted yearly during the decade from 95.8% in 2009 to 77.2 in 2018 (**Figure 2-d**). Women with labor induction or caesarean section accounted for approximately 35% of the entire population over the decade (**Figure 2-f**). Proportion of women initiated prenatal care visit in the first trimester of pregnancy increased from 39.9% in 2009 to 91.7% in 2018 (Figure 2-g). Prenatal care utilization has improved with a drastic increase in the proportion of adequate plus utilization group from 5.4% in 2009 to 44.8% in 2018 (**Figure 2-h**). The male-to-female sex ratio in Baoan, Shenzhen stayed around 117:100 over the decade in our study (**Figure 2-i**). Since 2014, fertility treatment had become slightly more prevalent among live births in Baoan, from no cases during 2009-2013 to 0.06% in 2014 and 0.73% in 2018 (**supplementary file: Table 3**).

Contributions of transitions in sociodemographic factors to variations of preterm birth rate

The preterm birth rate increased from 5.66% during 1 January 2009 and 30 June 2016 to 6.18% between 1 July 2016 and 31 December 2018, with 88% of the increase attributed to late preterm birth. The increase of overall preterm rate mainly came from the increase of medically induced preterm birth rate, while rate of preterm labor (S-PTB) decreased after June 2016. We compared preterm birth rates subcategorized by sociodemographic factors including maternal age, maternal education, parity, multiple pregnancy, prenatal care utilization and infant gender, as well as the percent compositions of these factors in **Table 3**. Except for the adequate plus group of prenatal care utilization, preterm birth rates increased in all the categories after the policy. Contributions of sociodemographic factors to the variations of overall and subtypes of preterm birth rates between two periods were visualized with population attribution risk fraction in **Figure 3 (supplementary file: Table 4)**. Maternal age and multiple pregnancy were drivers behind the increment of overall preterm birth rate whereas maternal education, parity, prenatal care utilization and infant gender had contributed to the rate reduction. Particularly, maternal education level increased, especially in the group College and Above, from 18.03% to 35.76% and an attributed 0.223% reduction of overall preterm birth rate, an 0.001% decrease of PROM-PTB rate, an 0.143% decrease of S-PTB and an 0.052% decline of MI-PTB rate were evaluated respectively. Births with inadequate prenatal care utilization (<50%) decreased obviously from 32.16% to 7.69%, which contributed to a 0.446% decrease of overall preterm birth rate, 0.006% increase of PROM-PTB rate, 0.272% decrease of S-PTB 0.142% reduction of MI-PTB. Even with a small composition change, from 1.99% to 2.49%, multiple pregnancy had contributed to over half of the increase (0.278%/0.52%) in overall preterm birth rate with the major effect on MI-PTB. Maternal age contributed to an increase in the rate of MI-PTB but a decrease in S-PTB. The proportion of younger maternal age dropped from 5.59% to 2.75% while advanced maternal age (≥36) grew from 6.86% to 11.07%, contributing a 0.03% increase of preterm birth rate. Multiparous births expanded from 50.43% to 60.33% and had made a 0.06% decrease of preterm birth rate. The infant gender ratio kept stable during two periods and its contribution to the change of preterm birth rate was very small.

Table 3
Preterm Birth Rate and Distribution of Risk Factors in Baoan, Shenzhen, 2009 - 2018[a]

	Preterm birth rate (%)		Distribution percentage (%)[c]	
	2009.01-2016.06	**2016.07-2018.12**	**2009.01-2016.06**	**2016.07-2018.12**
All live birth	5.66	6.18	72.40	27.60
PROM-PTB	0.08	0.10	-	-
S-PTB	3.23	2.84	-	-
MI-PTB	2.35	3.24	-	-
Gestational age(week)				
< 28	0.05	0.11	0.84	1.78
28 -< 32	0.56	0.56	9.86	9.05
32 -< 37	5.05	5.51	89.30	89.17
Maternal age(year)				
≤ 20	7.84	8.49	5.59	2.75
21-35	5.32	5.77	87.55	86.18
≥ 36	8.23	8.79	6.86	11.07
Maternal education				
Primary school and below	5.74	7.76	4.38	1.16
Secondary and high school	5.78	6.47	77.59	63.08
College and above	5.15	5.62	18.03	35.76
Parity				
0	5.94	6.64	49.57	39.67
≥1	5.39	5.88	50.43	60.33
Multiple pregnancy				
No	4.91	5.06	98.01	97.51
Yes	42.69	50.17	1.99	2.49
Prenatal care utilization				

rate[b]				
< 50%	6.11	8.86	32.16	7.69
50% -< 110%	4.79	5.16	58.11	58.40
≥ 110%	9.44	7.34	9.73	33.91
Infant Gender				
Female	5.21	5.55	45.75	46.45
Male	6.04	6.73	54.25	53.55

- a. 476997 live births were included after removing 1047 records due to missing values in any risk factor.
- b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
- c. The distribution percentage for each category is the number of cases divided by the total number of preterm births.

Discussion

To date, the persistency of increasing preterm birth rate remains a challenging public health issue facing the world and limited studies have focused on the temporal trends of preterm birth during a sociodemographic transition period in recent decades. In this retrospective cohort study, a statistical analysis of 478,044 birth records demonstrated the drivers of the time trends in preterm birth among a mixed population under the sociodemographic transition background in Shenzhen. The findings of this study highlight the importance of safeguarding the health and well-being of women to reduce preterm birth, especially through improving maternal education and prenatal care service coverage.

During the sociodemographic transition period between 2009 and 2018, the overall preterm birth rate of 5.82% in Baoan was at a relatively lower level compared with the global preterm birth rate ranging from 5% in northern European countries to 18% in African countries [6]. It is also lower than the weighted national incidence of 6.7% in China during 2015-2016 [34]. However, compared with the whole Shenzhen preterm birth rate of 5.7% during 2003-2012, it was slightly higher during 2009-2018 [20]. Consistent with the global trend of the rising preterm birth rate reported by many countries in recent years, the prevalence of preterm birth in Baoan increased from 5.65% in 2009 to 6.18% in 2018 under the sociodemographic transition background [5, 35]. Compared with the whole Shenzhen birth population research during 2003-2012, both S-PTB rate and MI-PTB rate of births in Baoan during 2009-2018 increased while there was a 0.46% decrease in PROM-PTB rate (Supplementary Table 5) [20]. MI-PTB and late preterm had driven the majority of increase in preterm birth rates both in our research and the study among whole Shenzhen birth population during 2003-2012 [20]. In our analysis of risk factors of preterm birth, multiple pregnancy had a strong effect on preterm birth, especially MI-PTB and more than half of the increase of overall preterm birth rate between two periods (before and after implementation of the universal two-child policy) could be explained by it. Our results were consistent with other studies which found that multiple pregnancy was a strong risk factor for preterm birth with a 7 to10 time higher risk than singletons [36-37]. Concerns have been raised in many studies about the increasing trend of multiple pregnancy reported both in China and worldwide, which was associated with the global rising of advanced maternal age, infertility treatments and obstetric interventions performed before 37 gestational weeks, especially in 34-36 weeks [38-42].

In contrast with multiple pregnancy, the improvements in maternal education and prenatal care utilization have contributed to the reduction of overall preterm birth rate as well as the subtype-specific preterm birth rates, which coincided with the overall socio-economic developments in China with the launch of laws and policies including 9-Year Compulsory Education for All and National Commitment to Maternal and Child Survival and Health [43, 44]. Particularly, the proportion of pregnant women with inadequate prenatal care utilization narrowed down obviously after implementation of the universal two-child policy and contributed to a 0.45% decline in preterm birth rate. The positive effect of prenatal care on preterm birth during 2009-2018 was estimated to be larger than the period 2003-2012 in the whole Shenzhen birth population [20]. The timing of prenatal care initiation among our study population moved up a lot over the decade years, from 39.94% of women in the first trimester in 2009 to 91.73% in 2018. But it did not show much significant and independent association with overall and subtypes of preterm birth rates. As suggested by the Born Too Soon Group, further studies are needed to clarify the association between the quality of prenatal care visits and preterm birth [45]. Additionally, 0.22% of reduction in preterm birth rate could be explained by the expansion of maternal educational attainment during 2009-2018. However, the effect of maternal education found in this study is contrary to the result in the Shenzhen preterm birth research during 2003-2012, which demonstrated that the education improvement had contributed to 0.2% of rise in preterm birth rate [20]. It should be noted that the proportion of multiparous births increased continuously over the decade, and a near 10% increment after the implementation of the universal two-child policy, which has brought a small reduction in preterm birth rate. The percentage of multiparity in this study was around 15.28% higher than the Shenzhen birth population during 2003-2012 and also higher than the national level [20, 25]. The male-to-female sex ratio in Baoan during 2009-2018 remained abnormal compared with the natural sex ratio at birth, which indicated that the more balanced sex ratio as one of the expected benefits of the universal two-child policy has not been achieved yet [46, 47].

The present study is unique in reporting the new information about time trends in preterm birth under a rapid sociodemographic transition setting over 10 years. Both contributions of sociodemographic factors to preterm birth and to the incidence changes were calculated for a more comprehensive and quantitative understanding of their pathogenesis of temporal trends in preterm birth. Subtypes of preterm birth including spontaneous preterm and iatrogenic preterm were analyzed together with the overall preterm. Percent compositions of sociodemographic factors in each year have been presented to give a better landscape of the socio-economic transition in this area. Few missing information on prenatal care utilization and parity unlikely impacted hugely on the results. However, data about maternal socioeconomic status and employment, as well as maternal obesity were not available. Increased risks of preterm rate were significantly related with maternal obesity in a cohort study of 1,599,551 live singleton births in Sweden from 1992 to 2010 [48]. Similar results were also found in a nationwide study of 7,141,630 singleton live births from the US during 2016 and 2017 [49].

As a result, analysis about whether income and employment factors mediated the time trends of specific preterm birth was not available. Meanwhile, among the risk factors analysed in this study, only sociodemographic transitions in maternal age and multiple pregnancy have been identified as contributors to the rising preterm birth rate in Baoan, Shenzhen during 2009-2018, which indicated that about half the change is unexplained. Other important factors including non-medically indicated labour, induction and cesarean section deliveries, assisted reproductive technologies need to be analysed in future studies.

Conclusions

In conclusion, the present study provides unique information about the temporal trends in preterm birth among a mixed population under the rapid sociodemographic transition setting in China during the last decade. The observed increment in preterm birth rate was significantly associated with the expansion of multiple pregnancy. Fortunately, maternal educational attainment and prenatal care utilization have improved obviously during the period and positive contributions to the decline in preterm birth incidence have been made. The study findings highlight that the investment in girls' education, quality reproductive and maternal healthcare may render significant reductions in the rate of babies born too soon and economic burden of preterm birth. More studies need to be conducted to discover the hidden risk factors that drive the increase of preterm birth rate and finally to reduce the prevalence of preterm birth and its global burden.

Acknowledgments

We would like to thank the staff who provided us with limited but accredited access to the Shenzhen Birth Registry Database and suggestions on the use of this database.

References

1. Romero R, Dey SK, Fisher SJ. Preterm labor: one syndrome, many causes. *Science* 2014;345(6198):760-765.
2. Maghsoudlou S, Yu ZM, Beyene J, *et al*. Phenotypic Classification of Preterm Birth Among Nulliparous Women: A Population-Based Cohort Study. *J Obstet Gynaecol Can* 2019;41(10):1423-1432 e1429.
3. Lawn JE, Kinney MV, Belizan JM, *et al*. Born too soon: accelerating actions for prevention and care of 15 million newborns born too soon. *Reprod Health* 2013;10 Suppl 1:S6.
4. United Nations Inter-agency Group for Child Mortality Estimation (UNIGME). Levels & Trends in Child Mortality: Report 2019, Estimates developed by the United Nations Inter-agency Group for Child Mortality Estimation. United Nations Children's Fund, New York, 2019.
5. Chawanpaiboon S, Vogel JP, Moller AB, *et al*. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *Lancet Glob Health* 2019; 7(1):e37-e46.
6. Blencowe H, Cousens S, Chou D, *et al*. Born too soon: the global epidemiology of 15 million preterm births. *Reprod Health* 2013;10 Suppl 1:S2.
7. Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes; Behrman RE, Butler AS. Preterm Birth: Causes, Consequences, and Prevention. *National Academies Press (US)* 2007.
8. Johnston KM, Gooch K, Korol E, *et al*. The economic burden of prematurity in Canada. *BMC Pediatr* 2014;14:93.
9. Boerma T. Countdown to 2030: tracking progress towards universal coverage for reproductive, maternal, newborn, and child health. *Lancet* 2018;391(10129):1538-1548.
10. Rahman A, Rahman M, Pervin J, *et al*. Time trends and sociodemographic determinants of preterm births in pregnancy cohorts in Matlab, Bangladesh, 1990-2014. *BMJ Glob Health* 2019;4(4):e001462.
11. Sakata S, Konishi S, Ng CFS, *et al*. Preterm birth rates in Japan from 1979 to 2014: Analysis of national vital statistics. *J Obstet Gynaecol Res* 2018;44(3):390-396.
12. Lopez Orellana P. Increase in Preterm Birth during Demographic Transition in Chile from 1991 to 2012. *Biomed Res Int* 2015;2015:845968.
13. Sadovsky ADI, Matijasevich A, Santos IS, *et al*. Socioeconomic inequality in preterm birth in four Brazilian birth cohort studies. *J Pediatr (Rio J)* 2018;94(1):15-22.
14. Glinianaia, SV, Ghosh, R, Rankin, J, *et al*. No improvement in socioeconomic inequalities in birthweight and preterm birth over four decades: a population-based cohort study. *BMC public health* 2013, 13: 345.
15. Yang M, Dijst M, Helbich M. Mental Health among Migrants in Shenzhen, China: Does it Matter Whether the Migrant Population is Identified by Hukou or Birthplace? *Int J Environ Res Public Health*. 2018;15(12):2671.
16. Shenzhen Statistics Bureau. Shenzhen Statistical Yearbook 2019. Date accessed: December 30, 2019. Available online: http://www.sz.gov.cn/attachment/0/405/405056/6616865.pdf.
17. Shenzhen Baoan Statistics Bureau. Shenzhen Baoan Statistical Yearbook 2017. Date accessed: November 30, 2018. Available online: http://sso.sz.gov.cn/pub/baqzfzx2017/tjj/ywgz_136262/tjsj_137617/tjnj_137621/201811/P020181130433800362927.pdf.
18. Shenzhen Baoan Statistics Bureau. Shenzhen Baoan Statistical Yearbook 2012. Date accessed: February 24, 2014. Available online:

http://sso.sz.gov.cn/pub/baqzfzx2017/tjj/ywgz_136262/tjsj_137617/tjnj_137621/201404/P020140429367563038549.pdf.
19. Liang Z, Lin Y, Ma Y, et al. The association between ambient temperature and preterm birth in Shenzhen, China: a distributed lag non-linear time series analysis. *Environ Health* 2016;15(1):84.
20. Li C, Liang Z, Bloom MS, *et al*. Temporal trends of preterm birth in Shenzhen, China: a retrospective study. *Reprod Health* 2018;15(1):47.
21. WHO. Recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. Modifications recommended by FIGO as amended October 14, 1976. *Acta Obstet Gynecol Scand* 1977;56(3):247-253.
22. Tang K, Wang H, Tan SH, *et al*. Association between maternal education and breast feeding practices in China: a population-based cross-sectional study. *BMJ Open* 2019;9(8):e028485.
23. Zhao, Q, Huang, ZJ, Yang, S, et al. The utilization of antenatal care among rural-to-urban migrant women in Shanghai: a hospital-based cross-sectional study. BMC public health. 2012;12:1012.
24. Osterman MJK, Martin JA. Timing and Adequacy of Prenatal Care in the United States, 2016. *Natl Vital Stat Rep* 2018;67(3):1-14.
25. Li HT, Xue M, Hellerstein S, et al. Association of China's universal two child policy with changes in births and birth related health factors: national, descriptive comparative study. *BMJ* 2019;366:l4680.
26. McHugh ML. The chi-square test of independence. *Biochem Med (Zagreb*) 2013, 23(2):143-149.
27. Thabane L, Mbuagbaw L, Zhang S, *et al*. A tutorial on sensitivity analyses in clinical trials: the what, why, when and how. *BMC Med Res Methodol* 2013;13:92.
28. Sperandei S. Understanding logistic regression analysis. *Biochem Med (Zagreb)* 2014;24(1):12-18.
29. Goldenberg RL, Culhane JF, Iams JD, *et al*. Epidemiology and causes of preterm birth. *Lancet* 2008;371(9606):75-84.
30. Auger N, Le TU, Park AL, *et al*. Association between maternal comorbidity and preterm birth by severity and clinical subtype: retrospective cohort study. *BMC Pregnancy Childbirth* 2011;11:67.
31. VanderWeele TJ, Lantos JD, Lauderdale DS. Rising preterm birth rates, 1989-2004: changing demographics or changing obstetric practice? *Soc Sci Med* 2012;74(2):196-201.
32. Chang HH, Larson J, Blencowe H, *et al*. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. *Lancet* 2013;381(9862):223-234.
33. Greenland S, Senn SJ, Rothman KJ, *et al*. Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations. *Eur J Epidemiol* 2016;31(4):337-350.
34. Chen C, Zhang J, Xia H, *et al*. Epidemiology of preterm birth in China in 2015 and 2016: a nationwide survey. *The Lancet* 2018;392:S73.
35. Chang HH, Larson J, Blencowe H, et al. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. *Lancet* 2013;381(9862):223-234.
36. Dodd JM, Grivell RM, CM OB, *et al*. Prenatal administration of progestogens for preventing spontaneous preterm birth in women with a multiple pregnancy. *Cochrane Database Syst Rev* 2019;2019(11).
37. Blondel B, Macfarlane A, Gissler M, *et al*. General obstetrics: Preterm birth and multiple pregnancy in European countries participating in the PERISTAT project. *BJOG* 2006;113(5):528-535.
38. Deng C, Dai L, Yi L, *et al*. Temporal trends in the birth rates and perinatal mortality of twins: A population-based study in China. *PLoS One* 2019;14(1):e0209962.
39. Pison G, Monden C, Smits J. Twinning Rates in Developed Countries: Trends and Explanations. *Population and Development Review* 2015;41(4):629-649.

40. Richards JL, Kramer MS, Deb-Rinker P, Rouleau J, Mortensen L, Gissler M, Morken NH, Skjaerven R, Cnattingius S, Johansson S *et al*. Temporal Trends in Late Preterm and Early Term Birth Rates in 6 High-Income Countries in North America and Europe and Association With Clinician-Initiated Obstetric Interventions. *JAMA* 2016;316(4):410-419.
41. Fox H, Callander E, Lindsay D, Topp S. Evidence of overuse? Patterns of obstetric interventions during labour and birth among Australian mothers. *BMC Pregnancy and Childbirth* 2019;19(1):226.
42. Zhong N. Achieving Lower Preterm Birth Rates in China via Reductions in Iatrogenic Preterm Births. *Am J Public Health* 2019;109(11):1489-1490.
43. He C, Liu L, Chu Y, *et al*. National and subnational all-cause and cause-specific child mortality in China, 1996-2015: a systematic analysis with implications for the Sustainable Development Goals. *Lancet Glob Health* 2017;5(2):e186-e197.
44. Guo Y, Bai J, Na H. The history of China's maternal and child health care development. *Semin Fetal Neonatal Med* 2015;20(5):309-314.
45. Requejo J, Merialdi M, Althabe F, *et al*. Born too soon: care during pregnancy and childbirth to reduce preterm deliveries and improve health outcomes of the preterm baby. *Reprod Health* 2013;10 Suppl 1:S4.
46. Shah PS, Knowledge Synthesis Group on Determinants of LBWPTb. Parity and low birth weight and preterm birth: a systematic review and meta-analyses. *Acta Obstet Gynecol Scand* 2010;89(7):862-875.
47. Zeng Y, Hesketh T. The effects of China's universal two-child policy. *Lancet* 2016; 388(10054): 1930-1938.
48. Cnattingius S, Villamor E, Johansson S, et al. Maternal obesity and risk of preterm delivery. JAMA. 2013;309(22):2362-2370.
49. Liu B, Xu G, Sun Y, et al. Association between maternal pre-pregnancy obesity and preterm birth according to maternal age and race or ethnicity: a population-based study. Lancet Diabetes Endocrinol. 2019;7(9):707-714.

Footnotes

Contributors: LYZ, LZ and RM developed the study concept and design. RM, YLL and QX collected data. RM cleaned the data and performed data analysis. RM and LYZ drafted the manuscript. LYZ, LZ, YLL, JW, YXZ, HYS, XR provided oversight and expert advice for the research and the written paper. All authors revised and approved the final paper.

Funding: This study is supported by the National Natural Science Foundation of China (grant number: 31771468)

Disclaimer: The funding sources had no involvement in any aspect of this study.
Competing interests: None declared.
Patient consent for publication: Not required.
Ethics approval: This study was approved by the medical ethics committee of Shenzhen Baoan Women's and Children's Hospital, Jinan University, China (number LLSC-2019-07-01). All data used in this study have been completely anonymized before accession and were analysed anonymously.
Provenance and peer review: Not commissioned; externally peer reviewed.
Data sharing statement: Data are available upon reasonable request to the corresponding author.

Figure Legends:

Figure 1.
Temporal Trends in Preterm Birth Rate among 478,044 Livebirths (2801 ineligible birth records were excluded) Subcategorized by Risk Factors in Baoan, Shenzhen, 2009-2018. a. Overall and subtypes b. Gestational age c. Maternal age d. Maternal education e. Immigration f. Parity g. Multiple pregnancy h. Delivery mode i. Fertility treatment j. First visit trimester k. Prenatal care utilization l. Infant gender

Figure 2.
Temporal Trends in the Distribution of Sociodemographic Factors in Baoan, Shenzhen, 2009-2018. a. Gestational age b. Maternal age c. Maternal education d. Immigration e. Parity f. Delivery mode g. First visit trimester h. Prenatal care utilization i. Infant gender

Figure 3.
Analysis of Sociodemographic Factors Contributing to the Variations of Preterm Birth Rate in Baoan, Shenzhen, 2009-2018. PROM-PTB, preterm birth following premature rupture of membranes; MI-PTB, medically induced preterm birth; S-PTB, spontaneous preterm labor.

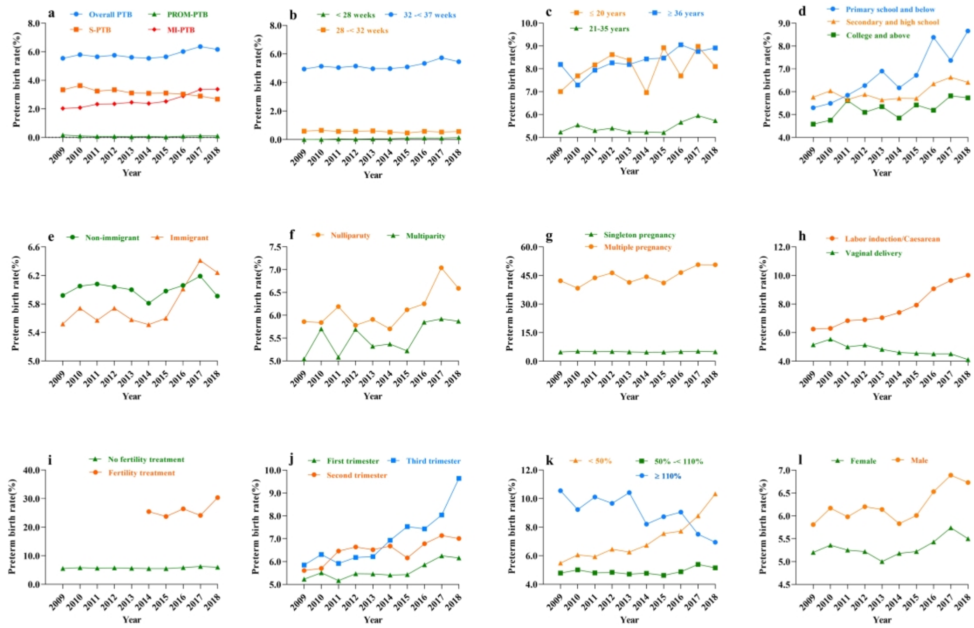


Figure 1. Temporal Trends in Preterm Birth Rate among 478,044 Livebirths (2801 ineligible birth records were excluded) Subcategorized by Risk Factors in Baoan, Shenzhen, 2009-2018. a. Overall and subtypes b. Gestational age c. Maternal age d. Maternal education e. Immigration f. Parity g. Multiple pregnancy h. Delivery mode i. Fertility treatment j. First visit trimester k. Prenatal care utilization l. Infant gender

291x194mm (300 x 300 DPI)

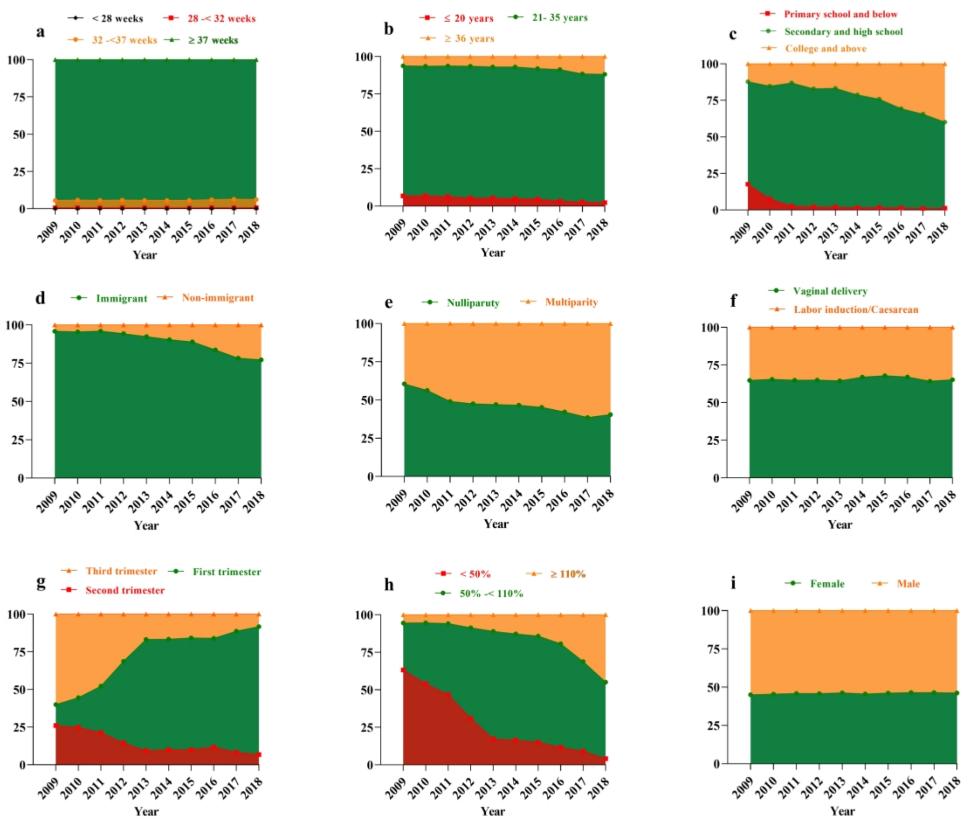


Figure 2. Temporal Trends in the Distribution of Sociodemographic Factors in Baoan, Shenzhen, 2009-2018. a. Gestational age b. Maternal age c. Maternal education d. Immigration e. Parity f. Delivery mode g. First visit trimester h. Prenatal care utilization i. Infant gender

232x200mm (300 x 300 DPI)

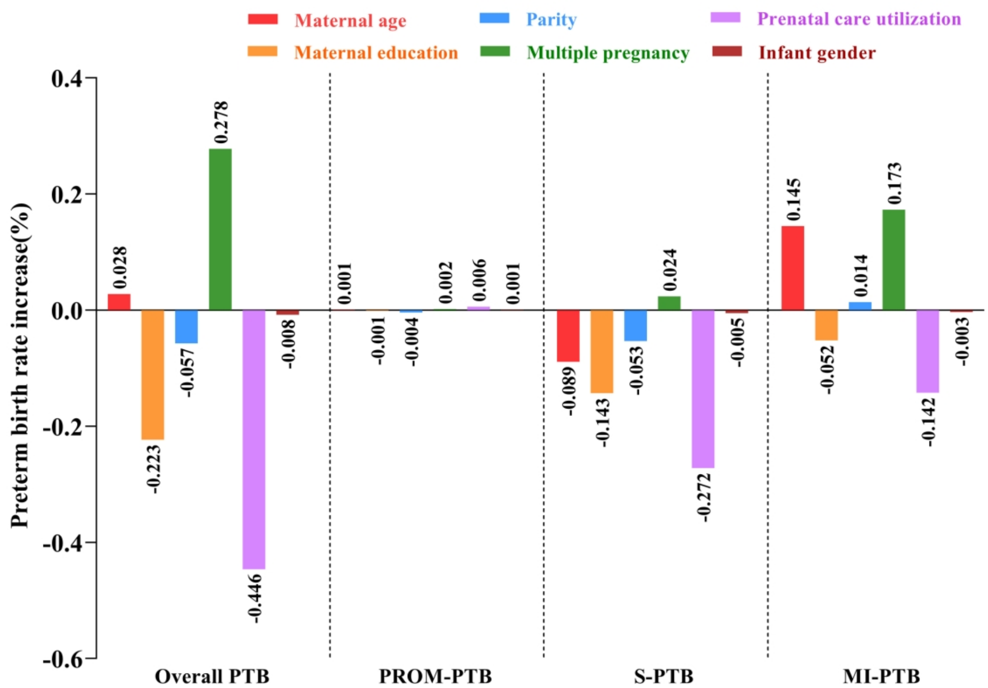


Figure 3. Analysis of Sociodemographic Factors Contributing to the Variations of Preterm Birth Rate in Baoan, Shenzhen, 2009-2018. PROM-PTB, preterm birth following premature rupture of membranes; MI-PTB, medically induced preterm birth; S-PTB, spontaneous preterm labor.

183x132mm (300 x 300 DPI)

Supplementary Materials

Ten-year time trends in preterm birth during a sociodemographic transition period: a retrospective cohort study in Shenzhen, China

Supplementary Figure 1. Flowchart of Study Population

Births among women in Baoan from the Shenzhen Birth Registration System
(From 1 January, 2009 to 31 December, 2018)
(n=480,845)

↓

Excluded (n= 2,801):
- Stillbirths or births with unknown results (n=2,561)
- Births with miss gestational age (n= 8)
- Births with miss maternal age (n=0)
- Births with maternal age <13 yr or >50 yr (n=182)
- Births at <22 wk or >46 wk gestation (n=50)

↓

Live births included in the study population
(n= 478,044)

Supplementary Table 1. Temporal Trends in Preterm Birth Rate (%) in Baoan, Shenzhen, 2009 - 2018

	Year									
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Overall Preterm Birth Rate	5.54	5.80	5.65	5.76	5.61	5.54	5.65	6.02	6.36	6.16
PROM-PTB	0.17	0.10	0.07	0.07	0.04	0.07	0.03	0.09	0.11	0.10
S-PTB	3.34	3.63	3.24	3.34	3.11	3.09	3.10	3.03	2.90	2.68
MI-PTB	2.03	2.08	2.33	2.35	2.46	2.38	2.52	2.90	3.35	3.38
Gestational age(week)										
< 28	0.00	0.01	0.04	0.03	0.05	0.05	0.10	0.11	0.10	0.14
28 -< 32	0.59	0.65	0.57	0.58	0.61	0.52	0.46	0.58	0.53	0.56
32 -< 37	4.94	5.14	5.04	5.15	4.96	4.97	5.09	5.34	5.73	5.46
Maternal age(year)										
≤ 20	7.00	7.69	8.17	8.62	8.38	6.96	8.92	7.69	8.98	8.10
21-35	5.23	5.54	5.30	5.40	5.24	5.23	5.21	5.66	5.95	5.73
≥ 36	8.19	7.29	7.94	8.26	8.19	8.43	8.47	9.05	8.76	8.91
Maternal education										
Primary school and below	5.30	5.49	5.85	6.27	6.90	6.17	6.72	8.38	7.37	8.66
Secondary and high school	5.76	6.04	5.65	5.88	5.64	5.71	5.70	6.35	6.63	6.41
College and above	4.58	4.75	5.61	5.10	5.35	4.85	5.42	5.19	5.82	5.73
Immigrant										
No	5.92	6.05	6.08	6.04	6.00	5.81	5.98	6.06	6.19	5.91
Yes	5.52	5.74	5.57	5.74	5.58	5.51	5.60	6.01	6.41	6.24
Parity										
0	5.86	5.84	6.19	5.78	5.91	5.7	6.12	6.25	7.04	6.59
≥ 1	5.04	5.7	5.08	5.69	5.32	5.37	5.22	5.85	5.92	5.87
Multiple pregnancy										
No	4.84	5.23	4.96	5.06	4.87	4.71	4.80	5.00	5.23	4.94
Yes	42.24	38.32	43.78	46.37	41.40	44.32	41.06	46.51	50.68	50.65
Delivery mode										
Vaginal delivery	5.15	5.54	5.00	5.14	4.83	4.61	4.56	4.52	4.52	4.11
Labour induction/ Caesarean section	6.25	6.30	6.84	6.90	7.04	7.41	7.93	9.07	9.65	10.02
Fertility treatment										

No	5.54	5.80	5.65	5.76	5.61	5.52	5.53	5.85	6.26	5.99
Yes	-[b]	-[b]	-[b]	-[b]	-[b]	25.45	23.75	26.43	24.11	30.34
First visit trimester										
First trimester	5.23	5.51	5.17	5.47	5.46	5.41	5.43	5.86	6.25	6.16
Second trimester	5.61	5.70	6.46	6.64	6.52	6.68	6.16	6.78	7.14	5.51
Third trimester	5.85	6.31	5.92	6.18	6.22	6.93	7.83	7.03	7.50	9.64
Prenatal care utilization rate[a]										
< 50%	5.48	6.06	5.93	6.46	6.26	6.73	7.55	7.72	8.79	10.33
50% - < 110%	4.78	5.01	4.8	4.84	4.71	4.77	4.62	4.88	5.39	5.15
≥ 110%	10.55	9.23	10.11	9.66	10.42	8.21	8.73	9.05	7.5	6.94
Infant gender										
Female	5.20	5.36	5.25	5.22	5.00	5.18	5.22	5.43	5.74	5.50
Male	5.81	6.17	5.98	6.20	6.14	5.83	6.01	6.53	6.89	6.73

a. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.

b. During 2009-2013, there were no records of fertility treatments in the database.

Supplementary Table 2. Sensitivity Analysis of Temporal Trends for Overall Preterm Birth Rates in Baoan, Shenzhen, 2009 - 2018

Year	Preterm birth rate(%)	Risk Ratio(95%CI)	P Value
2009	5.54	Reference	
2010	5.80	1.003(0.999,1.006)	0.104
2011	5.65	1.001(0.998,1.004)	0.493
2012	5.76	1.002(0.999,1.006)	0.148
2013	5.61	1.001(0.998,1.004)	0.626
2014	5.54	1.000(0.997,1.003)	0.986
2015	5.65	1.001(0.998,1.004)	0.494
2016	6.02	1.005(1.002,1.008)	0.002
2017	6.36	1.009(1.005,1.012)	0.000
2018	6.16	1.007(1.003,1.010)	0.000

Supplementary Table 3. Temporal Trends in the Distribution Percentage (%) of Sociodemographic Factors in Baoan, Shenzhen, 2009 - 2018[a]

	Year									
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
All live births	38590	41912	46617	54957	46861	50063	45872	51328	52823	49021
Gestational age(week)										
< 28	0.00	0.01	0.04	0.03	0.05	0.05	0.10	0.11	0.10	0.14
28 -< 32	0.59	0.65	0.57	0.58	0.61	0.52	0.46	0.58	0.53	0.56
32 -< 37	4.94	5.14	5.04	5.15	4.96	4.97	5.09	5.34	5.73	5.46
≥ 37	94.46	94.20	94.35	94.24	94.39	94.46	94.35	93.98	93.64	93.84
Maternal age(year)										
≤ 20	6.81	6.92	6.41	5.36	5.48	5.05	4.72	3.37	2.80	2.29
21-35	86.99	86.63	87.32	88.21	87.60	88.03	87.23	87.91	85.61	85.81
≥ 36	6.20	6.45	6.27	6.43	6.93	6.92	8.05	8.72	11.58	11.90
Maternal education										
Primary school and below	17.59	7.60	2.64	2.12	1.92	1.62	1.62	1.37	1.08	1.20
Secondary and high school	70.19	77.18	84.35	80.87	81.39	77.18	74.22	68.01	64.57	58.91
College and above	12.22	15.22	13.01	17.01	16.69	21.20	24.16	30.62	34.35	39.88
Immigrant										
No	4.16	4.54	4.05	5.69	7.65	9.66	11.04	16.33	21.67	22.8
Yes	95.84	95.46	95.95	94.31	92.35	90.34	88.96	83.67	78.33	77.2
Parity										
0	60.54	56.25	49.06	47.50	47.05	46.66	45.18	42.19	38.51	40.47
≥ 1	39.46	43.75	50.94	52.50	52.95	53.34	54.82	57.81	61.49	59.53
Multiple pregnancy										

No	98.13	98.26	98.24	98.30	97.95	97.91	97.66	97.54	97.51	97.33
Yes	1.87	1.74	1.76	1.70	2.05	2.09	2.34	2.46	2.49	2.67
Delivery mode										
Vaginal deliveries	64.82	65.49	64.84	64.92	64.48	66.97	67.88	67.03	64.18	65.24
Labor induction/ Caesarean section	35.18	34.51	35.16	35.08	35.52	33.03	32.12	32.97	35.82	34.76
Fertility treatment										
No	100	100	100	100	100	99.96	99.35	99.18	99.47	99.27
Yes	0	0	0	0	0	0.04	0.65	0.82	0.53	0.73
First visit trimester										
First trimester	39.94	44.58	52.18	68.74	83.2	83.35	84.18	83.95	88.67	91.73
Second trimester	26.07	24.89	21.35	14.47	9.36	10.02	9.98	11.8	8.27	6.81
Third trimester	33.99	30.54	26.47	16.79	7.44	6.63	5.85	4.24	3.06	1.46
Prenatal care utilization rate[b]										
< 50%	63.24	54.13	46.82	30.96	17.33	16.44	15.05	11.72	9.05	4.11
50% - <110%	31.33	40.49	47.30	60.38	71.64	70.88	70.70	68.97	59.72	51.05
≥ 110%	5.43	5.38	5.88	8.67	11.02	12.68	14.24	19.32	31.24	44.84
Infant Gender										
Female	45.02	45.44	45.90	45.77	46.26	45.58	46.14	46.46	46.43	46.17
Male	54.98	54.56	54.10	54.23	53.74	54.42	53.86	53.54	53.57	53.83

a. The distribution percentage (%) for each category is the number of cases divided by the total number of preterm births.
b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.

Supplementary Table 4. Analysis of Sociodemographic Factors Contributing to Variations of Preterm Birth Rate in Baoan, Shenzhen, 2009-2018[a]

	Overall PTB		PROM-PTB		S-PTB		MI-PTB	
	AOR	Rate change	AOR	Rate change	AOR	Rate change	AOR	Rate change
Maternal age(year)								
≤20	1.544		1.194		2.185		0.593	
21-35	Reference	0.028%	Reference	0.001%	Reference	-0.089%	Reference	0.145%
≥36	1.491		1.294		0.984		1.932	
Maternal education								
Primary school and below	1.439		1.536		1.832		1.074	
Secondary and high school	1.256	-0.223%	0.970	-0.001%	1.412	-0.143%	1.112	-0.052%
College and above	Reference		Reference		Reference		Reference	
Parity								
0	1.102	-0.057%	1.700	-0.004%	1.230	-0.053%	0.954	0.014%
≥ 1	Reference		Reference		Reference		Reference	
Multiple pregnancy								
No	Reference		Reference		Reference		Reference	
Yes	18.338	0.278%	6.461	0.002%	2.861	0.024%	29.937	0.173%
Prenatal care utilization rate[b]								
< 50%	1.330		0.580		1.423		1.219	
50% - <110%	0.744	-0.446%	0.653	0.006%	0.781	-0.272%	0.731	-0.142%
≥ 110%	Reference		Reference		Reference		Reference	
Infant Gender								
Female	Reference		Reference		Reference		Reference	
Male	1.268	-0.008%	1.460	0.001%	1.316	-0.005%	1.185	-0.003%
Projected Increase	-	0.239%	-	-0.003%		-0.044%		0.221%

a. 131787 live births after the policy were included in the logistic regression model.
b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
c. The distribution percentage for each category is the number of cases divided by the total number of preterm births.
d. AOR: adjusted odds ratio
e. AFp: Attributable risk fraction for the population.
f. Preterm birth rate change is calculated by multiplying AFp with the preterm birth rate after the policy and substract the result for before the policy.

Supplementary Table 5. Comparisons of Preterm Birth Rates and Risk Factor Distribution Percentages in Baoan, Shenzhen, 2003-2018[a]

	Distribution percentage(%)[c]		Preterm birth rate(%)	
	2003-2012[c]	**2009-2018**	**2003-2012[c]**	**2009-2018**
Overall Preterm Birth				
PROM-PTB	-		0.54	0.08
S-PTB	-		2.89	3.13
MI-PTB	-		2.21	2.61
Gestational age(week)				
<28 weeks	10.27	1.12	0.58	0.07
28-<32 weeks	12.79	9.65	0.72	0.56
32-<37 weeks	76.94	89.23	4.34	5.19
Maternal age(year)				
≤20	5.88	4.82	6.97	8.01
21-35	88.79	87.15	5.40	5.46
≥36	5.33	8.03	8.34	8.47
Maternal education				
Less than high school	43.27	34.59	5.71	5.82
High school and college	35.98	55.17	5.82	5.93
Bachelor	19.04	8.89	5.21	5.29
Postgraduate	1.71	1.35	5.35	4.69
Parity				
0	62.08	46.83	5.77	6.10
≥ 1	37.92	53.17	5.42	5.55
Prenatal care utilization rate[b]				
< 50%	45.88	25.52	7.14	6.38
50% - <110%	39.88	58.10	5.28	4.89
≥ 110%	14.23	16.38	1.86	8.24
Infant Gender				
Female	45.72	45.95	5.26	5.32
Male	54.28	54.05	5.97	6.25

a. Li C, Liang Z, Bloom MS, et al. Temporal trends of preterm birth in Shenzhen, China: a retrospective study. *Reprod Health* 2018;15(1):47.
b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
c. The distribution percentage for each category is the number of cases divided by the total number of preterm births.

STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	4
		(*b*) For matched studies, give matching criteria and the number of controls per case	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, explain how matching of cases and controls was addressed	
		(*e*) Describe any sensitivity analyses	4
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	5-8

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Ten-year time trends in preterm birth during a sociodemographic transition period: a retrospective cohort study in Shenzhen, China

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-037266.R2
Article Type:	Original research
Date Submitted by the Author:	07-Sep-2020
Complete List of Authors:	Ma, Rui; Shenzhen City Baoan District Womens and Childrens Hospital, Center for Big Data Research in Health Luo, Yali; Shenzhen City Baoan District Womens and Childrens Hospital, Department of Prevention & Health Care Wang, Jun; Shenzhen City Baoan District Womens and Childrens Hospital, Center for Big Data Research in Health Zhou, Yanxia; Shenzhen City Baoan District Womens and Childrens Hospital, Centre for Big Data Research in Health Sun, Haiyang; Shenzhen City Baoan District Womens and Childrens Hospital, Centre for Big Data Research in Health Ren, Xi; Shenzhen City Baoan District Womens and Childrens Hospital, Centre for Big Data Research in Health Xu, Quan; Shenzhen City Baoan District Womens and Childrens Hospital, Department of Prevention & Health Care Zhang, Lian; Shenzhen City Baoan District Womens and Childrens Hospital, Department of Neonatology Zou, Lingyun; Shenzhen City Baoan District Womens and Childrens Hospital, Center for Big Data Research in Health
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health, Epidemiology
Keywords:	EPIDEMIOLOGY, PUBLIC HEALTH, Maternal medicine < OBSTETRICS, Child protection < PAEDIATRICS

SCHOLARONE™
Manuscripts

Ten-year time trends in preterm birth during a sociodemographic transition period: a retrospective cohort study in Shenzhen, China

Rui Ma[1], Yali Luo[2], Jun Wang[1], Yanxia Zhou[1], Haiyang Sun[1], Xi Ren[1], Quan Xu[2], Lian Zhang[3*], Lingyun Zou[1*]

Author affiliations
[1] Center for Big Data Research in Health, Shenzhen Baoan Women's and Children's Hospital, Jinan University, Shenzhen, China
[2] Department of Prevention & Health Care, Shenzhen Baoan Women's and Children's Hospital, Jinan University, Shenzhen, China
[3] Department of Neonatology, Shenzhen Baoan Women's and Children's Hospital, Jinan University, Shenzhen, China

***Correspondence to**
Dr Lingyun Zou, Center for Big Data Research in Health, Shenzhen Baoan Women's and Children's Hospital, Jinan University, Shenzhen, 518102, China; +86 755 23202015; lingyun.zou@gmail.com

Dr Lian Zhang, Department of Neonatology, Shenzhen Baoan Women's and Children's Hospital, Jinan University, Shenzhen, 518102, China; +86 755 23202015; zhliande@qq.com

Wordcount: 4385

Abstract

Objectives To investigate time trends of preterm birth and estimate the contributions of risk factors to the changes in preterm birth rates over a decade (2009-2018) of transitional period in Shenzhen, China.

Design Retrospective cohort study between 2009 and 2018.

Setting All births in Baoan during January 2009 and December 2018 registered in the Shenzhen Birth Registry Database.

Participants 478,044 live births were included with sociodemographic and medical records for both women and infants.

Outcome measures The incidence rate of preterm birth stratified by different maternal and infant characteristics. Multiple logistic regression was used to identify significant risk factors associated with preterm birth. The population attributable risk fraction of each factor was calculated to estimate its contribution to variations of preterm birth rate over the ten years.

Results A total of 27,829 preterm births from 478,044 live births (5.8%) was recorded and the preterm birth rate increased from 5.7% in 2009 to 6.2% in 2018. Medically induced preterm birth rate increased from 2.0% in 2009 to 3.4% in 2018 while spontaneous preterm labor rate decreased from 3.3% to 2.7% over the decade years. Risk factors including multiple pregnancy (0.28% increase) drove the rise of preterm birth rate whereas changes in maternal educational attainment (0.22% reduction) and prenatal care utilization (0.45% reduction) had contributed to the decline in preterm birth rate.

Conclusions An uptrend of preterm birth rate was observed in an area under rapid sociodemographic transitions during 2009-2018 and the changes were associated with these sociodemographic transitions. Continued investments in girls' education and prenatal care have the potential of reducing preterm birth rate.

Strengths and limitations of this study

- A complete and large-scale dataset of over 480,000 births across the recent 10-year period was analysed in this study to present long-term time trends in preterm birth and associated factors.
- Preterm births were classified into three specific subtypes including both spontaneous preterm births and iatrogenic preterm births to further examine the impact of risk factors on each type of preterm birth.
- Population attribution risk fraction was used to quantify the contributions of changes in risk factors to the variations of preterm birth rate before and after the two-child policy initiation.
- Preterm birth subtypes were unavailable in the Shenzhen Birth Registry Database and the classification was based on delivery mode and surgical indications.
- Possible risk factors including family income, maternal employment, maternal obesity and more were unavailable in the database and have not been analysed in the study.

Introduction

Preterm birth, which is defined as birth of a neonate before 37 completed weeks of gestation, is a syndrome with many causes and multiple phenotypes [1, 2]. Globally, approximately 15 million neonates were born preterm in 2014, and over one million children die each year due to preterm birth complications, contributing to approximately 16% of all deaths and 35% of newborn deaths in 2019 [3, 4]. Despite decades of substantial research, the increasing prevalence of preterm birth continued to rise in many countries worldwide, resulting in a worldwide increase from 9.8% in the year of 2000 to 10.6% in the year of 2014 [5]. Even fortunate survivors may experience lifetime disabilities, including neurodevelopmental and physical impairments, as well as behavioural effects, which impose a heavy burden on the family and society[6]. The economic burden associated with preterm birth complications was at least $26.2 billion in the United States in 2005 and $587.1 million in Canada in 2014 [7, 8]. Addressing risk factors for preterm birth and determining the cause of the incremental incidence are critical to informing public health policies aimed at reducing the global burden of preterm births and achieving the Global Strategy for Women's, Children's and Adolescents' Health under the Sustainable Development Goals [9].

Sociodemographic transitions have been shown to be associated with time trends in preterm birth, especially in areas during the industrialisation period. A cohort study from Bangladesh revealed that 27% of the decline in preterm birth rate could be attributed to the decrease in parity and expansion of maternal education during 1990-2014 [10]. Maternal age at delivery could explain the secular trends of preterm birth in Japan from 1979 to 2014 based on national birth data [11]. During the Chilean sociodemographic transition period 1991-2012, the increase in advanced maternal age (35 years or older) was evaluated to significantly increase the risk of preterm birth significantly [12]. Economic inequalities were also found in relation to preterm births in four Brazilian birth cohort studies conducted between 1982 and 2011 [13]. A population-based cohort study on births in Newcastle upon Tyne in Northern England over four decades confirmed the widened preterm birth gap between the most and least deprived socioeconomic groups [14].

China accounted for 7.8% (1.17 million) of preterm births worldwide, with the second largest number of preterm neonates [5]. From 2000 to 2014, the estimated preterm birth rate in China increased from 6.35% to 6.94% [5]. As the first special economic zone located in the Pearl River Delta of South China, Shenzhen has undergone rapid urbanisation and has attracted millions of migrant labourers since the beginning of the 1980s [15]. Baoan epitomizes this urbanisation as the largest district in Shenzhen, with a more than 3.26 million year-end permanent population in 2018 and approximately 82% are migrants from other parts of China [16]. During 2012 and 2018, the de jure population of Baoan rapidly expanded from 2.68 million to 3.26 million, and the gross domestic product per capita grew from $8556 in 2008 to $15981 in 2017 [16-18]. In addition, the proportion of labourers in the tertiary sector of the economy increased from 15.7% in 2012 to 22.6% in 2017 [16, 17].

However, limited studies on long-term time trends in preterm birth are available in areas under drastic sociodemographic transitions in China during recent decades. Transitions in the society and their contributions to the changes in preterm birth rate are still unclear. The present study was based on all births in Baoan during 2009-2018 registered in the Shenzhen Birth Registry Database. We assessed the temporal trends in preterm birth and associated risk factors among a large proportion of the migrant population. We further estimated the quantitative contributions of these factors to the changes in preterm birth rates over the last decade.

Methods

Study design and data collection

This cohort study was based on data of all births in Baoan from 1 January 2009 to 31 December 2018, extracted from the Shenzhen Birth Registry Database, which has served as a system for birth registration and maternal and infant health management since 2000 [19]. Demographic and clinical records of both mothers and new-borns were available for the identification of preterm birth and risk factors. Only live births were included in this study and ineligible records were excluded to ensure the coherence and continuity of preterm birth rate calculations based on prior related research: (1) Stillbirths or births with unknown results; (2) births with missing gestational age or gestational age < 22 weeks or > 46 weeks; and (3) births with missing maternal age or maternal age < 13 years or > 50 years. The flowchart of data selection is shown in the supplementary file: Figure 1 [5, 20].

Patient and public involvement

This study used routinely collected administrative health data and no patients were involved in the conception, design and conduct of the research. The results will be disseminated through open access publication.

Ethics approval

This study was approved by the Medical Ethics Committee of Baoan Women's and Children's Hospital, Jinan University. Data collection was in the study were anonymous, and no individually identifiable information was available for the analysis.

Definition and measurements

Preterm birth is defined by the World Health Organization as all births before 37 completed weeks of gestation or fewer than 259 days since the first day of a woman's last menstrual period [3, 21]. Based on gestational age, it was further classified as extremely preterm (<28 weeks), very preterm (28 - <32 weeks) and late preterm (32 - <37 weeks). Preterm birth rate was calculated using the number of live births in a specific preterm category divided by all live births multiplied by 100 in a specific time period [21].

Based on the delivery mode and surgical indications recorded in the database, we categorised preterm birth into three subtypes: two spontaneous preterm birth subtypes, including preterm premature rupture of membranes (PROM-PTB) and preterm labour (S-PTB), and the third subtype medically induced preterm birth (MI-PTB). PROM-PTB was defined as preterm birth with premature rupture of membranes, S-PTB was defined as non-PROM with vaginal deliveries and MI-PTB was defined as preterm birth with either induction of labour or caesarean section delivery but without PROM [20].

Potential risk factors related to preterm birth were selected and analysed based on a literature review [10-14]. Variables including gestational age, maternal age, maternal education, maternal ethnicity , immigrant, smoking, drinking, parity, delivery mode, fertility treatment, gestational age at the first prenatal care visit, number of prenatal care visits, gestational hypertension, gestational diabetes, preeclampsia or eclampsia, infant sex, and date of delivery were included in our analysis. Numeric variables including gestational age, maternal age and gestational age at the first prenatal care visit were categorised into ordinal subgroups. We classified maternal education into 3 categories for a more balanced population and clear data interpretation: primary school and below, secondary and high school and college and above [22]. Prenatal care utilisation is recommended by the Law of the People's Republic of China on Maternal and Infant Health Care with the initiation of antenatal care during the first trimester of pregnancy and consisting of five or more antenatal care visits [23]. Three first visit trimester groups were generated based on the gestational age at the first prenatal care visit [24]. The number of prenatal care visits was transformed into the prenatal care utilisation rate, by calculating the ratio between the actual number of visits and the recommended number of visits. The ratio was then classified into three groups: inadequate (< 50%), intermediate and appropriate (50-

110%) and adequate plus (≥ 110%) [24]. To analyse the effect of the universal two-child policy, we classified births into two groups based on the time of delivery: births taking place before or within nine months after the implementation of the universal two-child policy in October 2015 (June 2016) and births taking place nine months after the policy [25].

Statistical analysis

The chi-square test was used to evaluate significant differences in frequencies of both overall and subtypes of preterm birth between each maternal and infant group in this study [26]. Annual overall preterm birth rates for each risk factor subcategory were calculated to present the temporal trends stratified by different characteristics over the decade. Yearly percent compositions of each risk factor were calculated to show the changes in sociodemographic indicators. Sensitivity analysis was performed to examine changes in linear trends of annual overall preterm birth rates by calculating risk ratios, with the year 2009 as a reference [27]. Multivariable binomial logistic regression models were applied to estimate adjusted odds ratios (AORs) and 95% confidence intervals (95% CI) of covariates for overall preterm birth and subtype-specific preterm birth [28]. Possible independent variables were selected based on their significance in univariate analyses ($p<0.05$) and their probable associations with preterm birth judged by prior domain knowledge [29].

To examine the contribution of risk factors to preterm birth incidence in the entire study population over the last decade, we measured the population attributable risk fraction using formula (1) where AFp_i is the population attributable risk fraction for risk factor i, PF_j is the proportion of the total population and RR_j is the risk ratio for the exposure category j ($j = 1, 2, ..., m$) of risk factor i ($i = 1, 2, ..., n$). RR_j was approximated by using OR_i to avoid overlap from different risk factors [30, 31]. AFp was then calculated using formula (2) to measure the total population attributable risk fraction across all risk factors.

$$AFp_i = \frac{\sum_1^m PF_j * (RR_j - 1)}{1 + \sum_1^m PF_j * (RR_j - 1)} \quad (1)$$

$$AFp = 1 - \prod_i^n (1 - AFp_i) \quad (2)$$

We evaluated sociodemographic changes after implementation of the universal two-child policy and their contributions to the variations of preterm birth rate with approaches: (1) calculate PF for each selected factor in two time periods, (2) identify the risk of preterm birth for these factors with odds ratios (ORs) in a logistic regression among births after the policy, (3) estimate AFp for each factor before and after the policy (AFp_{before} was calculated by PF_{before} and OR_{after} whereas AFp_{after} was calculated by PF_{after} and OR_{after}), and (4) calculate the total contribution to the changes in preterm birth rate between two periods by multiplying AFp with the preterm birth rate after the policy and subtracting the result before the policy with formula (3) [20, 32].

$$Increased\ Rate = AFp_{after} * Rate_{after} - AFp_{before} * Rate_{after} \quad (3)$$

All analyses were conducted using Python software (version 3.6.6; Python Software Foundation). Alpha levels of 0.001, 0.01 and 0.05 indicated statistical significance for a two-tailed test separately [33]. Missing values of several variables were included in the descriptive analysis but were removed from the logistic regression analyses.

Results

Preterm birth rates in Baoan, Shenzhen

A total of 480,845 births in Baoan, Shenzhen were identified in the Shenzhen Birth Registry Database from 2009 to 2018. Furthermore, 478,044 (99.4%) live births were included in the final study population after excluding 2801 (0.6%) ineligible birth records: 2561 (0.5%) stillbirths or births with unknown results, 182 (0.04%) live births with maternal age under 13 years or over 50 years and 58 (0.01%) live births with missing gestational age or gestational age lower than 22 weeks or higher than 46 weeks. There were 27,829 (5.8%) preterm births in Baoan from 2009 to 2018 with 312 (0.1%) extremely preterm births, 2686 (0.6%) very preterm births and 24,831 (5.2%) late preterm births respectively. The rates of PROM-PTB, S-PTB and MI-PTB were 0.1%, 3.1% and 2.6%, accounting for 1.42%, 53.8% and 44.8% of the overall preterm births, respectively. The overall preterm birth rates and subtype-specific preterm birth rates among the different exposure categories for each maternal and infant group are presented in **Table 1**.

Table 1 Descriptive Statistics of Preterm Birth Subtypes in Baoan, Shenzhen, 2009–2018

	Live births	Preterm births	P value[e]	PROM-PTB	P value[e]	S-PTB	P value[e]	MI-PTB	P value[e]
	N(%[c])	N(%[d]) [e]		N(%[d]) [e]		N(%[d]) [e]		N(%[d]) [e]	
All live births	478044	27829(5.8)		394(0.08)		14982(3.1)		12453(2.6)	
Maternal age (year)									
≤20	23055(4.8)	1846(8.0)		14(0.1)		1473(6.4)		359(1.6)	
21-35	416608(87.2)	22734(5.5)	<0.001	327(0.1)	<0.001	123923.0)	<0.001	10015(2.4)	<0.001
≥36	38381(8.0)	3249(8.5)		53(0.1)		1117(2.9)		2079(5.4)	
Maternal education									
Primary school and below	16687(3.5)	994(6.0)		25(0.2)		562(3.4)		407(2.4)	
Secondary and high school	351920(73.6)	20973(6.0)	<0.001	263(0.1)	<0.001	11806(3.4)	<0.001	8904(2.5)	<0.001
College and above	109437(22.9)	5862(5.4)		106(0.1)		2614(2.4)		3142(2.9)	
Maternal ethnicity									
Non-Han	25851(5.4)	1589(6.2)	0.222	17(0.1)	0.396	896(3.5)	0.002	676(2.6)	0.933
Han	452193(94.6)	26240(5.8)		377(0.1)		14084(3.1)		11777(2.6)	
Immigrant									
No	53014(11.1)	3234(6.1)	0.004	64(0.1)	0.001	1304(2.5)	<0.001	1866(3.5)	<0.001
Yes	425031(88.9)	24595(5.8)		330(0.1)		12678(3.2)		10587(2.5)	
Smoking									
No	477964(100.0)	27825(5.8)	0.094	394(0.1)	-	14980(3.1)	0.518	12450(2.6)	0.770
Yes	80(0.0)	4(5.0)		0(0.0)		1(1.3)		3(3.8)	
Drinking									
No	477954(99.9)	27826(5.8)	0.433	394(0.1)	-	14980(3.1)	0.846	12452(2.6)	0.576
Yes	90(0.0)	3(3.3)		0(0.0)		2(2.2)		1(1.1)	
Parity									
0	223429(46.7)	13640(6.1)		232(0.1)		7785(3.5)		5623(2.5)	
≥1	253680(53.1)	14076(5.6)	<0.001	159(0.1)	<0.001	7129(2.8)	<0.001	6788(2.7)	<0.001
Missing	935(0.2)	-		935		-		-	
Multiple pregnancy									
No	467871(97.9)	23233(5.0)	<0.001	339(0.1)	<0.001	14033(3.0)	<0.001	8861(1.9)	<0.001
Yes	10173(2.1)	4596(45.2)		55(0.5)		949(9.3)		3592(35.3)	
Delivery mode									
Vaginal delivery	313532(65.6)	14983(4.8)	<0.001	1(0.0)	<0.001	14982(4.8)	-	0(0.0)	-
Labour induction/ Caesarean section	164512(34.4)	12846(7.8)		393(0.2)		0(0.0)		12453(7.6)	
Fertility treatment									
No	476667(99.7)	27463(5.8)	<0.001	386(0.1)	<0.001	14939(3.1)	<0.957	12138(2.6)	<0.001
Yes	1377(0.3)	366(26.6)		8(0.6)		43(3.1)		315(22.9)	
First visit trimester									

First trimester	350437(73.3)	19860(5.7)	<0.001	288(0.1)	0.138	10383(3.0)	<0.001	9189(2.6)	<0.001
Second trimester	66110(13.8)	4080(6.2)		61(0.1)		2040(3.1)		1979(3.0)	
Third trimester	61497(12.9)	3889(6.3)		45(0.1)		2559(4.2)		1285(2.1)	
Prenatal care utilization rate[a]									
< 50%	121974(25.5)	7780(6.4)	<0.001	97(0.1)	<0.001	4941(4.1)	<0.001	2742(2.3)	<0.001
50% - < 110%	277690(58.1)	13579(4.9)		183(0.1)		7304(2.6)		6092(2.2)	
≥ 110%	78283(16.4)	6454(8.2)		114(0.2)		2728(3.5)		3612(4.6)	
Missing	97(0.0)	-	-	-		-		-	
Gestational hypertension									
No	477826(99.9)	27803(5.8)	<0.001	394(0.1)	-	14979(3.1)	<0.195	12430(2.6)	<0.001
Yes	218(0.1)	26(11.9)		0(0.00)		3(1.4)		23(10.6)	
Gestational diabetes									
No	477682(99.9)	27804(5.8)	0.441	389(0.1)	<0.001	14981(3.1)	0.002	12434(2.6)	0.003
Yes	362(0.1)	25(6.9)		5(1.4)		1(0.3)		19(5.3)	
Preeclampsia or eclampsia									
No	477552(99.9)	27662(5.8)	<0.001	394(0.1)	-	14969(3.1)	0.619	12299(2.6)	<0.001
Yes	492(0.1)	167(33.9)		0(0.0)		13(2.6)		154(31.3)	
Two-child policy[b]									
No	346225(72.4)	19677(5.7)	<0.001	264(0.1)	<0.001	11237(3.3)	<0.001	8176(2.4)	<0.001
Yes	131819(27.6)	8152(6.2)		130(0.1)		3745(2.8)		4277(3.2)	
Infant Gender									
Female	219629(45.9)	11683(5.3)		167(0.1)		6130(2.8)		5386(2.5)	
Male	258396(54.1)	16139(6.3)	<0.001	227(0.1)	0.019	8847(3.4)	<0.001	7065(2.7)	<0.001
Missing	19(0.0)	-	-	19		-		-	

a. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.

b. The universal two-child policy effect time is defined as the delivery time before 1 July 2016, nine months after the policy was announced in October 2015

c. Distributions of maternal characteristics among the whole study population were calculated by the number of women in each subcategory divided by the total number of women, 478044.

d. Overall and subtype preterm birth rates were calculated by the number of preterm births divided by the number of women in each subcategory.

e. Preterm birth frequencies among subcategories of each variable were compared with the Chi-Square test.

Temporal trends in preterm birth rate

The annual overall preterm birth rates for the uncategorised study population and each exposure category of the selected risk factors during 2009-2018 are shown in **Figure 1 (Supplementary File: Table 1)**. The overall preterm birth rate fluctuated between 5.5% and 5.8% during 2009-2015 and surpassed 6.0% in 2016, reaching the highest rate in 2017 (6.4%) (**Figure 1-a**). Spontaneous preterm birth rates decreased, with an approximately 0.07% decline in PROM-PTB and a 0.7% decline in S-PTB. However, the MI-PTB rate had increased year by year, from 2.0% in 2009 to 3.4% in 2018 (**Figure 1-a**). Annual changes in late preterm were more obvious than those in extremely preterm and very preterm infants (**Figure 1-b**). Generally, the rising trends in preterm birth were observed in exposure subcategories of maternal age (**Figure 1-c**), maternal education (**Figure 1-d**), immigration (**Figure 1-e**), parity (**Figure 1-f**), multiple pregnancy (**Figure 1-g**), labour induction or caesarean delivery mode (**Figure 1-h**), fertility treatment (**Figure 1-i**), first visit trimester (**Figure 1-j**), inadequate prenatal care utilisation (**Figure 1-k**), and infant sex(**Figure 1-l**). The results of the sensitivity analysis (**Supplementary File: Table 2**) indicated that statistically significant changes in annual preterm birth rates occurred only in the years 2016, 2017 and 2018 compared with 2009. The overall preterm birth trends for smoking, drinking, gestational hypertension, gestational diabetes, preeclampsia or eclampsia were not measured as they made up a small proportion in the positive results.

Risk factors for preterm birth

Based on the results of the chi-square test of possible maternal characteristics in **Table 1**, statistically significant risk factors for both overall preterm birth and subtypes of preterm birth including maternal age, education level, immigration, parity, multiple pregnancy, fertility treatment, first prenatal care visit trimester, prenatal care utilisation, two-child policy and infant sex were further analysed using multivariable logistic regression. Gestational hypertension, diabetes and preeclampsia or eclampsia were not included in the regression model as they made up a small proportion in subgroups of preterm birth, even with significant associations with preterm birth (**Table 1**). The corresponding adjusted odds ratios for each characteristic are presented in **Table 2.** Maternal age, maternal education, parity, multiple pregnancy, prenatal care utilization and infant gender still showed significant associations with both overall preterm birth and subtypes of preterm birth. For example, women with multiple pregnany had a higher risk of preterm than the reference group (adjusted odds ratio [AOR] 15.2, 95% CI: 14.6, 15.9; $p<0.001$) with the highest risk of MI-PTB (adjusted odds ratio [AOR] 25.6, 95% CI: 24.4, 26.8; *p<0.001*) and lower risk of PROM-PTB (adjusted odds ratio [AOR] 5.7, 95% CI: 4.2, 7.7; *p<0.001*) and S-PTB (adjusted odds ratio [AOR] 3.5, 95% CI: 3.3, 3.8; *p<0.001*). Births with maternal fertility treatment had a much higher risk of preterm birth rate, especially PROM-PTB rate and MI-PTB rate (**Table 1**), but the strength of association was reduced by other risk factors in our multivariable logistic regression analysis (**Table 2**).

Table 2
Multivariable Logistic Regression of Risk Factors for Overall Preterm Birth and Subtypes of preterm Birth in Baoan, Shenzhen, 2009–2018[a]

	Overall PTB		PROM-PTB		S-PTB		MI-PTB	
	β[d]	AOR[e] (95% CI)[f]	β[d]	AOR[e] (95% CI)[f]	β[d]	AOR[e] (95% CI)[f]	β[d]	AOR[e] (95% CI)[f]
Maternal age (year)								
≤ 20	0.44	1.6(1.5,1.6)*	-0.31	0.7(0.4,1.3)	0.65	1.9(1.8,2.0)*	-0.23	0.8(0.7,0.9)*
21-35	-	Reference	-	Reference	-	Reference	-	Reference
≥ 36	0.44	1.5(1.5,1.6)*	0.55	1.7(1.3,2.4)*	0.01	1.0(1.0.,1.1)	0.72	2.1(1.9,2.2)*
Maternal education								
Primary school and below	0.17	1.2(1.0,1.3)*	0.80	2.2(2.0,3.6)$	0.27	1.3(1.2,1.4)*	0.02	1.0(0.9,1.1)
Secondary and high school	0.22	1.2(1.0,1.3)*	0.11	1.1(0.9,1.5)	0.31	1.4(1.3,1.4)*	0.08	1.1(1.0,1.1)#
College and above	-	Reference	-	Reference	-	Reference	-	Reference
Immigrant								
No	-	Reference	-	Reference	-	Reference	-	Reference
Yes	0.07	1.1(1.0,1,1)#	-0.17	0.8(0.6,1.1)	0.12	1.1(1.1,1.2)*	0.03	1.0(1.0,1.1)
Parity								
0	-	Reference	-	Reference	-	Reference	-	Reference
≥ 1	-0.09	0.9(0.9,0.9)*	-0.57	0.6(0.5,0.7)*	-0.18	0.8(0.8,0.9)*	0.07	1.1(1.0,1.1)#
Multiple pregnancy								
No	-	Reference	-	Reference	-	Reference	-	Reference
Yes	2.72	15.2 (14.6,15.9)*	1.74	5.7 (4.2,7.7)*	1.25	3.5 (3.3,3.8)*	3.24	25.6 (24.4,26.8)*
Fertility treatment								
No	-	Reference	-	Reference	-	Reference	-	Reference
Yes	-0.01	1.0(0.9,1.1)	0.39	1.5(0.7,3.1)	-0.75	0.5(0.4,0.7)*	0.16	1.2(1.0,1.4)$
First visit trimester								
First trimester	-	Reference	-	Reference	-	Reference	-	Reference

Second trimester	0.04	1.0(1.0,1.1)[$]	0.25	1.3(1.0,1.7)	-0.10	0.9(0.9,1.0)[*]	0.20	1.2(1.2,1.3)[*]
Third trimester	0.02	1.0(1.0,1.1)	-0.05	1.0(0.6,1.4)	-0.03	1.0(1.0,1.1)	-0.05	1.0(0.9,1.0)
Prenatal care utilization rate[b]								
< 50%	-0.19	0.8(0.8,0.9)[*]	-0.36	0.7(0.5,1.0)	-0.01	1.0(0.9,1.1)	-0.39	0.68(0.63,0.73)[*]
50% - < 110%	-0.46	0.6(0.6,0.7)[*]	-0.55	0.6(0.5,2.4)[*]	-0.37	0.7(0.7,0.7)[*]	-0.49	0.61(0.58,0.64)[*]
≥ 110%	-	Reference	-	Reference	-	Reference	-	Reference
Two-child policy[c]								
No	-	Reference	-	Reference	-	Reference	-	Reference
Yes	0.07	1.1(1.0,1.1)[*]	0.19	1.2(1.0,1.5)	-0.03	1.0(0.9,1.0)	0.16	1.2(1.1,1.2)[*]
Infant Gender								
Female	-	Reference	-	Reference	-	Reference	-	Reference
Male	0.20	1.2(1.2,1.3)[*]	0.17	1.2(1.0,1.4)	0.22	1.3(1.2,13)[*]	0.14	1.2(1.1,1.2)[*]

a. 476,997 live births were included after removing 1047 records due to missing values in any risk factor.
b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
c. The universal two-child policy is defined as the delivery time before 1 July 2016, nine months after the policy was announced in October 2015.
d. β, coefficients of risk factors in the multivariable binomial logistic regression model.
e. AOR, adjusted odds ratio; CI, confidence interval.
f. [$]: P<0.05; [#]: P<0.01; [*]: P<0.001.

Temporal trends in the distribution of sociodemographic factors

The distributions of sociodemographic factors including maternal age, education, immigration, parity, multiple pregnancy, delivery mode, first prenatal care visit trimester, prenatal care utilisation and infant sex are shown in **Figure 2** (**Supplementary File: Table 3**). Preterm births and the increase in preterm birth rate mainly occurred in the late preterm group (gestational age 32 - <37 weeks) (**Figure 2-a**). The advanced maternal age group (≥36 years) expanded from 6.2% in 2009 to 11.9% in 2018 (**Figure 2-b**). Improvement in maternal educational attainment is presented in **Figure 2-c**, showing that the proportion of women with education level of primary school and below decreased from 17.6% in 2009 to 1.2% in 2018. The percentage of immigrants decreased yearly during the decade from 95.8% in 2009 to 77.2% in 2018 (**Figure 2-d**). However, multiparity group expanded during the study period, from 39.5% in 2009 to 59.5% in 2018 (**Figure 2-e**). Women with labour induction or caesarean section accounted for approximately 35% of the entire population over the decade (**Figure 2-f**). The proportion of women who initiated prenatal care visits in the first trimester of pregnancy increased from 39.9% in 2009 to 91.7% in 2018 (**Figure 2-g**). Prenatal care utilisation improved with a drastic increase in the proportion of adequate plus utilization group from 5.4% in 2009 to 44.8% in 2018 (**Figure 2-h**). The male-to-female sex ratio in Baoan, Shenzhen stayed around 117:100 over the decade in our study (**Figure 2-i**). Since 2014, fertility treatment had become slightly more prevalent among live births in Baoan, from no cases during 2009-2013 to 0.1% in 2014 and 0.7% in 2018 (**Supplementary File: Table 3**).

Contributions of transitions in sociodemographic factors to variations in preterm birth rate

The preterm birth rate of from 5.7% from 1 January 2009 to 30 June 2016 increased to 6.2% from 1 July 2016 to 31 December 2018, with 88% of the increase attributed to late preterm birth. The increase in the overall preterm rate mainly came from the increase in medically induced preterm birth rate, while rate of preterm labour (S-PTB) decreased after June 2016. We compared preterm birth rates subcategorised by sociodemographic factors including maternal age, maternal education, parity, multiple pregnancy, prenatal care utilisation and infant sex, as well as the percent compositions of these factors (**Table 3**). Except for the adequate plus group of prenatal care utilisation, preterm birth rates increased in all the categories after the policy. The contributions of sociodemographic factors to the variations in the overall and subtypes of preterm birth rates between the two periods are visualised with population attribution risk fraction in **Figure 3 (Supplementary File: Table 4)**. Maternal age and multiple pregnancy were drivers underlying the increment of the overall preterm birth rate, whereas maternal education, parity, prenatal care utilisation and infant sex contributed to the rate reduction. In particularl, maternal education level increased, especially in the group of college and above, from 18.0% to 35.8% and an attributed 0.22% reduction in the overall preterm birth rate, a 0.14% decrease in S-PTB and a 0.05% decline in MI-PTB rate were evaluated, respectively. Births with inadequate prenatal care utilisation (<50%) decreased from 32.2% to 7.7%, which contributed to a 0.45% decrease in the overall preterm birth rate, 0.01% increase of PROM-PTB rate, 0.27% decrease of S-PTB and 0.14% reduction of MI-PTB. Even with a small change in composition, from 2.0% to 2.5%, multiple pregnancy had contributed to over half of the increase (0.28%/0.52%) in the overall preterm birth rate, with a major effect on MI-PTB. Maternal age contributed to an increase in the rate of MI-PTB but a decrease in the rate of S-PTB. The proportion of younger maternal age dropped from 5.6% to 2.8% while advanced maternal age (≥36 years) grew from 6.9% to 11.1%, contributing to a 0.03% increase in preterm birth rate. Multiparous births increased from 50.4% to 60.3% and had made a 0.06% decrease in preterm birth rate. The infant sex ratio remained during the two periods and its contribution to the change in preterm birth rate was very small.

Table 3
Preterm Birth Rate and Distribution of Risk Factors in Baoan, Shenzhen, 2009 - 2018[a]

	Preterm birth rate (%)		Distribution percentage (%)[c]	
	2009.01-2016.06	2016.07-2018.12	2009.01-2016.06	2016.07-2018.12
All live birth	5.7	6.2	72.4	27.6
PROM-PTB	0.1	0.1	-	-
S-PTB	3.2	2.8	-	-
MI-PTB	2.4	3.2	-	-
Gestational age(week)				
< 28	0.1	0.1	0.8	1.8
28 -< 32	0.6	0.6	9.9	9.1
32 -< 37	5.1	5.5	89.3	89.2
Maternal age(year)				
≤ 20	7.8	8.5	5.6	2.8
21-35	5.3	5.8	87.6	86.2
≥ 36	8.2	8.8	6.9	11.1
Maternal education				
Primary school and below	5.7	7.8	4.4	1.2
Secondary and high school	5.8	6.5	77.6	63.1
College and above	5.2	5.6	18.0	35.8
Parity				
0	5.9	6.6	49.6	39.7
≥1	5.4	5.9	50.4	60.3
Multiple pregnancy				
No	4.9	5.1	98.0	97.5
Yes	42.7	50.2	2.0	2.5
Prenatal care utilization rate[b]				
< 50%	6.1	8.9	32.2	7.7
50% -< 110%	4.9	5.2	58.1	58.4

≥ 110%	9.4	7.3	9.7	33.9
Infant Gender				
Female	5.2	5.6	45.8	46.5
Male	6.0	6.7	54.3	53.6

- a. 476,997 live births were included after removing 1047 records due to missing values in any risk factor.
- b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
- c. The distribution percentage for each category is the number of cases divided by the total number of preterm births.

Discussion

To date, the persistent increase in preterm birth rate remains a challenging public health issue facing the world and limited studies have focussed on the temporal trends of preterm birth during a sociodemographic transition period in recent decades. In this retrospective cohort study, a statistical analysis of 478,044 birth records demonstrated the drivers of the time trends in preterm birth among a mixed population, under the background of sociodemographic transition in Shenzhen. The findings of this study highlight the importance of safeguarding the health and well-being of women to reduce preterm birth, especially through improving maternal education and prenatal care service coverage.

During the sociodemographic transition period from 2009 to 2018, the overall preterm birth rate of 5.8% in Baoan was at a relatively lower level compared with the global preterm birth rate ranging from 5% in northern European countries to 18% in African countries [6]. It is also lower than the weighted national incidence of 6.7% in China during 2015-2016 [34]. However, it was slightly higher than the Shenzhen preterm birth rate of 5.7% during 2003-2012, it was slightly higher during 2009-2018 [20]. Consistent with the global trend of the rising preterm birth rates reported by many countries in recent years, the prevalence of preterm birth in Baoan increased from 5.7% in 2009 to 6.2% in 2018 under the background of sociodemographic transition [5, 35]. Compared with the whole Shenzhen birth population during 2003-2012, both the S-PTB rate and MI-PTB rate in Baoan increased during 2009-2018, while there was a 0.5% decrease in the PROM-PTB rate (**Supplementary Table 5**) [20]. MI-PTB and late preterm drove the majority of the increase in preterm birth rates both in both our research and the study of the entire Shenzhen birth population during 2003-2012 [20]. In our analysis of risk factors, multiple pregnancy had a strong effect on preterm birth, especially MI-PTB and more than half of the increase in the overall preterm birth rate between the two periods (before and after implementation of the universal two-child policy) could be explained by it. Findings from other studies indicated that multiple pregnancy was a strong risk factor for preterm birth with a 7 to10 times higher risk than that of singletons [36-37]. Concerns have been raised in many studies about the increasing trend of multiple pregnancy reported both in China and worldwide, which was associated with the global rise in advanced maternal age, infertility treatments and obstetric interventions performed before 37 gestational weeks, especially at 34-36 weeks [38-42].

In contrast with multiple pregnancy, the improvements in maternal education and prenatal care utilisation have contributed to the reduction in the overall preterm birth rate as well as the subtype-specific preterm birth rates, which has coincided with socio-economic developments in China with the launch of laws and policies, including 9-year compulsory education for all and national commitment to maternal and child survival and health [43, 44]. In particular, the proportion of pregnant women with inadequate prenatal care utilisation decreased after implementation of the universal two-child policy and contributed to a 0.5% decline in the preterm birth rate. The positive effect of prenatal care on preterm birth during 2009-2018 was estimated to be larger than the period 2003-2012 in the whole Shenzhen birth population [20]. Although the proportion of women who initiated prenatal care in the first trimester increased from 39.9% in 2009 to 91.7 in 2018, this was not significantly associated with the overall and subtypes of preterm birth rates. As suggested by the Born Too Soon Group, further studies are needed to clarify the association between the quality of prenatal care visits and preterm birth [45]. Additionally, the 0.2% of reduction in preterm birth rate could be explained by the expansion of maternal educational attainment during 2009-2018. However, the effect of maternal education on preterm birth in this study is contrary to the result in the Shenzhen preterm birth research during 2003-2012, which demonstrated that the education improvement had contributed to 0.2% of the rise in preterm birth rate [20]. It should be noted that the proportion of multiparous births increased continuously over the decade, including and a near 10% increment after the implementation of the universal two-child policy, which resulted in a small reduction in the preterm birth rate. The percentage of multiparity in this study was approximately 15.3% higher than that in the Shenzhen birth population during 2003-2012 and also higher than the national level [20, 25]. The male-to-female sex ratio in Baoan during 2009-2018 remained abnormal compared with the natural sex ratio at birth, which indicated that a more balanced sex ratio, one of the expected benefits of the universal two-child policy, had not yet been achieved [46, 47].

The present study is unique in reporting time trends in preterm birth under a setting of rapid sociodemographic transition over 10 years. Contributions of sociodemographic factors to preterm birth and to the incidence changes were calculated to provide a more comprehensive and quantitative understanding of the pathogenesis of temporal trends in preterm birth. Overall and subtypes of preterm birth, including spontaneous preterm and iatrogenic preterm, were analysed respectively. Percent compositions of sociodemographic factors in each year have been presented to provide a better landscape of the socio-economic transition in this area. Missing information on prenatal care utilisation and parity were unlikely to have impacted the results.

However, the study results were limited by data collection and analysis methods. Firstly, misclassification of preterm birth subtypes was possible because subtype of preterm birth was unavailable in the Shenzhen Birth Registry Database. Fortunately, the classification method based on delivery mode and surgical indications has been adapted by similar research and reliability of the database has been verified by previous study [19, 20]. Secondly, there were many important factors we did not cover in this study as the limitation of the database. For example, data on maternal employment, family income, and maternal obesity were not available. Increased risks of preterm birth were significantly related to maternal obesity in a cohort study of 1,599,551 live singleton births in Sweden from 1992 to 2010 [48]. Similar results were also found in a nationwide study of 7,141,630 singleton live births from the US during 2016 and 2017 [49]. Finally, sociodemographic transitions in maternal age and multiple pregnancy have been identified as contributors to the rising preterm birth rate in Baoan, Shenzhen during 2009-2018 in this study. More possible important factors, including maternal employment, family income, non-medically indicated labour, induction and caesarean section deliveries, assisted reproductive technologies need to be studied to present a more comprehensive understanding about the impact of sociodemographic transitions on preterm birth.

Conclusions

In conclusion, the present study provides unique information about the temporal trends in preterm birth in the setting of rapid sociodemographic transition in China during the last decade. The observed increase in preterm birth rate was significantly associated with the increase of multiple pregnancy. Fortunately, maternal educational attainment and prenatal care utilisation have improved significantly during this period, and have made positive contributions to the decline in preterm birth incidence. The study findings highlight that the investment in girls' education, quality reproductive and maternal healthcare may significantly reduce the rate of babies born too soon and the economic burden of preterm birth. More studies need to be conducted to discover the hidden risk factors that drive the increase in preterm birth rate and finally to reduce the prevalence of preterm birth and its global burden.

Acknowledgments

We would like to thank the staff who provided us with limited but accredited access to the Shenzhen Birth Registry Database and suggestions on the use of this database.

References

1. Romero R, Dey SK, Fisher SJ. Preterm labor: one syndrome, many causes. *Science* 2014;345(6198):760-765.
2. Maghsoudlou S, Yu ZM, Beyene J, *et al*. Phenotypic Classification of Preterm Birth Among Nulliparous Women: A Population-Based Cohort Study. *J Obstet Gynaecol Can* 2019;41(10):1423-1432 e1429.
3. Lawn JE, Kinney MV, Belizan JM, *et al*. Born too soon: accelerating actions for prevention and care of 15 million newborns born too soon. *Reprod Health* 2013;10 Suppl 1:S6.
4. United Nations Inter-agency Group for Child Mortality Estimation (UNIGME). Levels & Trends in Child Mortality: Report 2019, Estimates developed by the United Nations Inter-agency Group for Child Mortality Estimation. United Nations Children's Fund, New York, 2019.
5. Chawanpaiboon S, Vogel JP, Moller AB, *et al*. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *Lancet Glob Health* 2019; 7(1):e37-e46.
6. Blencowe H, Cousens S, Chou D, *et al*. Born too soon: the global epidemiology of 15 million preterm births. *Reprod Health* 2013;10 Suppl 1:S2.
7. Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes; Behrman RE, Butler AS. Preterm Birth: Causes, Consequences, and Prevention. *National Academies Press (US)* 2007.
8. Johnston KM, Gooch K, Korol E, *et al*. The economic burden of prematurity in Canada. *BMC Pediatr* 2014;14:93.
9. Boerma T. Countdown to 2030: tracking progress towards universal coverage for reproductive, maternal, newborn, and child health. *Lancet* 2018;391(10129):1538-1548.
10. Rahman A, Rahman M, Pervin J, *et al*. Time trends and sociodemographic determinants of preterm births in pregnancy cohorts in Matlab, Bangladesh, 1990-2014. *BMJ Glob Health* 2019;4(4):e001462.
11. Sakata S, Konishi S, Ng CFS, *et al*. Preterm birth rates in Japan from 1979 to 2014: Analysis of national vital statistics. *J Obstet Gynaecol Res* 2018;44(3):390-396.
12. Lopez Orellana P. Increase in Preterm Birth during Demographic Transition in Chile from 1991 to 2012. *Biomed Res Int* 2015;2015:845968.
13. Sadovsky ADI, Matijasevich A, Santos IS, *et al*. Socioeconomic inequality in preterm birth in four Brazilian birth cohort studies. *J Pediatr (Rio J)* 2018;94(1):15-22.
14. Glinianaia, SV, Ghosh, R, Rankin, J, *et al*. No improvement in socioeconomic inequalities in birthweight and preterm birth over four decades: a population-based cohort study. *BMC public health* 2013, 13: 345.
15. Yang M, Dijst M, Helbich M. Mental Health among Migrants in Shenzhen, China: Does it Matter Whether the Migrant Population is Identified by Hukou or Birthplace? *Int J Environ Res Public Health*. 2018;15(12):2671.
16. Shenzhen Statistics Bureau. Shenzhen Statistical Yearbook 2019. Date accessed: December 30, 2019. Available online: http://www.sz.gov.cn/attachment/0/405/405056/6616865.pdf.
17. Shenzhen Baoan Statistics Bureau. Shenzhen Baoan Statistical Yearbook 2017. Date accessed: November 30, 2018. Available online: http://sso.sz.gov.cn/pub/baqzfzx2017/tjj/ywgz_136262/tjsj_137617/tjnj_137621/201811/P020181130433800362927.pdf.
18. Shenzhen Baoan Statistics Bureau. Shenzhen Baoan Statistical Yearbook 2012. Date accessed: February 24, 2014. Available online:

http://sso.sz.gov.cn/pub/baqzfzx2017/tjj/ywgz_136262/tjsj_137617/tjnj_137621/201404/P020140429367563038549.pdf.

19. Liang Z, Lin Y, Ma Y, et al. The association between ambient temperature and preterm birth in Shenzhen, China: a distributed lag non-linear time series analysis. *Environ Health* 2016;15(1):84.
20. Li C, Liang Z, Bloom MS, *et al*. Temporal trends of preterm birth in Shenzhen, China: a retrospective study. *Reprod Health* 2018;15(1):47.
21. WHO. Recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. Modifications recommended by FIGO as amended October 14, 1976. *Acta Obstet Gynecol Scand* 1977;56(3):247-253.
22. Tang K, Wang H, Tan SH, *et al*. Association between maternal education and breast feeding practices in China: a population-based cross-sectional study. *BMJ Open* 2019;9(8):e028485.
23. Zhao, Q, Huang, ZJ, Yang, S, et al. The utilization of antenatal care among rural-to-urban migrant women in Shanghai: a hospital-based cross-sectional study. BMC public health. 2012;12:1012.
24. Osterman MJK, Martin JA. Timing and Adequacy of Prenatal Care in the United States, 2016. *Natl Vital Stat Rep* 2018;67(3):1-14.
25. Li HT, Xue M, Hellerstein S, et al. Association of China's universal two child policy with changes in births and birth related health factors: national, descriptive comparative study. *BMJ* 2019;366:l4680.
26. McHugh ML. The chi-square test of independence. *Biochem Med (Zagreb*) 2013, 23(2):143-149.
27. Thabane L, Mbuagbaw L, Zhang S, *et al*. A tutorial on sensitivity analyses in clinical trials: the what, why, when and how. *BMC Med Res Methodol* 2013;13:92.
28. Sperandei S. Understanding logistic regression analysis. *Biochem Med (Zagreb)* 2014;24(1):12-18.
29. Goldenberg RL, Culhane JF, Iams JD, *et al*. Epidemiology and causes of preterm birth. *Lancet* 2008;371(9606):75-84.
30. Auger N, Le TU, Park AL, *et al*. Association between maternal comorbidity and preterm birth by severity and clinical subtype: retrospective cohort study. *BMC Pregnancy Childbirth* 2011;11:67.
31. VanderWeele TJ, Lantos JD, Lauderdale DS. Rising preterm birth rates, 1989-2004: changing demographics or changing obstetric practice? *Soc Sci Med* 2012;74(2):196-201.
32. Chang HH, Larson J, Blencowe H, *et al*. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. *Lancet* 2013;381(9862):223-234.
33. Greenland S, Senn SJ, Rothman KJ, *et al*. Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations. *Eur J Epidemiol* 2016;31(4):337-350.
34. Chen C, Zhang J, Xia H, *et al*. Epidemiology of preterm birth in China in 2015 and 2016: a nationwide survey. *The Lancet* 2018;392:S73.
35. Chang HH, Larson J, Blencowe H, et al. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. *Lancet* 2013;381(9862):223-234.
36. Dodd JM, Grivell RM, CM OB, *et al*. Prenatal administration of progestogens for preventing spontaneous preterm birth in women with a multiple pregnancy. *Cochrane Database Syst Rev* 2019;2019(11).
37. Blondel B, Macfarlane A, Gissler M, *et al*. General obstetrics: Preterm birth and multiple pregnancy in European countries participating in the PERISTAT project. *BJOG* 2006;113(5):528-535.
38. Deng C, Dai L, Yi L, *et al*. Temporal trends in the birth rates and perinatal mortality of twins: A population-based study in China. *PLoS One* 2019;14(1):e0209962.
39. Pison G, Monden C, Smits J. Twinning Rates in Developed Countries: Trends and Explanations. *Population and Development Review* 2015;41(4):629-649.

40. Richards JL, Kramer MS, Deb-Rinker P, Rouleau J, Mortensen L, Gissler M, Morken NH, Skjaerven R, Cnattingius S, Johansson S *et al*. Temporal Trends in Late Preterm and Early Term Birth Rates in 6 High-Income Countries in North America and Europe and Association With Clinician-Initiated Obstetric Interventions. *JAMA* 2016;316(4):410-419.
41. Fox H, Callander E, Lindsay D, Topp S. Evidence of overuse? Patterns of obstetric interventions during labour and birth among Australian mothers. *BMC Pregnancy and Childbirth* 2019;19(1):226.
42. Zhong N. Achieving Lower Preterm Birth Rates in China via Reductions in Iatrogenic Preterm Births. *Am J Public Health* 2019;109(11):1489-1490.
43. He C, Liu L, Chu Y, *et al*. National and subnational all-cause and cause-specific child mortality in China, 1996-2015: a systematic analysis with implications for the Sustainable Development Goals. *Lancet Glob Health* 2017;5(2):e186-e197.
44. Guo Y, Bai J, Na H. The history of China's maternal and child health care development. *Semin Fetal Neonatal Med* 2015;20(5):309-314.
45. Requejo J, Merialdi M, Althabe F, *et al*. Born too soon: care during pregnancy and childbirth to reduce preterm deliveries and improve health outcomes of the preterm baby. *Reprod Health* 2013;10 Suppl 1:S4.
46. Shah PS, Knowledge Synthesis Group on Determinants of LBWPTb. Parity and low birth weight and preterm birth: a systematic review and meta-analyses. *Acta Obstet Gynecol Scand* 2010;89(7):862-875.
47. Zeng Y, Hesketh T. The effects of China's universal two-child policy. *Lancet* 2016; 388(10054): 1930-1938.
48. Cnattingius S, Villamor E, Johansson S, et al. Maternal obesity and risk of preterm delivery. JAMA. 2013;309(22):2362-2370.
49. Liu B, Xu G, Sun Y, et al. Association between maternal pre-pregnancy obesity and preterm birth according to maternal age and race or ethnicity: a population-based study. Lancet Diabetes Endocrinol. 2019;7(9):707-714.

Footnotes

Contributors: LYZ, LZ and RM developed the study concept and design. RM, YLL and QX collected data. RM cleaned the data and performed data analysis. RM and LYZ drafted the manuscript. LYZ, LZ, YLL, JW, YXZ, HYS, XR provided oversight and expert advice for the research and the written paper. All authors revised and approved the final paper.

Funding: This study is supported by the National Natural Science Foundation of China (grant number: 31771468)

Disclaimer: The funding sources had no involvement in any aspect of this study.
Competing interests: None declared.
Patient consent for publication: Not required.
Ethics approval: This study was approved by the medical ethics committee of Shenzhen Baoan Women's and Children's Hospital, Jinan University, China (number LLSC-2019-07-01). All data used in this study have been completely anonymized before accession and were analysed anonymously.
Provenance and peer review: Not commissioned; externally peer reviewed.
Data sharing statement: Data are available upon reasonable request to the corresponding author.

Figure Legends:

Figure 1.
Temporal Trends in Preterm Birth Rate among 478,044 Livebirths (2801 ineligible birth records were excluded) Subcategorized by Risk Factors in Baoan, Shenzhen, 2009-2018. a. Overall and subtypes b. Gestational age c. Maternal age d. Maternal education e. Immigration f. Parity g. Multiple pregnancy h. Delivery mode i. Fertility treatment j. First visit trimester k. Prenatal care utilization l. Infant gender

Figure 2.
Temporal Trends in the Distribution of Sociodemographic Factors in Baoan, Shenzhen, 2009-2018. a. Gestational age b. Maternal age c. Maternal education d. Immigration e. Parity f. Delivery mode g. First visit trimester h. Prenatal care utilization i. Infant gender

Figure 3.
Analysis of Sociodemographic Factors Contributing to the Variations of Preterm Birth Rate in Baoan, Shenzhen, 2009-2018. PROM-PTB, preterm birth following premature rupture of membranes; MI-PTB, medically induced preterm birth; S-PTB, spontaneous preterm labor.

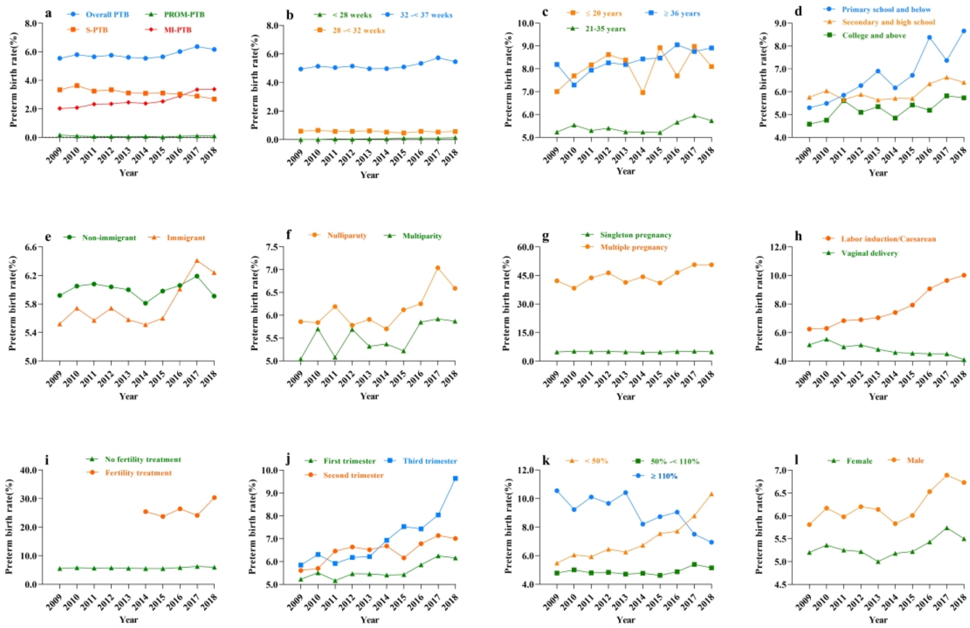


Figure 1. Temporal Trends in Preterm Birth Rate among 478,044 Livebirths (2801 ineligible birth records were excluded) Subcategorized by Risk Factors in Baoan, Shenzhen, 2009-2018. a. Overall and subtypes b. Gestational age c. Maternal age d. Maternal education e. Immigration f. Parity g. Multiple pregnancy h. Delivery mode i. Fertility treatment j. First visit trimester k. Prenatal care utilization l. Infant gender

291x194mm (600 x 600 DPI)

Figure 2. Temporal Trends in the Distribution of Sociodemographic Factors in Baoan, Shenzhen, 2009-2018.
a. Gestational age b. Maternal age c. Maternal education d. Immigration e. Parity f. Delivery mode g. First visit trimester h. Prenatal care utilization i. Infant gender

232x200mm (600 x 600 DPI)

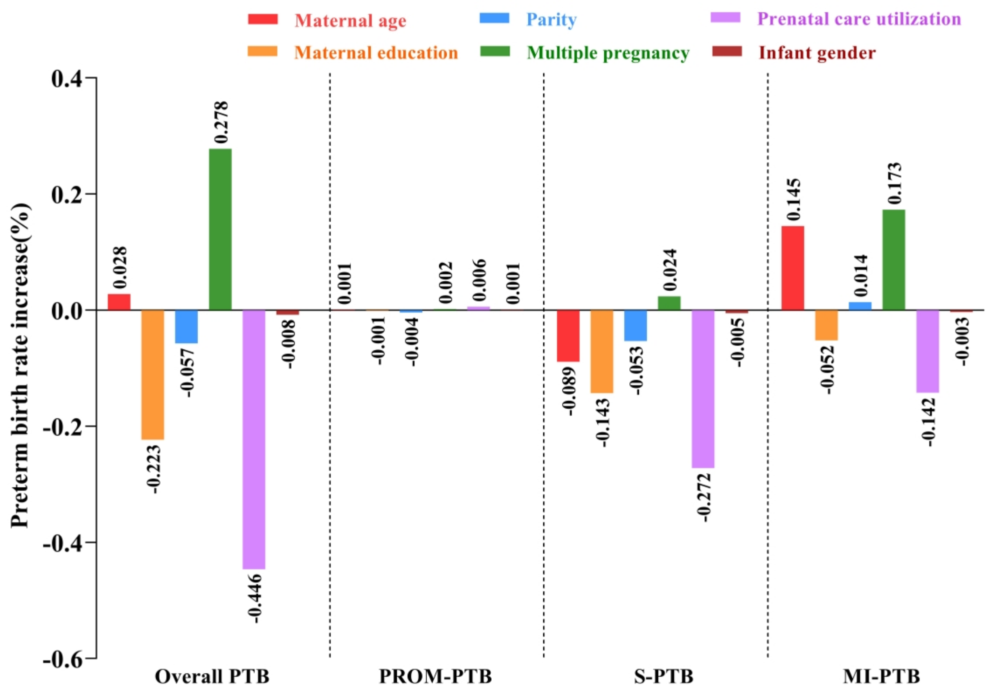


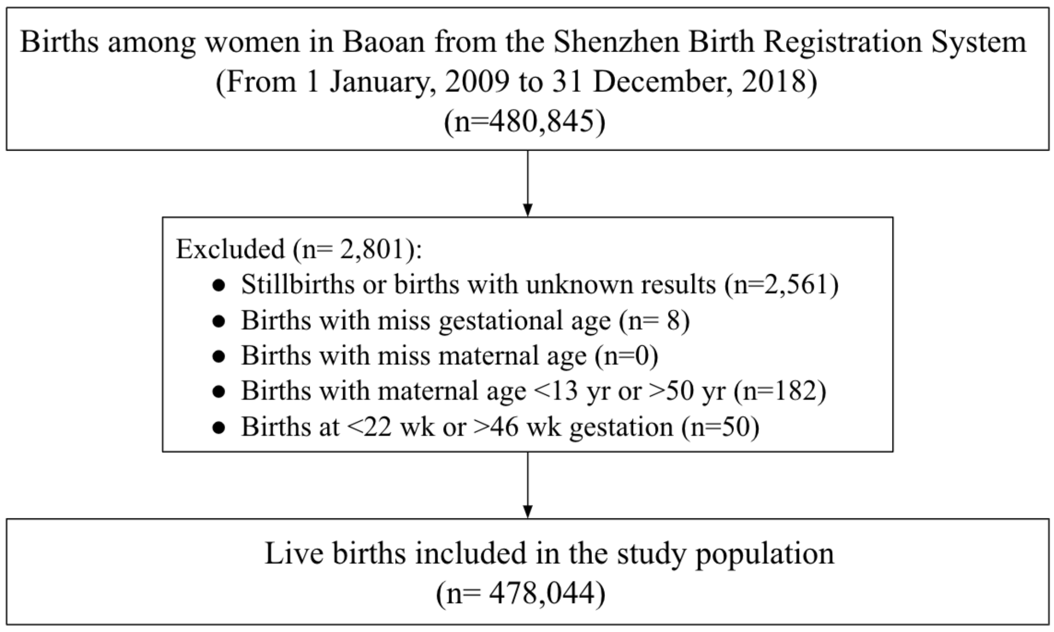
Figure 3. Analysis of Sociodemographic Factors Contributing to the Variations of Preterm Birth Rate in Baoan, Shenzhen, 2009-2018. PROM-PTB, preterm birth following premature rupture of membranes; MI-PTB, medically induced preterm birth; S-PTB, spontaneous preterm labor.

183x132mm (600 x 600 DPI)

Supplementary Materials

Ten-year time trends in preterm birth during a sociodemographic transition period: a retrospective cohort study in Shenzhen, China

Supplementary Figure 1. Flowchart of Study Population



Supplementary Table 1. Temporal Trends in Preterm Birth Rate (%) in Baoan, Shenzhen, 2009 - 2018

	Year									
	2009	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Overall Preterm Birth Rate	5.5	5.8	5.7	5.8	5.6	5.5	5.7	6.0	6.4	6.2
PROM-PTB	0.2	0.1	0.1	0.1	0.0	0.1	0.0	0.1	0.1	0.1
S-PTB	3.3	3.6	3.2	3.3	3.1	3.1	3.1	3.0	2.9	2.7
MI-PTB	2.0	2.1	2.3	2.4	2.5	2.4	2.5	2.9	3.4	3.4
Gestational age(week)										
< 28	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1
28 -< 32	0.6	0.7	0.6	0.6	0.6	0.5	0.5	0.6	0.5	0.6
32 -< 37	4.9	5.1	5.0	5.2	5.0	5.0	5.1	5.3	5.7	5.5
Maternal age(year)										
≤20	7.0	7.7	8.2	8.6	8.4	7.0	8.9	7.7	9.0	8.1
21-35	5.2	5.5	5.3	5.4	5.2	5.2	5.2	5.7	6.0	5.7
≥ 36	8.2	7.3	7.9	8.3	8.2	8.4	8.5	9.1	8.8	8.9
Maternal education										
Primary school and below	5.3	5.5	5.9	6.3	6.9	6.2	6.7	8.4	7.4	8.7
Secondary and high school	5.8	6.0	5.6	5.9	5.6	5.7	5.7	6.4	6.6	6.4
College and above	4.6	4.8	5.6	5.1	5.4	4.9	5.4	5.2	5.8	5.7
Immigrant										
No	5.9	6.1	6.1	6.0	6.0	5.8	6.0	6.1	6.2	5.9
Yes	5.5	5.7	5.6	5.7	5.6	5.5	5.6	6.0	6.4	6.2
Parity										
0	5.9	5.8	6.2	5.8	5.9	5.7	6.1	6.3	7.0	6.6
≥ 1	5.0	5.7	5.1	5.7	5.3	5.4	5.2	5.9	5.92	5.9
Multiple pregnancy										
No	4.8	5.2	5.0	5.1	4.9	4.7	4.8	5.0	5.2	4.9
Yes	42.2	38.3	43.8	46.4	41.4	44.3	41.1	46.5	50.7	50.7
Delivery mode										
Vaginal delivery	5.2	5.5	5.0	5.1	4.8	4.6	4.6	4.5	4.5	4.1
Labour induction/ Caesarean section	6.3	6.3	6.8	6.9	7.0	7.4	7.9	9.1	9.7	10.0

Fertility treatment										
No	5.5	5.8	5.7	5.8	5.6	5.5	5.5	5.9	6.3	6.0
Yes	-[b]	-[b]	-[b]	-[b]	-[b]	25.5	23.8	26.4	24.1	30.3
First visit trimester										
First trimester	5.2	5.5	5.2	5.5	5.5	5.4	5.4	5.9	6.3	6.2
Second trimester	5.6	5.7	6.5	6.6	6.5	6.7	6.2	6.8	7.1	5.5
Third trimester	5.9	6.3	5.9	6.2	6.2	6.9	7.8	7.0	7.5	9.6
Prenatal care utilization rate[a]										
< 50%	5.5	6.1	5.9	6.5	6.3	6.7	7.6	7.7	8.8	10.3
50% - < 110%	4.8	5.0	4.8	4.8	4.7	4.8	4.6	4.9	5.4	5.2
≥110%	10.6	9.2	10.1	9.7	10.4	8.2	8.7	9.1	7.5	6.9
Infant gender										
Female	5.2	5.4	5.3	5.2	5.0	5.2	5.2	5.4	5.7	5.5
Male	5.8	6.2	6.0	6.2	6.1	5.8	6.0	6.5	6.9	6.7

a. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.

b. During 2009-2013, there were no records of fertility treatments in the database.

Supplementary Table 2. Sensitivity Analysis of Temporal Trends for Overall Preterm Birth Rates in Baoan, Shenzhen, 2009 - 2018

Year	**Preterm birth rate(%)**	**Risk Ratio(95%CI)**	**P Value**
2009	5.5	Reference	
2010	5.8	1.0(1.0,1.0)	0.104
2011	5.7	1.0(1.0,1.0)	0.493
2012	5.8	1.0(1.0,1.0)	0.148
2013	5.6	1.0(1.0,1.0)	0.626
2014	5.5	1.0(1.0,1.0)	0.986
2015	5.7	1.0(1.0,1.0)	0.494
2016	6.0	1.0(1.0,1.0)	0.002
2017	6.4	1.0(1.0,1.0)	0.000
2018	6.2	1.0(1.0,1.0)	0.000

Supplementary Table 3. Temporal Trends in the Distribution Percentage (%) of Sociodemographic Factors in Baoan, Shenzhen, 2009 - 2018[a]

	Year									
	2009	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
All live births	38590	41912	46617	54957	46861	50063	45872	51328	52823	49021
Gestational age(week)										
< 28	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1
28 -< 32	0.6	0.7	0.6	0.6	0.6	0.5	0.5	0.6	0.5	0.6
32 -< 37	4.9	5.1	5.0	5.2	5.0	5.0	5.1	5.3	5.7	5.5
≥ 37	94.5	94.2	94.4	94.2	94.4	94.5	94.4	94.0	93.6	93.8
Maternal age(year)										
≤20	6.8	6.9	6.4	5.4	5.5	5.1	4.7	3.4	2.8	2.3
21-35	87.0	86.6	87.3	88.2	87.6	88.0	87.2	87.9	85.6	85.8
≥36	6.2	6.5	6.3	6.4	6.9	6.9	8.1	8.7	11.6	11.9
Maternal education										
Primary school and below	17.6	7.6	2.6	2.1	1.9	1.6	1.6	1.4	1.1	1.2
Secondary and high school	70.2	77.2	84.4	80.9	81.4	77.2	74.2	68.0	64.6	58.9
College and above	12.2	15.2	13.0	17.0	16.7	21.2	24.2	30.6	34.4	39.9
Immigrant										
No	4.2	4.5	4.1	5.7	7.7	9.7	11.0	16.3	21.7	22.8
Yes	95.8	95.6	96.0	94.3	92.4	90.3	89.0	83.7	78.3	77.2
Parity										
0	60.5	56.3	49.1	47.5	47.1	46.7	45.2	42.2	38.5	40.5
≥ 1	39.5	43.8	50.9	52.5	53.0	53.3	54.8	57.8	61.5	59.5

Multiple pregnancy										
No	98.1	98.3	98.2	98.3	98.0	97.9	97.7	97.5	97.5	97.3
Yes	1.9	1.7	1.8	1.7	2.1	2.1	2.3	2.5	2.5	2.7
Delivery mode										
Vaginal deliveries	64.8	65.5	64.8	64.9	64.5	67.0	67.9	67.0	64.2	65.2
Labor induction/ Caesarean section	35.2	34.5	35.	35.1	35.5	33.0	32.1	33.0	35.8	34.8
Fertility treatment										
No	100.0	100.0	100.0	100.0	100.0	100.0	99.4	99.2	99.5	99.3
Yes	0.0	0.0	0.0	0.0	0.0	0.0	0.7	0.8	0.5	0.7
First visit trimester										
First trimester	39.9	44.6	52.2	68.7	83.	83.4	84.2	84.0	88.7	91.7
Second trimester	26.1	24.9	21.4	14.5	9.4	10.0	10.0	11.8	8.3	6.8
Third trimester	34.0	30.5	26.5	16.8	7.4	6.6	5.9	4.2	3.1	1.5
Prenatal care utilization rate[b]										
< 50%	63.2	54.1	46.8	31.0	17.3	16.4	15.1	11.7	9.1	4.1
50% - <110%	31.3	40.5	47.3	60.4	71.6	70.9	70.7	69.0	59.7	51.1
≥110%	5.4	5.4	5.9	8.7	11.0	12.7	14.2	19.3	31.2	44.8
Infant Gender										
Female	45.0	45.4	45.9	45.8	46.3	45.6	46.1	46.5	46.4	46.2
Male	55.0	54.6	54.1	54.2	53.7	54.4	53.9	53.5	53.6	53.8

a. The distribution percentage (%) for each category is the number of cases divided by the total number of preterm births.
b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.

Supplementary Table 4. Analysis of Sociodemographic Factors Contributing to Variations of Preterm Birth Rate in Baoan, Shenzhen, 2009-2018[a]

	Overall PTB		PROM-PTB		S-PTB		MI-PTB	
	AOR	Rate change	AOR	Rate change	AOR	Rate change	AOR	Rate change
Maternal age(year)								
≤20	1.5		1.2		2.2		0.6	
21-35	Reference	0.03%	Reference	0.00%	Reference	-0.09%	Reference	0.15%
≥36	1.5		1.3		1.0		1.9	
Maternal education								
Primary school and below	1.4		1.5		1.8		1.1	
Secondary and high school	1.3	-0.22%	1.0	-0.00%	1.4	-0.14%	1.1	-0.05%
College and above	Reference		Reference		Reference		Reference	
Parity								
0	1.1	-0.06%	1.7	-0.00%	1.2	-0.05%	1.0	0.01%
≥1	Reference		Reference		Reference		Reference	
Multiple pregnancy								
No	Reference		Reference		Reference		Reference	
Yes	18.3	0.28%	6.5	0.00%	2.9	0.02%	29.9	0.17%
Prenatal care utilization rate[b]								
< 50%	1.3		0.6		1.4		1.2	
50% - <110%	0.7	-0.45%	0.7	0.01%	0.8	-0.27%	0.7	-0.14%
≥110%	Reference		Reference		Reference		Reference	
Infant Gender								
Female	Reference		Reference		Reference		Reference	
Male	1.3	-0.01%	1.5	0.00%	1.3	-0.01%	1.2	-0.00%
Projected Increase	-	0.24%	-	-0.00%		-0.04%		0.22%

a. 131,787 live births after the policy were included in the logistic regression model.
b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
c. The distribution percentage for each category is the number of cases divided by the total number of preterm births.
d. AOR: adjusted odds ratio
e. AFp: Attributable risk fraction for the population.
f. Preterm birth rate change is calculated by multiplying AFp with the preterm birth rate after the policy and subtract the result for before the policy.

Supplementary Table 5. Comparisons of Preterm Birth Rates and Risk Factor Distribution Percentages in Baoan, Shenzhen, 2003-2018[a]

	Distribution percentage(%)[c]		Preterm birth rate(%)	
	2003-2012[c]	**2009-2018**	**2003-2012[c]**	**2009-2018**
Overall Preterm Birth				
PROM-PTB	-		0.5	0.1
S-PTB	-		2.9	3.1
MI-PTB	-		2.2	2.6
Gestational age(week)				
<28 weeks	10.3	1.1	0.6	0.1
28-<32 weeks	12.8	9.7	0.7	0.6
32-<37 weeks	76.9	89.2	4.3	5.2
Maternal age(year)				
≤20	5.9	4.8	7.0	8.0
21-35	88.8	87.2	5.4	5.5
≥36	5.3	8.0	8.3	8.5
Maternal education				
Less than high school	43.3	34.6	5.7	5.8
High school and college	36.0	55.2	5.8	5.9
Bachelor	19.0	8.9	5.2	5.3
Postgraduate	1.7	1.4	5.4	4.7
Parity				
0	62.1	46.8	5.8	6.1
≥ 1	37.9	53.2	5.4	5.6
Prenatal care utilization rate[b]				
< 50%	45.9	25.5	7.1	6.4
50% - <110%	39.9	58.1	5.3	4.9
≥110%	14.2	16.4	1.9	8.2
Infant Gender				
Female	45.7	46.0	5.3	5.3
Male	54.3	54.1	6.0	6.3

a. Li C, Liang Z, Bloom MS, et al. Temporal trends of preterm birth in Shenzhen, China: a retrospective study. *Reprod Health* 2018;15(1):47.
b. Prenatal care utilization rate is defined as the ratio between the actual number of visits and the recommended number.
c. The distribution percentage for each category is the number of cases divided by the total number of preterm births.

STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	4
		(*b*) For matched studies, give matching criteria and the number of controls per case	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, explain how matching of cases and controls was addressed	
		(*e*) Describe any sensitivity analyses	4
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	5-8

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.