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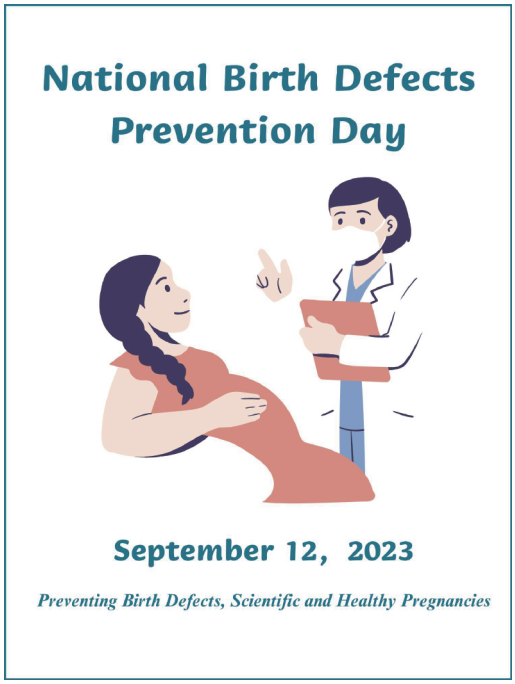

BIRTH DEFECTS PREVENTION ISSUE

Foreword

Preplanned Studies

ISSN 2096-7071

This week's issue was organized by Guest Editor Jufen Liu.

Foreword

Preventing Birth Defects: Implications and Prospects

Jufen Liu[1,2,#]

Efforts to lower maternal and neonatal mortality rates and enhance the quality of maternal and child care are pivotal, particularly in low- and middle-income countries (LMICs). These initiatives are critical for the realization of the Sustainable Development Goals by 2030. In 2019, congenital anomalies ranked as the tenth leading cause of global health loss (*1*). These conditions, also known as birth defects (BDs), are structural changes present at birth that can impact virtually any body part (e.g., heart, brain, foot). They are a significant contributor to early miscarriage, stillbirth, and fetal death. Individuals who survive these conditions often face disabilities, developmental delays, and a lifetime need for specialized medical care and health services. Therefore, comprehensive efforts to prevent BDs could substantially improve population health.

A sizable prospective cohort study conducted in China in the early 1990s found that daily periconceptional intake of 0.4 mg of folic acid could significantly reduce the risk of neuraltube defects (NTDs) (*2*), congenital limb reduction defects (*3*), and various other abnormalities. A nationwide folic acid supplementation program was not implemented until over a decade later, in 2009. Following the initiation of this program, there were marked increases in the rate of periconceptional folic acid supplementation and plasma folate concentration (*4*–*5*). Correspondingly, the prevalence of both NTDs and non-isolated NTDs with concurrent malformations dropped noticeably (*6*–*7*).

China implemented the universal two-child policy in 2016 and extended it to a three-child policy in 2021, anticipated to have a notable effect on maternal and infant health. In 2015, the Beijing Municipal Commission of Health and Family Planning innovated secondary prevention of BDs, establishing an integrated service management model of prenatal screening and diagnostic testing. Currently, non-invasive prenatal testing (NIPT), a superior accuracy high-throughput sequencing technology, has been instituted in 110 prenatal screening institutions and 10 prenatal diagnostic testing institutions in Beijing. The improved socioeconomic status and health literacy among the reproductive population prompted scientists to examine the influence of population policies and novel technology use on BDs epidemiology. This special issue contains four Preplanned Studies that address this question. Xia et al. reported an increased prevalence of chromosomal abnormalities (CAs) and their subtypes in Beijing over the last decade, based on hospital-based BDs surveillance data (*8*). Wang et al. revealed a significant decrease of both total BDs and NTDs in northern China over the past two decades (*9*). Wu et al. discovered, in Beijing, an increase in noncritical congenital defects (non-CCHDs) while the survival rate for critical congenital heart defects (CCHDs) remained stagnant despite advanced detection (*10*). Finally, Zhang et al. affirmed that strong compliance considerably mitigated the risk for NTDs (*11*).

Recent recommendations reaffirm that individuals intending to, or who may become pregnant, should consume a daily supplement containing 0.4 to 0.8 mg (400 to 800 μg) of folic acid, a widely supported prophylactic measure to prevent NTDs in their offspring. This recommendation, based on substantial evidence, bolsters the effectiveness of folic acid supplementation in disease prevention (*12*). In 2009, the Ministry of Health (previous) of the People's Republic of China launched the major public health project of "Folic Acid Supplementation to Prevent Neural Tube Defects", providing free folic acid supplements for women with registered residence and family planning in rural areas. Since 2019, extensive national efforts have been made to include folic acid supplementation in the National Basic Public Health Service Project in China. It is heartening to note that such efforts persist and were incorporated into the National Basic Public Service Standards as of July 30, 2023, providing an optimal platform for preventing NTDs and other BDs. A sustained educational effort remains vital to ensure compliance with supplementation guidelines, including earlier initiation and appropriate supplementation durations (*5*). Concurrent advancements in diagnostic techniques and tools underscore the need for ongoing epidemiological research into folic acid-resistant NTDs, congenital heart defects (CHDs), and comorbid malformations (*7*). It is also crucial to explore the etiology including genomics (*13*), exposomics (*14*), and epigenomics in future studies.

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Preplanned Studies

Trends in the Prevalence of Births with Chromosomal Abnormalities — Haidian District, Beijing Municipality, China, 2013–2022

Shuangbo Xia[1,2,&]; Chao Meng[3,&]; Xiao Cheng[1,2]; Duoduo Wang[1,2]; Yaxian Wu[1,2]; Zhiwen Li[1,2]; Yuan Wei[4,#]; Jufen Liu[1,2,#]

Summary

What is already known about this topic?

The primary causes of early miscarriage and stillbirth are chromosomal abnormalities (CAs) whose prevalence has been observed to increase in recent years.

What is added by this report?

According to data received from a hospital-based birth-defect surveillance system in the Haidian District, Beijing, there was a significant increase in the prevalence of CAs along with most subtypes from 2013 to 2022. This noted increase in the reported prevalence is potentially attributable to factors such as a rise in maternal age, alongside the enhanced detection efficacy resulting from the utilization of noninvasive prenatal testing.

What are the implications for public health practice?

The escalating prevalence of sex CAs and other previously rare CAs pose novel challenges for genetic counseling and healthcare practitioners. These professionals are tasked with the accurate evaluation and interpretation of detection data, which must then be conveyed appropriately to patients. Furthermore, it is imperative to intensify health education efforts to assist women in making informed treatment decisions, considering the diverse prognoses associated with different CAs.

Chromosomal abnormalities (CAs), which encompass both numerical and structural variants, present as common birth defects. These defects are a predominant factor behind early miscarriage and stillbirth (*1*). Moreover, they can lead to congenital anomalies such as mental retardation, developmental delays, and multiple malformations in newborns (*2*). Although recent studies in certain regions have indicated an uptick in the prevalence of CAs, there is an ongoing need for more research into some underlying subtypes (*3*–*4*). In this study, we assessed the trends and prevalence of CAs in Beijing's Haidian District from 2013 to 2022. Our findings revealed a substantial increase in the prevalence of CAs in the Haidian District, with the rate rising from 29.46/10,000 in 2013 to 82.74/10,000 in 2022. Additionally, the prevalence of some subtypes, such as autosomal trisomies, sex CAs (SCAs), and microdeletion/microduplication, evidenced a significant rising trend. The escalating prevalence of SCAs and other previously rare CAs necessitates new strategies for genetic counseling and poses fresh challenges for health professionals. It's critical that healthcare practitioners accurately evaluate these detection results and interpret them appropriately to patients. Strengthening health education initiatives will support women in making informed treatment decisions based on the diverse prognoses of CAs.

This study analyzed data from a hospital-based birth defect surveillance system in the Haidian District, details of which were discussed in a previous publication (*5*). Briefly, all pertinent healthcare institutions (inclusive of 18 community health service centers, midwifery agencies, and children's hospitals) within the Haidian District are mandated to complete unified forms, registration cards, and report the total count of perinatal infants, alongside detailed individual information on cases of birth defects and infant mortality. Pregnant women were advised to undergo non-invasive prenatal screenings to detect CAs. Owing to technological progression, detection methods have evolved from maternal prenatal serum screening to non-invasive prenatal testing (NIPT). According to the guidelines set out by the Beijing Municipal Health Commission, a prenatal diagnostic rate exceeding 90% is required, with further diagnoses for newborns presenting post-birth abnormalities. The categorization of CAs was conducted in line with the International

Statistical Classification of Diseases and Related Health Problems, 10th Edition. Depending on the clinical examination, different CAs were classified under three primary groups: autosomal trisomies, SCAs, and other CAs (*6*). CAs of a structural nature (microdeletions, microduplications, translocations, inversions) were further delineated. The annual CAs incidence was calculated by dividing the total count of reported CAs cases by the total number of perinatal infants within that year. A Joinpoint regression model was developed using Joinpoint software (version 4.9.1, Information Management Services, Inc.Calverton, MD, USA) to estimate the average annual percentage change (AAPC) in the prevalence of CAs. Two periods were distinguished according to the Joinpoint regression analysis, and the chi-square test and Fisher's exact test were carried out using R software (version 4.0.5, R Development Core Team, Vienna, Austria) to compare the characteristics distributions in births with CAs between different periods. *P* values equal to or less than 0.05 (two-tailed) were deemed statistically significant.

Between 2013 and 2022, a total of 364,758 births were recorded, along with 1,676 cases of CAs resulting in a prevalence of 45.95 per 10,000 births. The types of CAs and their prevalence over this time period are displayed in Table 1. Over this period, the prevalence of CAs manifested an increasing trend, escalating from 29.46 per 10,000 in 2013 to 82.74 per 10,000 in 2022, which equates to an AAPC of 13.4% [95% confidence interval (*CI*): 8.3%, 18.8%].

The prevalence of autosomal trisomies climbed from 19.18 per 10,000 in 2013 to 29.67 per 10,000 in 2022 (AAPC=7.5%, 95% *CI*: 5.7%, 9.4%). Specifically, trisomy 21 and trisomy 18 syndromes displayed a significant upward trend in prevalence (Trisomy 21: AAPC=6.9%, 95% *CI*: 4.6%, 9.2%; Trisomy 18: AAPC=8.2%, 95% *CI*: 4.7%, 11.9%), whereas trisomy 13 syndrome did not (AAPC=1.0%, 95% *CI*: −17.2%, 23.2%).

SCAs prevalence increased from 4.91 per 10,000 in 2013 to 20.89 per 10,000 in 2022 (AAPC=21.3%, 95% *CI*: 15.9%, 27.0%). Individual SCAs subtypes (chimerism, 47XXY, 47XYY, 47XXX, 45X) all demonstrated significant increasing trends over the same period, all with AAPC values greater than 0% and *P*-values less than 0.05.

The prevalence of other CAs also increased over the past 10 years (AAPC=22.6%, 95% *CI*: 16.5%, 30.1%) with significant upward trends observed in microdeletion/microduplication, translocation, and inversion (each with AAPC values greater than 0% and *P*-values less than 0.05).

TABLE 1. Prevalence and trends of chromosomal abnormalities in Haidian District, Beijing, China, from 2013 to 2022 (*N* expressed as 1/10,000).

Chromosomal Abnormalities	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	Trend test	
											AAPC (95% *CI*)	*P*
Autosomal trisomies	19.18	16.96	20.22	19.71	25.08	23.94	30.34	31.19	29.44	29.67	7.5 (5.7, 9.4)	<0.001
Trisomy 21 syndrome	15.20	13.24	14.62	14.67	18.01	15.77	22.61	23.49	20.57	23.40	6.9 (4.6, 9.2)	<0.001
Trisomy 18 syndrome	3.51	3.31	4.63	4.35	5.93	7.04	4.87	6.16	7.66	5.85	8.2 (4.7, 11.9)	0.001
Trisomy 13 syndrome	0.47	0.41	0.97	0.69	1.14	1.13	2.86	1.54	1.21	0.42	1.0 (−17.2, 23.2)	0.924
Sex chromosome aneuploidies	4.91	5.59	5.36	6.19	10.26	15.49	10.30	15.02	27.03	20.89	21.3 (15.9, 27.0)	<0.001
Sex chromosome chimerism	0.70	1.86	0.97	1.83	2.51	2.25	1.43	1.93	4.44	2.93	13.4 (5.5, 22.0)	0.004
47XXY	1.64	1.66	1.22	1.37	3.19	3.94	4.29	5.78	10.49	6.27	26.4 (18.0, 35.4)	<0.001
47XYY	0.47	0.41	0.49	0.92	0.91	1.97	0.86	1.54	3.63	2.51	25.8 (18.3, 33.7)	<0.001
47XXX	0.47	0.62	0.49	0.46	1.14	3.38	2.58	1.54	2.82	1.67	22.6 (7.2, 40.1)	0.008
45X	1.64	1.03	1.71	1.15	1.37	2.82	1.14	2.31	1.61	2.93	6.6 (2.8, 10.5)	0.004
Other chromosomal abnormalities	5.38	6.20	5.85	7.34	11.18	11.82	18.03	22.74	25.40	35.10	22.6 (15.6, 30.1)	<0.001
Microdeletion/microduplication	1.64	1.45	3.9	3.21	5.02	3.94	9.73	13.1	16.94	19.22	34.9 (29.3, 40.6)	<0.001
Translocation	1.87	2.48	0.49	1.15	3.19	3.38	3.72	4.62	4.03	7.52	20.8 (5.7, 38.0)	0.012
Inversion	0.70	1.03	0.73	0.46	2.05	1.97	2.29	1.93	2.42	5.85	23.2 (11.6, 36.0)	0.001
Others	1.17	1.24	0.73	2.52	0.92	2.53	2.29	3.09	2.01	2.51	12.5 (7.0, 18.3)	0.001
Total	29.46	28.76	30.95	32.77	44.91	49.85	58.39	66.63	77.45	82.74	13.4 (8.3, 18.8)	<0.001

Abbreviation: AAPC=average annual percent change; *CI*=confidence interval.

TABLE 2. Trends in the annual prevalence of chromosomal abnormalities in Haidian District, Beijing, China, from 2013 to 2022 using Joinpoint regression analysis.

Segments*	Year	APC (95% *CI*)	*P*
Trend 1	2013–2015	3.4 (−20.2, 33.9)	0.754
Trend 2	2015–2022	16.4 (13.5,19.5)	<0.001
Full range	2013–2022	13.4 (8.3,18.8)	<0.001

Abbreviation: APC=annual percentage change; *CI*=confidence interval.
* The implementation of universal two-child policy was in 2016 and the application of noninvasive prenatal testing was 2017.

Table 2 illustrates an inflection point in CAs prevalence identified by Joinpoint regression modeling in 2015. The initial trend indicates an escalation in annual prevalence from 29.46/10,000 in 2013 to 30.95/10,000 in 2015 (APC=3.4%, 95% *CI*: −20.2%, 33.9%). The subsequent trend demonstrates a significant upsurge from 30.95/10,000 in 2015, escalating to 77.45/10,000 in 2022 (APC=16.4%, 95% *CI*: 13.5%, 19.5%).

Table 3 delineates the variation in characteristics of CAs across distinct periods. Among all CAs instances, significant increases from 2013–2015 to 2016–2022 were observed for maternal age (P<0.001), gravidity (P=0.002), parity (P<0.001), and prenatal diagnostics (P<0.001). For trisomy 21 syndrome cases specifically, disparate distributions in maternal age, parity, gestational weeks, prognosis, therapeutic abortion, and timing of diagnosis were evident across varying periods (all P<0.05). In SCAs scenarios, a marked increase in prenatal diagnostics was shown, from 87.7% in 2013–2015 to 98.9% in 2016–2022 (P<0.001). Furthermore, in cases involving microdeletion and microduplication, there was an observed augmentation in gravidity (P=0.020) and the rate of therapeutic abortion (P=0.026) during the period from 2013–2015 to 2016–2022.

DISCUSSION

Data derived from a hospital-based birth-defect surveillance system in Haidian District, Beijing indicates a steady rise in the prevalence of CAs over the past decade. The data further reveals a significant increase in the prevalence of most CAs subtypes from 2013 to 2022. Interestingly, the year 2015 marked a major turning point in this trend wherein the prevalence growth rate significantly escalated post-2015.

Globally, CAs occur in approximately 4 to 9 out of every thousand newborns (*6*). In the Haidian District of Beijing, the prevalence of CAs is relatively low, with 4.595 per thousand. It is important to mention, however, that this prevalence has seen a steady increase, reaching 8.274 per thousand in 2022. Due to regional differences in detection rates and capabilities, it would be inaccurate to directly compare the prevalence of CAs between different regions. Nonetheless, a similar increasing trend in prevalence, as seen in this study, has been reported in several prior studies. For instance, the prevalence of trisomy 21, trisomy 18, and trisomy 13 syndromes in Europe showed an escalation between 2005 and 2021 (*3*). In Zhejiang Province, the overall prevalence of CAs rose from 1.209 per thousand to 3.922 per thousand between 2014 and 2020, with varying degrees of increase in the prevalence of trisomy 21 syndrome, SCAs, and microdeletions/microduplications (*4*). Similarly, in Guangdong Province, the prevalence of trisomy 21 syndrome surged from 0.465 per thousand to 1.364 per thousand between 2011 and 2018 (*7*).

In our investigation, it was observed that the maternal age for children suffering from CAs during the period 2016–2022 was statistically higher compared to 2013–2015. This change coincided with China's transition from a one-child to a universal two-child policy in 2016. As a result, there was a noticeable increase in the percentage of pregnancies associated with older mothers, multiple pregnancies, and multiparous women from 2016 to 2022 in contrast to the numbers recorded between 2013 and 2015. Earlier research determined that advanced maternal age significantly raises the risk for CAs (*8*). Consequently, it can be posited that the shift in birth policy may have indirectly increased maternal age, gravidity, and parity, thereby causing a surge in the prevalence of CAs post-2016 (*9*).

Conversely, the observed surge in reported cases of CAs might represent advancements in prenatal diagnostic methods in Haidian District and increased awareness among expectant mothers. The National Health Commission of the People's Republic of China initiated a nationwide pilot program for this technology in 2016 and the NIPT technology was applied in 2017 in Beijing (*10*). Evidently, NIPT

TABLE 3. Variations in characteristics of chromosomal abnormality cases over select time periods in Haidian District, Beijing, China, *n* (%).

Variable	Total CAs		*P**	Trisomy 21 syndrome		*P**	SCAs		*P**	Microdeletions/microduplications		*P**
	2013–2015	2016–2022		2013–2015	2016–2022		2013–2015	2016–2022		2013–2015	2016–2022	
Total	392	1,284		189	444		70	280		30	208	
Age, years			<0.001			0.006			0.077			0.054
≤30	113 (31.0)	265 (20.7)		45 (26.0)	67 (15.2)		26 (37.1)	69 (24.6)		15 (50.0)	60 (28.8)	
30–35	124 (34.0)	456 (35.7)		54 (31.2)	148 (33.5)		27 (38.6)	114 (40.7)		10 (33.3)	84 (40.4)	
>35	128 (35.1)	557 (43.6)		74 (42.8)	227 (51.4)		17 (24.3)	97 (34.6)		5 (16.7)	64 (30.8)	
Gravidity			0.002			0.065			0.211			0.020
1	154 (39.3)	399 (31.1)		73 (38.6)	138 (31.1)		33 (47.1)	109 (38.9)		16 (53.3)	66 (31.7)	
≥2	238 (60.7)	885 (68.9)		116 (61.4)	306 (68.9)		37 (52.9)	171 (61.1)		14 (46.7)	142 (68.3)	
Parity			<0.001			<0.001			0.100			0.745
Nulliparous	193 (49.2)	433 (34.5)		103 (54.5)	173 (39.0)		33 (47.1)	102 (36.4)		11 (36.7)	70 (33.7)	
Multiparous	199 (50.8)	851 (66.3)		86 (45.5)	271 (61.0)		37 (52.9)	178 (63.6)		19 (63.3)	138 (66.3)	
Gestational week			0.675			<0.001			0.888			0.134
<28	284 (72.4)	944 (73.5)		155 (82.0)	425 (95.7)		47 (67.1)	184 (65.7)		14 (46.7)	127 (61.1)	
≥28	108 (27.6)	340 (26.5)		34 (18.0)	19 (4.3)		23 (32.9)	96 (34.3)		16 (53.3)	81 (38.9)	
Number of embryos			0.291			0.997			0.778			0.656
Single birth	342 (94.0)	1,222 (95.3)		165 (95.9)	425 (95.9)		62 (95.4)	260 (93.2)		28 (96.6)	200 (96.6)	
Multiple births	22 (6.0)	60 (4.7)		7 (4.1)	18 (4.1)		3 (4.6)	19 (6.8)		1 (3.4)	7 (3.4)	
Prognosis			0.510†			<0.001†			1.000†			1.000†
Live birth	88 (24.2)	273 (21.4)		26 (15.1)	10 (2.3)		20 (30.8)	88 (31.5)		12 (41.4)	47 (22.7)	
Early fetus loss and stillbirths	274 (75.3)	998 (78.1)		146 (84.3)	432 (97.5)		45 (69.2)	190 (68.1)		16 (55.2)	155 (74.9)	
Early neonatal deaths	2 (0.5)	7 (0.5)		1 (0.6)	1 (0.2)		0 (0.0)	1 (0.4)		1 (3.4)	5 (2.4)	
Therapeutic abortion			0.270			<0.001			0.774			0.026
No	93 (25.5)	292 (22.8)		27 (15.7)	14 (3.2)		20 (30.8)	91 (32.6)		13 (44.8)	52 (25.1)	
Yes	271 (74.5)	990 (77.2)		145 (84.3)	429 (96.8)		45 (69.2)	188 (67.4)		16 (55.2)	155 (74.9)	
Time of diagnosis			<0.001			<0.001			<0.001			0.741
Prenatal	324 (89.0)	1,249 (97.4)		146 (84.9)	438 (98.9)		57 (87.7)	276 (98.9)		28 (96.6)	197 (95.2)	
Postpartum	40 (11.0)	33 (2.6)		26 (15.1)	5 (1.1)		8 (12.3)	3 (1.1)		1 (3.4)	10 (4.8)	

Abbreviation: CAs=chromosomal abnormalities; SCAs=sex chromosomal abnormalities.

* Differences between the 2013–2015 period and 2016–2022 period, using Chi-square test.

† Differences between the 2013–2015 period and 2016–2022 period, as determined by Fisher's exact test.

technology exhibits high performance in early detection of CAs, managing to identify certain variants of CAs that proved challenging via traditional methods. Owing to its elevated sensitivity, the prevalence of missed diagnosis prior to pregnancy is minimized, which may partially account for the rising prevalence of CAs noted in this study.

The NIPT not only enhances the efficacy of detection for autosomal trisomies, but also proves useful in identifying certain types of SCAs, such as 47 XYY and 47 XXY, and other CAs (*4*). Ethical considerations necessitate that any decision to proceed with therapeutic abortion for CAs must fully respect the patient's wishes. Therefore, healthcare practitioners need to deliver individualized and detailed genetic counseling based on the detection information. For severe cases like trisomy 21 syndrome, healthcare practitioners may provide conclusive advice allowing the patient to consider therapeutic abortion before the 28 weeks gestation mark. However, certain CAs such as some SCAs subtypes and structural CAs are neither fatal nor severely debilitating. Here, practitioners' advice should take into account a variety of factors such as prognosis, the patient's physical condition, and financial capabilities. The final decision rests with the patient whether to proceed with abortion or explore different interventions. Limited counselling or insufficient explanation can lead to unnecessary abortions resulting in unwarranted intervention. The exemplary detection capacity of NIPT has led to an uptick in the proportion of hitherto rare SCAs and other CAs, posing fresh challenges for genetic counselling and healthcare practitioners.

Our findings indicate that the SCA abortion rate did not considerably rise post-2016, an encouraging sign. However, it is crucial to note that the abortion rate for microdeletion/microduplication was higher between 2016–2022 compared to 2013–2015. Looking ahead, the focus must be on increasing awareness and education among expectant women for a proper understanding. Healthcare practitioners must also strive for accurate interpretation and evaluation of test information, to aid patients in making appropriate treatment decisions in light of the varying prognoses associated with CAs.

The present study possesses several notable strengths. Primarily, Haidian District boasts a 100% rate of hospital-based delivery, making the district's hospital surveillance data an accurate representation of the population. Secondary strength lies in the district's high level of medical care, coupled with the established diagnostic proficiency of affiliated midwifery organizations. The deployed surveillance system, with its extensive review and rejection mechanisms for diagnostic results, bolsters data reliability at both the district and municipal levels. Moreover, the classification of CAs within the surveillance system — trisomy 21, trisomy 18, trisomy 13 syndrome, SCAs, and other CAs — was subdivided into more precise subtypes. This allows for a more nuanced analysis of CAs prevalence and also aids in enhancing future classification systems.

This study encompasses several limitations. Primarily, as a regional observational research, the findings are specifically indicative of the urban region in Beijing and may not be comprehensively representative of either the complete Beijing populace, or China overall. Additionally, the study did not incorporate an exhaustive categorization of structural CAs. Lastly, certain data categories such as specific exposure factors were omitted from collection in this research, limiting the study's scope to merely detailing the distribution of CAs rather than identifying potential risk factors.

The prevalence of CAs in Haidian, Beijing, has markedly risen from 2013 to 2022. This increase may be ostensibly linked to a rise in advanced maternal age and the utilization of NIPT. Heightened detection rates of CAs can expedite treatment for pregnant women diagnosed with poor prognosis conditions such as trisomy 21 syndrome, thus alleviating their burden. Conversely, attention must also be accorded to other CAs, such as SCAs, and women should be educated to form an accurate comprehension of these conditions. Achieving this requires healthcare practitioners to possess a comprehensive understanding of the advantages and disadvantages of prenatal diagnostic methods, patient preferences, and ethical evaluations.

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Preplanned Studies

Prevalence and Trends of Birth Defects — Five Counties, Shanxi Province, China, 2003–2022

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Summary

What is already known about this topic?

The Shanxi Province, located in northern China, holds the highest prevalence of birth defects (BDs) across the country. Following the implementation of a nationwide folic acid supplementation program in 2009, a significant reduction of 53.89% in the prevalence of neural tube defects (NTDs) was observed in Shanxi from 2012 to 2017. However, despite this decrease, the prevalence rate for congenital heart defects (CHDs) in 2017 was over four times that of the 2012 rate. Since 2014, CHDs have emerged as the most predominant BD in Shanxi.

What is added by this report?

The present study has identified a marked reduction in the prevalence of both total BDs and NTDs in five counties within Shanxi over the past two decades. As of 2017–2022, NTDs continue to be the most prevalent BDs recorded in this region. Contrarily, there has been a noteworthy increase in the prevalence of CHDs, ranking them among the top five most common BDs in the region between 2017 and 2022, though their rate remains below the national average. Additionally, the proportion of external anomalies remains high. Nevertheless, due to constrained access to primary healthcare services and diagnostic facilities, the early detection rate for internal anomalies, particularly CHDs, may be underestimated in the region.

What are the implications for public health practice?

The results of this study underscore the necessity for augmented efforts in promoting folic acid supplementation as a preventive measure for NTDs. Moreover, improvements in the distribution of medical resources within this region is recommended, particularly the introduction and enforcement of local training programs aimed at enhancing CHD screening and diagnostic processes in these respective counties.

Birth defects (BDs) present a substantial clinical and public health concern, notably contributing to infant mortality rates (*1*). Shanxi Province, in northern China, exemplifies this challenge, displaying the highest prevalence rate for BDs in the country and the highest incidence of neural tube defects (NTDs) worldwide (*2*). Nevertheless, the initiation of a folic acid supplementation program yielded a 52.49% reduction in NTDs within a span of five years across five counties in Shanxi (*3*). In contrast, the prevalence of congenital heart defects (CHDs) elevated from 13.23 per 10,000 in 2012 to 58.27 per 10,000 in 2017, and has remained the most common BD in Shanxi since 2014 (*4*).

Our study scrutinized the prevalence trends of total BDs, NTDs, and CHDs from 2003 to 2022 in five counties of Shanxi Province, leveraging data from a population-based BD surveillance system. We documented a marked decrease in total BDs and NTDs over the past two decades. Yet, NTDs, with a prevalence of 20.09 per 10,000, continued to be the most prevalent BDs in the region from 2017 to 2022. Moreover, while remaining below the national average, the incidence of CHDs notably increased from 1.24 per 10,000 in 2003 to 13.43 per 10,000 in 2022 and ranked among the top five most common BDs from 2017 to 2022.

Notwithstanding, the study observed a high proportion of external anomalies. Consequently, owing to restricted access to primary healthcare services and diagnostic facilities, the region's early diagnosis rates for internal anomalies, especially CHDs, may be underestimated. As such, it is crucial to enhance the screening and diagnostic procedures for CHDs in these counties.

The data for this study originates from a population-based BD surveillance system in five counties — Pingding, Xiyang, Taigu, Zezhou, and Shouyang — in Shanxi Province. BD diagnosis was conducted by local maternal-fetal medicine specialists and later confirmed by pediatricians at Peking University. Practice quality was assessed in 2004 by a survey, which confirmed that

95.6% of births were included in this dataset, with no underreporting of NTD (*5*). We have detailed the system in a prior publication (*3*).

This surveillance encompasses all pregnant women who have lived in the study area for over a year. It recorded all live births or stillbirths that occurred at 28 or more complete gestational weeks, along with terminations of pregnancies at any gestational age following the prenatal diagnosis of BDs. Data collected covered BD diagnostic criteria (coded in accordance with the 10th Edition of the International Statistical Classification of Diseases and Related Health Problems), sex, gestational weeks, birth outcomes, and maternal residential data. We previously described the classification of BD types in this surveillance (*6*). The study protocol was examined and approved by the Institutional Review Board of Peking University.

The study's prevalence denominator encompassed all live and still births of 28 or more complete gestational weeks, whereas the numerator included all live births, stillbirths, and pregnancy terminations that presented BDs. BDs categorized as perinatal were defined as incidences at 28 or more complete gestational weeks, while pre-perinatal BDs referred to cases identified prior to the 28-week gestational threshold and, subsequently, induced labor. The Joinpoint Regression Program (Version 5.0.2., 2023; Information Management Services, Inc., Calverton, MD, USA) was utilized to create a Joinpoint regression model, thereby estimating the average annual percentage change (AAPC) in the prevalence of total BDs, NTDs, and CHDs. The comparison of gestational week group, diagnosis, outcome, sex, and residence of CHDs and NTDs was accomplished using Chi-square tests and Fisher's exact tests in the SPSS software (version 26.0; IBM Corp., Armonk, NY, USA). Additionally, perinatal and pre-perinatal proportions, denoting cases of 28 or more and fewer than 28 gestational weeks, respectively, were calculated. Three distinct intervals were defined following population policy and public strategy. In the conducted analysis, a *P*-value less than 0.05 indicated statistical significance.

Between 2003 and 2022, the system logged a cumulative total of 288,987 births with 4,436 instances of BDs. This led to a prevalence rate of 153.50 per 10,000. A significant decline of 40.35% in the total prevalence of BDs was observed over the past two decades, with rates reduced from 195.81 per 10,000 in 2003 to 116.81 per 10,000 in 2022 [AAPC=−2.84%, 95% confidence interval (*CI*): −3.90%, −1.77%, *P*<0.001]. Further analysis of the joinpoint regression model in Table 1 pointed out a marked declining trend from 2003 to 2014 [annual percentage change (APC)=−4.39%, 95% *CI*: −5.66%, −3.11%, *P*<0.001]. However, a subsequent decrease in prevalence was observed from 2014 to 2022, though without statistical significance (APC=−0.66%, 95% *CI*: −2.78%, 1.51%, *P*=0.523). Moreover, external anomalies still constituted a significant proportion, with the five most prevalent BDs between 2017 and 2022, as displayed in Table 2, being: NTDs (20.09 per 10,000), polydactyly (22.25 per 10,000), cleft lip with or without cleft palate (11.12 per 10,000), external ear malformation (9.13 per 10,000), and CHDs (8.63 per 10,000).

Table 1 illustrates a substantial decline in the prevalence of NTDs, from 116.75 per 10,000 in 2003 to 18.80 per 10,000 in 2022. This decline proved to be statistically significant, with an AAPC of −9.58% (95% *CI*: −12.92%, −6.12%, *P*<0.001). Furthermore, the proportion of pre-perinatal NTDs exhibited a significant increase over the final three time periods, as depicted in Figure 1. Over the past two decades, all three subtypes of NTDs — primarily anencephaly and spina bifida — demonstrated a downward trend. NTD prevalence by subtype from 2000 to 2019 is detailed in

TABLE 1. Trends in the prevalence of total BDs, NTDs, and CHDs in five counties in Shanxi Province from 2003 to 2022, as determined by Joinpoint analysis.

Types of BDs	Period	APC (95% *CI*)	*P*
Total BDs			
Trend 1	2003–2014	−4.39 (−5.66, −3.11)	<0.001
Trend 2	2014–2022	−0.66 (−2.78, 1.51)	0.523
AAPC	2003–2022	−2.84 (−3.90, −1.77)	<0.001
NTDs			
Trend 1	2003–2011	−8.37 (−12.18, −4.39)	0.001
Trend 2	2011–2019	−14.41 (−18.75, −9.84)	<0.001
Trend 3	2019–2022	1.01 (−16.86, 22.72)	0.913
AAPC	2003–2022	−9.58 (−12.92, −6.12)	<0.001
CHDs			
Trend 1	2003–2012	5.35 (−4.82, 16.59)	0.291
Trend 2	2012–2022	20.63 (10.63, 31.53)	<0.001
AAPC	2003–2022	13.13 (6.45, 20.23)	<0.001

Note: Data from only four counties — Zezhou, Pingding, Taigu, and Shouyang — are presented for the year 2003. However, data from five counties are available for all other years.
Abbreviation: BDs=birth defects; NTD=neural tube defects; CHD=congenital heart defects; APC=annual percentage change; AAPC=average annual percentage change; *CI*=confidence interval.

TABLE 2. Prevalence of the top ten BDs in five counties of Shanxi Province from 2003 to 2022 (reported as prevalence per 10,000 births).

Ranking	2003–2009	2010–2016	2017–2022	Total
Number of births	129,824	98,923	60,240	288,987
First	NTDs (98.60)	NTDs (47.92)	NTDs (20.09)	NTDs (64.88)
Second	CL/P (19.95)	CL/P (20.32)	Polydactyly (20.25)	CL/P (18.24)
Third	Polydactyly (13.40)	Polydactyly (15.37)	CL/P (11.12)	Polydactyly (15.50)
Fourth	Congenital hydrocephalus (8.94)	Congenital hydrocephalus (6.57)	External ear malformation (9.13)	Congenital hydrocephalus (6.96)
Fifth	External ear malformation (4.54)	External ear malformation (5.36)	CHDs (8.63)	External ear malformation (5.78)
Sixth	Limb reduction defects (4.31)	Limb reduction defects (4.45)	Syndactyly (6.47)	Limb reduction defects (4.15)
Seventh	Congenital talipes equinovarus (3.39)	CHDs (3.64)	Down syndrome (4.32)	CHDs (3.91)
Eighth	Hypospadias (3.31)	Hypospadias (2.43)	Congenital hydrocephalus (3.32)	Syndactyly (3.15)
Nineth	Anorectal atresia or stenosis (without anus) (2.70)	Syndactyly (2.43)	Limb reduction defects (3.32)	Congenital talipes equinovarus (2.84)
Tenth	Syndactyly (2.16)	Congenital talipes equinovarus (2.12)	Congenital talipes equinovarus (2.82)	Hypospadias (2.77)

Note: Three distinct periods were demarcated based on changes in population policies and public strategies: 2003–2009, prior to the initiation of folic acid supplementation; 2010–2016, following folic acid supplementation but preceding the implementation of the universal two-child policy; and 2017–2022, following the implementation of the universal two-child policy.
Abbreviation: BDs=birth defects; NTDs=neural tube defects; CL/P=cleft lip with or without cleft palate; CHDs=congenital heart defects.

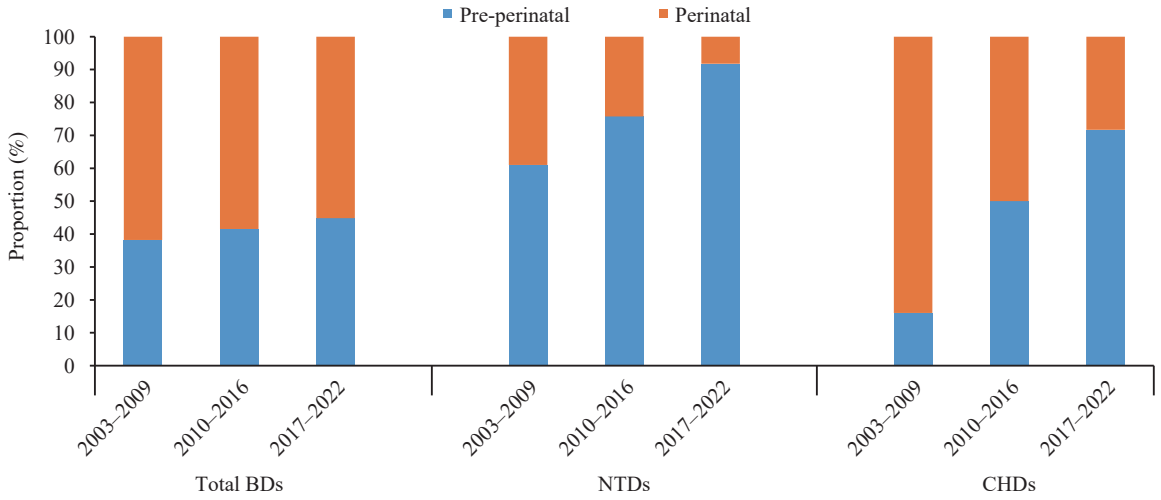

FIGURE 1. Proportion of BDs by gestational weeks and periods across five counties in Shanxi Province, 2003–2022.
Note: Three distinct periods were demarcated based on changes in population policies and public strategies: 2003–2009, prior to the initiation of folic acid supplementation; 2010–2016, following folic acid supplementation but preceding the implementation of the universal two-child policy; and 2017–2022, following the implementation of the universal two-child policy.
Abbreviation: BDs=birth defects; NTDs=neural tube defects; CHDs=congenital heart defects.
* Data pertaining to the gestational week for total BDs was unavailable for four cases, accounting for 0.09% of the data.

a prior publication (*6*).

Figure 2 presents a decline in the prevalence of the four types of outcomes among NTDs, along with a decreasing proportion of deaths within seven days. A joinpoint regression analysis identified three distinct trends in NTD prevalence. Initially, a notable statistical annual reduction from 116.75 per 10,000 in 2003 to 69.59 per 10,000 in 2011 was observed (APC=−8.37%, 95% *CI*: −12.18%, −4.39%, *P*=0.001). Subsequently, a sharp decrease from 69.59 per 10,000 in 2011 to 16.39 per 10,000 in 2019 was recorded (APC=−14.41%, 95% *CI*: −18.75%, −9.84%, *P*<0.001). This was then followed by a marginal fluctuation from 2019 to 2022 (APC=1.01%, 95% *CI*: −16.86%, 22.72%, *P*=0.913).

On the contrary, there was a significant ascending

trend in the prevalence of CHDs (AAPC=13.13%, 95% *CI*: 6.45%, 20.23%, *P*<0.001). The Joinpoint regression analysis, as outlined in Table 1, showed two distinct trends in the prevalence of CHDs. From 2003 to 2012, a relatively low level was observed with no significant trends (APC=5.35%, 95% *CI*: −4.82%, 16.59%, *P*=0.291), which was then followed by a steep and significant incline, from 0.64 per 10,000 in 2012 to 10.97 per 10,000 in 2022 (APC=20.63%, 95% *CI*: 10.63%, 31.53%, *P*<0.001). Figure 1 illustrates a considerable rise in the proportion of pre-perinatal CHDs during the last three periods.

Table 3 reveals that CHDs have a higher incidence of perinatal cases at or beyond 28 gestational weeks (47.37% *vs.* 33.28%, *P*=0.001) and mortality within seven days (39.22% *vs.* 18.93%, *P*<0.001), compared

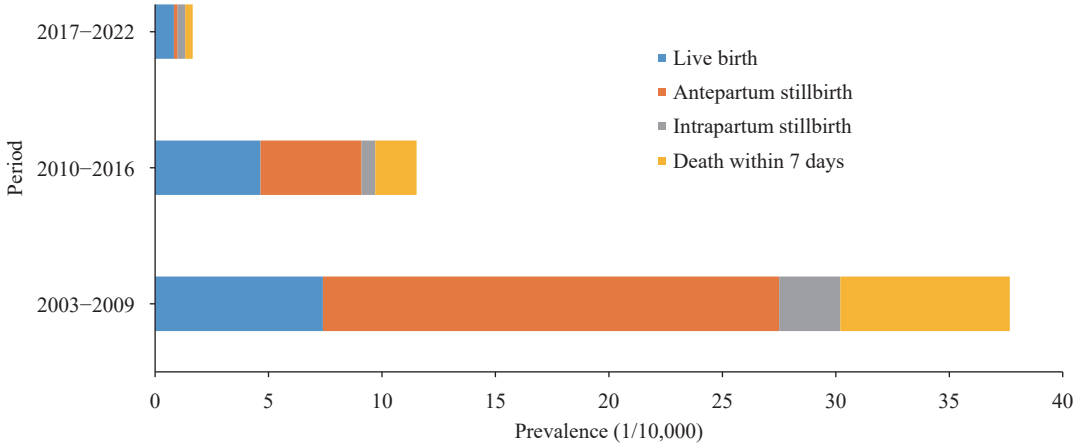

FIGURE 2. Prevalence of perinatal neural tube defects by outcomes and periods across five counties in Shanxi, 2003–2022.
Note: Three distinct periods were demarcated based on changes in population policies and public strategies: 2003–2009, prior to the initiation of folic acid supplementation; 2010–2016, following folic acid supplementation but preceding the implementation of the universal two-child policy; and 2017–2022, following the implementation of the universal two-child policy.

TABLE 3. Comparison of characteristics between NTDs and CHDs in five counties of Shanxi Province, 2003–2022 (*n*, %).

Variables	NTDs	CHDs	*P*-value
No. of cases	1,875 (42.27)	114 (2.57)	
Gestational weeks			0.002
<28 weeks	1,251 (66.72)	60 (52.63)	
≥28 weeks	624 (33.28)	54 (47.37)	
Diagnosed by ultrasound*	1,223 (99.27)	49 (98.04)	0.333
Outcome†			<0.001
Live birth	148 (23.95)	20 (39.22)	
Antepartum stillbirth	310 (50.16)	8 (15.69)	
Intrapartum stillbirth	43 (6.96)	3 (5.88)	
Death within 7 days	117 (18.93)	20 (39.22)	
Male§	847 (45.20)	61 (54.46)	0.054
Residence¶			<0.001
Urban	240 (12.80)	31 (27.43)	
Rural	1,635 (87.20)	82 (72.57)	

Abbreviation: NTDs=neural tube defects, CHDs=congenital heart defects.
* Diagnostic data were only procured for cases with a pre-perinatal age of less than 28 weeks; however, this information was unavailable for 22 cases, which represents 1.68% of the total cases studied.
† Outcome data were not available for nine cases, accounting for 1.33% of total instances.
§ For 3 cases (0.15%), sex data were unavailable, while 45 cases (2.40%) remained unidentified in terms of sex for NTDs.
¶ Data on residence were not available for 1 case (0.05%).

to NTDs. Both NTDs and CHDs were predominantly diagnosed using ultrasound (99.27% *vs*. 98.04%, P=0.333) and were predominantly found in women from rural areas (87.20% *vs*. 72.57%, P<0.001).

DISCUSSION

Our research uncovered a significant decline in the prevalence of BDs in select regions of Shanxi Province over the past two decades. This trend suggests that the area's comprehensive strategies for managing and preventing BDs were successful. The observed average prevalence rate of BDs from 2003 to 2022 was 153.50 per 10,000, mirroring the national average of 154.98 per 10,000 reported from 2010–2016 (*7*). The prevalence decreased substantially from 2003 to 2014 and then became stable from 2014 to 2022, which could be attributed to recent changes in China's birth policy. The Chinese government introduced a partial two-child policy in November 2013 and a universal two-child policy in January 2016. Following these changes, the incidence of high-risk pregnancies rose from 19.4% in 2013 to 24.7% in 2016, an increase from the 15.7% reported in 2008 (*8*). Additionally, the high rate of external anomalies signals that further improvements are needed in Shanxi's prenatal diagnostic capabilities.

Shanxi Province in northern China has the highest global prevalence of NTDs (*2*). NTD prevalence documented within this BD surveillance system saw a significant decline from 2011–2019 due to a comprehensive folic acid supplementation program implemented in 2009. Despite this, fluctuations were observed between 2019 and 2022, potentially resulting from a decrease in regional births mirroring the national trend (*9*), or signaling a plateau following the implementation of NTD reduction measures. Notably, NTD prevalence in this region exceeded the national average (1.45/10,000 in 2020) (*10*), with 20.09 per 10,000 in 2017–2022. This disparity might stem from inadequate adherence to folic acid intake during the periconceptional period. Although the number of women supplementing increased, rural women in the high-prevalence Shanxi population showed continued disparities compared to the low-prevalence Jiangsu population, possibly due to impeded preventive action prompted by late supplementation initiation (*11*). Consequently, an emphasis on health education is necessary to promote adherence to folic acid recommendations. Other factors, such as folic acid resistance, need to be investigated in future studies as potential contributors to NTD incidence.

CHD prevalence in our study area has seen a substantial increase over the past two decades, positioning it among the top five BDs in 2017–2022. Indeed, there has been a significant increase in pre-perinatal CHDs detected before 28 gestational weeks, despite the majority occurring at or after 28 gestational weeks. The rise in CHD prevalence may be attributed to improved detection methods, revisions in diagnostic standards, and the augmentation of neonatal CHD screening in China since 2018 (*12*). However, regional CHD prevalence falls short of national prevalence and that of other Chinese regions. Nationally, CHD incidence significantly escalated from 11.40 per 10,000 in 2000 to 173.20 per 10,000 in 2020 — significantly higher than the global average (94/10,000) — indicating CHDs as the most common BD since 2010 in China (*10*,*13*). Economic and medial resource disparities among regions may have resulted in this difference.

The substantial prevalence of external anomalies highlights the need for improving prenatal diagnostic capabilities. CHD prevalence may be influenced by prenatal diagnostic quality and neonatal physical examination techniques, which are affected by local perinatal healthcare availability and diagnostic tech proficiency (*7*). Coastal provincial-level administrative divisions (PLADs) have established CHD screening networks, but in economically deprived regions, many children with CHDs are undiagnosed or untreated. In Shaanxi Province, CHDs have the highest prevalence (77.32/10,000) among BDs, an economically worse-off and less medically developed region (*14*). On the other hand, the economically prosperous and medically advanced Zhejiang Province saw an increase in overall CHD incidence from 127 per 10,000 in 2014 to 206 per 10,000 in 2018 (*12*). The local primary healthcare's insufficient capacity may be the reason early CHD diagnoses are underestimated in Shanxi Province. It is crucial that diagnostic capabilities for internal anomalies, especially CHDs, be improved for perinatal infants in this region.

Our study boasts several key strengths. Primarily, the population-based BD surveillance system employed herein encompasses both perinatal and pre-perinatal BDs, offering a broader scope than the majority of studies, which frequently only report perinatal BDs at or beyond 28 gestational weeks within a hospital-based surveillance system. The incorporation of BDs prior to 28 weeks of gestation is fundamental in accurately

determining the true incidence of BDs, thereby establishing a robust foundation for evaluating the real-time effects of primary prevention measures. Furthermore, it serves to stimulate health authorities at all tiers to prioritize the enhancement of primary prevention strategy implementation in the future. Additionally, the span of two decades of consistent surveillance data encapsulates durable trends of change.

This study, however, presented several limitations. Primarily, the limited selection area, comprising predominantly rural counties in Shanxi Province, may constrain the applicability of our conclusions on a more expansive geographic scale, such as the entire PLADs or the nation as a whole. For more complete subsequent investigations, the inclusion of extensive individual exposure data is crucial to delve deeper into the origins of BDs.

In summary, the region has witnessed a marked decline in total BD prevalence over the past two decades, attributable to holistic preventive measures rolled out in the area. Importantly, the folic acid supplementation program, initiated broadly in 2009, resulted in a significant decrease in NTDs. This highlights the critical role of persistent folic acid supplementation promotion in forestalling NTDs. Alternatively, the region has seen a substantial rise in CHD prevalence. Less than optimal access to primary healthcare services and diagnostic facilities likely leads to an underestimation of early diagnosis rates for internal anomalies, particularly CHDs, in the region. Therefore, an immediate reallocation strategy favoring improved medical resources is vital, with particular emphasis on setting up local training programs geared towards enhancing internal anomaly screening and diagnostic capabilities, with a primary focus on CHDs in these counties.

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Preplanned Studies

Periconceptional Folic Acid Use and Its Effects on Neural Tube Defects — Five Counties, Shanxi Province, China, 2010–2016

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Summary

What is already known about this topic?

Robust evidence indicates that supplementing with folic acid periconceptionally may decrease the risk of neural tube defects (NTDs) in fetuses.

What is added by this report?

Over half of the mothers in both the NTD case group and the control group utilized folic acid supplements during the periconceptional period, showing no notable variations between the two groups. However, there was a significantly higher percentage of mothers with NTD cases who exhibited poor compliance in folic acid use compared to control mothers. A significantly lowered compliance with folic acid intake was observed among women facing unintended pregnancies and those with lower education levels.

What are the implications for public health practice?

Universal education regarding folic acid action for women of childbearing age should be strengthened to improve compliance with folic acid supplementation in the periconceptional period and further reduce the prevalence of NTDs.

Neural tube defects (NTDs) are profound congenital malformations of the brain and spinal cord that occur in fetuses in early pregnancy. Empirical evidence suggests that the periconceptional use of folic acid considerably reduces the risk of developing NTDs (*1*–*2*). In 2009, China's National Health Commission, formerly the Ministry of Health (MOH), rolled out a nationwide program aimed at promoting folic acid supplementation among women planning for pregnancy. The program aimed to motivate 70% of women to commence folic acid supplementation at least three months before conception (*3*–*4*). However, studies have indicated suboptimal adherence levels (below 40%), significantly short of the MOH's target (*5*–*6*), though the degree of adherence noticeably improved with higher maternal educational levels (*6*). This study investigates the use of folic acid, its protective effect against NTDs, and the significant features influencing adherence to the supplementation protocol in five counties within China's Shanxi Province following the rollout of the national supplementation program. These research findings indicate that more than half of the women in the case and control groups used folic acid during the periconceptional period. Nevertheless, cases of NTDs were significantly more prevalent among women who demonstrated poor adherence. Additionally, non-compliance was notably higher among women with unintended pregnancies and with lower educational levels. In order to reduce the prevalence of birth defects, particularly NTDs, there is a need to strengthen education regarding folic acid supplementation for childbearing-aged women with the aim of improving adherence during the periconceptional period.

A population-based, case-control study of major external birth defects, conducted between 2010 and 2016, identified 213 cases of NTDs and selected 442 normal controls in five counties of Shanxi Province (including Pingding, Xiyang, Shouyang, Taigu, and Zezhou). The population-based birth defect surveillance system had previously indicated these locations to have immensely high NTD prevalence before 2009. Each case was matched with a healthy newborn of the same sex and from the same county, having the closest conception date to the case's.

Trained health professionals collected data through structured interviews from participants within 10 days of delivery or pregnancy termination due to identified birth defects. The gathered information encompassed demographics, gravidity history, lifestyle behaviors, and folic acid intake practices.

From the initial group, 113 subjects (14.7%) were excluded due to incomplete folic acid intake data, resulting in a final sample size of 655 subjects. Compliance with folic acid supplementation was defined as consuming no less than a 60-day supply, beginning over a month prior to the last menstrual period (LMP) and extending to less than a month

post-LMP. Non-compliance was defined as consuming less than a 60-day supply or starting supplementation after one month post-LMP.

This study was granted approval by the Institutional Review Board of Peking University (IRB00001052–16061) and written informed consent was procured from all participants.

In order to assess the relationship between folic acid intake and the risk of NTDs, a logistic regression analysis was conducted. Unadjusted odds ratios (*OR*s) were calculated, including 95% confidence intervals (*CI*s). This was followed by the computation of adjusted odds ratios (*aOR*s) that also included 95% *CI*s, after accounting for potential confounding variables. These variables consisted of maternal age, pre-pregnancy body mass index (BMI), history of pregnancies affected by birth defects, incidences of fever or flu in early pregnancy, and exposure to secondhand smoke. The statistical analysis was conducted using SPSS software (version 24.0; SPSS Inc., Armonk, NY, USA).

A total of 213 cases of NTD and 442 control subjects were included in this analysis. The NTD cases comprised of 74 anencephaly cases, 115 spina bifida cases, and 24 encephalocele cases. Other malformations, such as orofacial clefts or gastroschisis, were present in 16 (7.5%) of the NTD cases. Mothers of NTD cases showed a lower level of education, an elevated rate of exposure to passive smoking, a more frequent history of pregnancies affected by birth defects, a higher prevalence of fever or flu contractions, and a higher rate of unintended pregnancies as compared to mothers of control subjects. Moreover, they were more likely to be 30 years or older and have a pre-pregnancy BMI of at least 25 kg/m^2 (Table 1).

In total, 51.6% (110/213) of mothers in the case group reported folic acid intake during the periconceptional period, a proportion slightly less than that of the control group, where 58.8% (260/442) reported intake. No significant differentiation was found between the two groups in terms of folic acid usage. However, a significant difference was observed concerning compliance, with the proportion of good compliance being significantly lower in the NTD case mothers (13.1%) compared to the control mothers (27.6%). After adjusting for factors such as maternal age, pre-pregnancy BMI, occurrences of fever or flu in early pregnancy, exposure to passive smoking during the periconceptional period, and history of birth defect-implicated pregnancies, the *aOR* for good compliance was calculated to be 0.517 (95% *CI*: 0.300–0.891) (Table 2).

Table 3 illustrates that there is a significant association between unintended pregnancy, lower education levels (defined as junior high school or less), and decreased compliance rate (all $P<0.05$). This association remains significant even after adjusting for potential confounding variables.

DISCUSSION

Over half of expectant women in Chinese regions with a high prevalence of NTDs reported taking folic acid supplements during the periconceptional period; no significant disparities in NTDs emerged between the case and control groups. After the implementation of a national folic acid supplementation program in 2009, periconceptional intake in these areas displayed an increasing trend, albeit remaining significantly lower than that in Beijing, which is at 97.2% (*6*). Considering that neural tube closure transpires within the first month of pregnancy, early supplementation during the periconceptional period and regular usage are crucial in preventing NTDs. Table 2 demonstrates that robust protective effects were observed whether women commenced folic acid intake more than 1 month prior to LMP, or from 1 month before to 1 month after LMP. The United States Preventive Services Task Force (USPSTF) advocates that women planning or capable of pregnancy should begin taking folic acid 1 month before conception and continue until 3 months post-conception, consuming at least 24 capsules monthly; in Western countries, 42.2% of women adhere to this recommendation (*7*). One study found a significantly lower prevalence of NTDs among women who used folic acid-containing multivitamins during the initial 6 weeks of pregnancy, compared to those who never used such supplements (prevalence ratio 0.27; 95% *CI*: 0.12–0.59) (*8*). In this study, merely 13.1% of mothers in the NTD case group demonstrated satisfactory compliance with supplementation, the figure lower than the control group (27.6%, $P<0.05$). However, applying the USPSTF standard, the fraction of sufficient compliance in the NTD group declined further to 6.6% (14/213). These findings unequivocally indicate that, despite this study's definition of satisfactory compliance being less strict, there was still a significant protective effect on NTDs (*aOR*: 0.517, 95% *CI*: 0.300–0.891).

TABLE 1. Demographic and lifestyle attributes of mothers of NTD cases and controls in five counties of Shanxi Province, China, 2010–2016.

Characteristics of mothers	NTD cases (*n*=213)*		Controls (*n*=442)*		*P*
	N	%	*N*	%	
Age (years)					0.031
<25	77	36.8	211	48.3	
25–29	74	35.4	140	32.0	
30–34	39	18.7	60	13.7	
≥35	19	9.1	26	6.0	
Prepregnancy BMI (kg/m^2)					<0.001
<18.5	20	9.8	40	9.2	
18.5–24.9	115	56.7	311	71.3	
≥25	68	33.5	85	19.5	
Occupation					0.221
Farmer	146	73.0	287	68.2	
Others	54	27.0	134	31.8	
Education					<0.001
Junior high school or lower	160	75.5	256	58.2	
Senior high school	33	15.6	101	22.9	
College or higher	19	8.9	83	18.9	
Parity					0.675
Primiparas	123	60.0	271	61.7	
Multiparas	82	40.0	168	38.3	
History of birth defect-affected pregnancy					0.010
Yes	9	4.3	5	1.1	
No	201	95.7	430	98.9	
Fever or flu in early pregnancy					<0.001
Yes	76	38.8	67	16.5	
No	120	61.2	339	83.5	
Passive smoking exposure					<0.001
Yes	124	60.5	135	31.1	
No	81	39.5	299	68.9	
Unintended pregnancy					<0.001
No	116	55.5	304	71.7	
Yes	93	44.5	120	28.3	

Abbreviation: NTDs=neural tube defects; BMI=body mass index.
* The total number may not be the sum of the values due to missing information for some subjects.

Our research identified notable disparities in folic acid adherence among women experiencing unintended pregnancies, which underscored by significantly lower compliance rates. After controlling for potential confounders, the association persisted (*aOR*: 2.753, 95% *CI*: 1.687–4.494). Unintended pregnancies proved prevalent, constituting 22.1% to 35.1% of all cases (*9*–*10*). Interestingly, mothers of NTD cases had higher rates of unintended pregnancies at 44.5%, exceeding the frequency seen in the broader population. Prior research discovered that 61% of women initiated supplementation upon realizing their pregnancy status (*10*), rendering adherence to recommended folic acid supplementation impossible for women with unexpected pregnancies. The study further revealed that the impact of education on compliance was modest, particularly among those women with lower education levels. Therefore, it is

TABLE 2. Associations between periconceptional folic acid supplementation and fetal NTDs in five counties of Shanxi Province, China, 2010–2016.

Factors	Case [*n* (%)]	Control [*n* (%)]	Crude *OR* (95% *CI*)	Adjusted *OR** (95% *CI*)
Folic acid supplementation				
No	103 (48.4)	182 (41.2)	1	1
Yes	110 (51.6)	260 (58.8)	1.338 (0.963–1.858)	1.023 (0.686–1.526)
When folic acid supplementation began†				
>1 month before LMP	20 (18.2)	70 (26.9)	0.418 (0.233–0.750)	0.458 (0.236–0.890)
From 1 month before to 1 month after LMP	21 (19.1)	89 (34.2)	0.345 (0.196–0.608)	0.322 (0.170–0.612)
>1 month after LMP	69 (62.7)	101 (38.9)	1	1
The total number of days taken folic acid supplementation†				
<60 days	47 (42.7)	71 (27.3)	1	1
≥60 days	63 (57.3)	189 (72.7)	0.501 (0.314–0.798)	0.497 (0.291–0.851)
Compliance with folic acid intake				
No folic acid intake	103 (48.4)	182 (41.2)	1	1
Poor	82 (38.5)	138 (31.2)	1.050 (0.729–0.252)	1.189 (0.771–1.834)
Good	28 (13.1)	122 (27.6)	0.406 (0.252–0.653)	0.517 (0.300–0.891)

Abbreviation: NTDs=neural tube defects; *OR*=odds ratio; *CI*=confidence interval; LMP=last menstrual period.
* Adjusted for variables such as maternal age, body mass index during pregnancy, history of pregnancies affected by birth defects, occurrence of fever or flu in early pregnancy, and exposure to passive smoking.
† Pertains to pregnant women who had consumed folic acid.

TABLE 3. Factors influencing compliance with folic acid intake in five counties of Shanxi Province, China, 2010–2016.

Factors	Compliance with folic acid intake§		Crude *OR* (95% *CI*)	Adjusted *OR*† (95% *CI*)
	Good [*n* (%)]	Poor or no intake [*n* (%)]		
Unintended pregnancy*				
No	120 (81.6)	300 (61.7)	1	1
Yes	27 (18.4)	186 (38.3)	2.756 (1.747–4.347)	2.753 (1.687–4.494)
Education*				
Junior high school or lower	68 (45.3)	348 (69.3)	4.204 (2.631–6.717)	2.632 (1.382-5.013)
Senior high school	36 (24.0)	98 (19.5)	2.236 (1.295–3.860)	1.733 (0.933–3.219)
College or higher	46 (30.7)	56 (11.2)	1	1

Abbreviation: *OR*=odds ratio; *CI*=confidence interval.
* Values may not sum to the total due to missing data from some subjects;
† Adjusted for factors including maternal age, body mass index during pregnancy, occupational status, historical incidence of birth defects, and parity;
§ Folic acid intake is categorized as good (coded as 0) or poor/no intake (coded as 1).

vital to amplify educational efforts promoting periconceptional supplementation of folic acid among women of childbearing age in the regions investigated.

This study possesses notable strengths. It utilizes a population-based birth-defect surveillance system distinguished by a high prevalence of NTDs and an impressive participation rate. Both cases and controls were culled from congruent regions, and the implemented evaluation of compliance with folic acid intake enabled an exhaustive analysis of how varied inception times and usage durations affect NTD risk. To our understanding, this stands as the inaugural study to concurrently investigate the status of folic acid use and its prophylactic effect on NTDs in these Chinese regions renowned for their high NTD prevalence, subsequent to the enforcement of the nationwide folic acid supplement program.

The present study was not without limitations. Folic acid intake, as reported by participating women during their postpartum period, presents the potential for recall bias, thus potentially influencing the study outcomes. Other significant factors that could likely affect compliance, such as awareness and intricate knowledge about folic acid, were not explored, thereby

limiting our ability to examine their impacts on adherence rates. It would be beneficial for forthcoming research to amalgamate data on folic acid intake with information on plasma folate concentrations, coupled with other important factors likely to affect folic acid use like understanding and disposition towards supplementation.

This study found that high adherence to folic acid supplementation was linked to a reduced risk of NTDs. However, the rate of adherence was markedly low among mothers with NTD-affected pregnancies, at just 13.1%, despite a nationwide folic acid supplementation program. Consequently, there is a clear need to intensify universal education on the benefits of folic acid for women of childbearing age. This will potentially enhance adherence to folic acid supplementation during the periconceptional period, and subsequently, decrease the occurrence rate of NTDs.

Conflicts of interest: No conflicts of interest.

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Preplanned Studies

A Hospital-Based Study on Congenital Heart Defects — Haidian District, Beijing Municipality, China, 2013–2022

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Summary

What is already known about this topic?

Congenital heart defects (CHDs) represent the most prevalent birth defects in China, exhibiting significant mortality and morbidity rates. Recent years have witnessed a steady increase in the occurrence of CHDs, highlighting a crucial need for rigorous research focus.

What is added by this report?

The cumulative birth prevalence of CHDs in Haidian District from 2013 to 2022 was 80.77 per 10,000 births, reflective of an upward trend primarily influenced by the diagnosis of minor, non-critical congenital defects (non-CCHDs). This increase can be attributed to advancements in diagnostic methodologies. Despite the progress in detection, the survival rate for CHDs did not correspondingly improve.

What are the implications for public health practice?

Policies need to be formulated to promote the graded management of CHDs. There should be timely updates to the diagnostic criteria to align with advancements in diagnostic techniques. Moreover, in instances where therapeutic abortion is not required, the provision of appropriate medical consultation post-diagnosis should be enhanced.

Congenital heart defects (CHDs) was the most prevalent birth defects in China during 2000–2011. It's 40.95 per 10,000 births in 2011 which accounted for 26.7% of all birth defects, data from hospital-based birth defects surveillence revealed (*1*). Of these, CHDs form the most common group, accounting for one-third of the total (*1*). The incidence of CHDs during the period from 2013 to 2021 was 82.00 per 10,000 births in Europe (*2*). For Shanghai, the incidence from 2016 to 2018 was recorded as 81.00 per 10,000 births (*3*), while Jinan demonstrated a lower incidence rate of 54.96 per 10,000 births from 2013 to 2020 (*4*).

CHDs can be complex and involve a variety of subtypes. Further, they can be categorized based on severity, as either critical CHDs (CCHDs) or non-critical CHDs (non-CCHDs). The World Health Organization (WHO) reports that CCHDs account for 25% of all CHDs, with infants diagnosed requiring intervention within the first year of life. In many countries, the incidence rate of non-CCHDs is increasing, whereas the rate of CCHDs has remained relatively stable.

This study aims to examine the trends and incidence rates of CHDs, providing data to inform governmental policy interventions. Our findings reveal an increasing incidence rate of CHDs in the Haidian District, Beijing, from 84.65 per 10,000 births in 2013 to 105.72 per 10,000 births in 2022, with non-CCHDs contributing significantly to this increase. Meanwhile, the incidence of CCHDs remained stable at an average of 19.00 per 10,000 births. Interestingly, improved diagnostic techniques have not coincided with improved survival rates for both CCHDs and non-CCHDs.

This study analyzes data from a hospital-based BD surveillance system in Haidian District. The surveillance system's details were highlighted in a prior publication (*5*). Each pertinent healthcare institution in the district (18 community health service centers, midwifery agencies, and children's hospitals) was obligated to complete unified forms and registration cards, reporting individual details about BDs and infant deaths. As per the Beijing Municipal Health Commission's protocols, a prenatal diagnosis rate exceeding 90% is required, with further examinations conducted on newborns exhibiting abnormalities. The diagnosis of CHDs followed the standards outlined by the International Statistical Classification of Diseases and Related Health Problems, 10th Edition. Joinpoint regression, facilitated by joinpoint software (version 4.9.1, Information Management Services, Inc., Calverton, MD, USA), was employed to calculate the annual percentage change (APC) and the average annual percentage change (AAPC) in CHDs prevalence. Statistical significance was marked by a

two-tailed *P* value of less than or equal to 0.05. The survival rate took the total number of CHDs into account in relation to live births, expressed as the number of live births per 100 CCHDs or non-CCHDs. The total perinatal infant count each year in Haidian District, China, formed the numerators to compute the annual prevalence, delineated as per 10,000 births.

In summary, 12 subtypes were recognized as CCHDs: common arterial trunk, double outlet right ventricle, complete transposition of great vessels, single ventricle, tetralogy of Fallot (TOF), congenital tricuspid stenosis, Ebstein's anomaly, hypoplastic left heart syndrome, interrupted aortic arch, pulmonary artery atresia, total anomalous pulmonary venous connection, and aortic coarctation.

RESULTS

Between the years 2013 and 2022, there were 364,758 births reported in the Haidian District, Beijing, China. During this period, a total of 2,946 CHDs cases were identified, corresponding to a prevalence rate of 80.77 per 10,000 births (95% *CI*: 77.89 to 83.72). Despite there being no prominent temporal trend observed for the total number of CHDs, a significant trend was noted upon the exclusion of patent ductus arteriosus (PDA). Specifically, there was an AAPC of 6.93% in CHDs cases excluding PDA (95% *CI*: 2.97% to 11.04%, *P*<0.001).

Over a ten-year span, the most frequently identified subtypes of CHDs included ventricular septal defect (VSD), PDA, atrial septal defect (ASD), persistent left superior vena cava (PLSVC), and TOF. It was observed that PDA and VSD combined, accounted for over half of total CHDs diagnoses (Figure 1). During 2013–2015, PDA was the prevalent subtype, but after 2015 VSD became predominant. There was an observed average annual decrease of 11.33% (AAPC: –11.33%, 95% *CI*: –19.67% to –2.12%, *P*<0.05) in PDA prevalence, whilst VSD and PLSVC saw an average annual increase of 7.79% (AAPC: 7.79%, 95% *CI*: 2.96% to 3.77%, *P*<0.01) and 15.13% (AAPC: 15.13%, 95% *CI*: 6.87% to 24.04%, *P*<0.001) respectively. No significant temporal trend was observed in the prevalence of ASD or TOF (AAPC: 0.65%, 95% *CI*: –10.15% to –12.69%, *P*=0.911; AAPC: 1.66%, 95% *CI*: –8.34% to –12.76%, *P*=0.723).

Figure 2 classifies CHDs into CCHDs and non-CCHDs. The average prevalence was noted as 19.00/10,000 for CCHDs and 61.77/10,000 for non-CCHDs. While the non-CCHDs indicated no significant temporal trend (AAPC: 0.86%; 95% *CI*: –5.98% to 8.08%; *P*=0.809), excluding from the count a common condition known as PDA resulted in a noteworthy trend, including an annual average increase of 9.36% (AAPC: 9.36%; 95% *CI*: 5.93% to 12.89%; *P*<0.001). However, no significant temporal trend was observed for the CCHDs category (AAPC: 2.46%; 95% *CI*: –3.93% to 9.28%; *P*=0.409). A minor

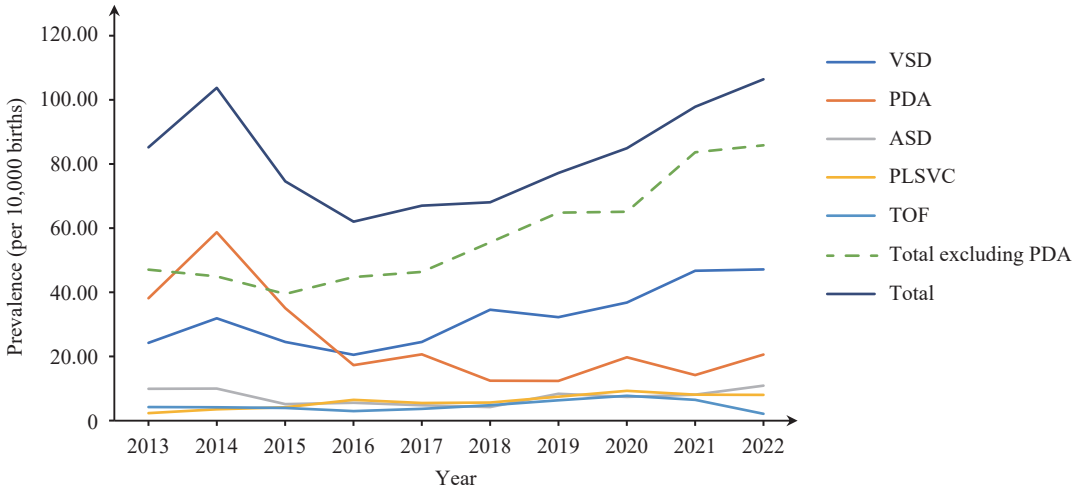

FIGURE 1. Prevalence of the five most common subtypes of congenital heart defects in Haidian District, Beijing Municipality, China, from 2013 to 2022.
Abbreviation: VSD=ventricular septal defect; PDA=patent ductus arteriosus; ASD=atrial septal defect; PLSVC=persistent left superior vena cava; TOF=tetralogy of Fallot.

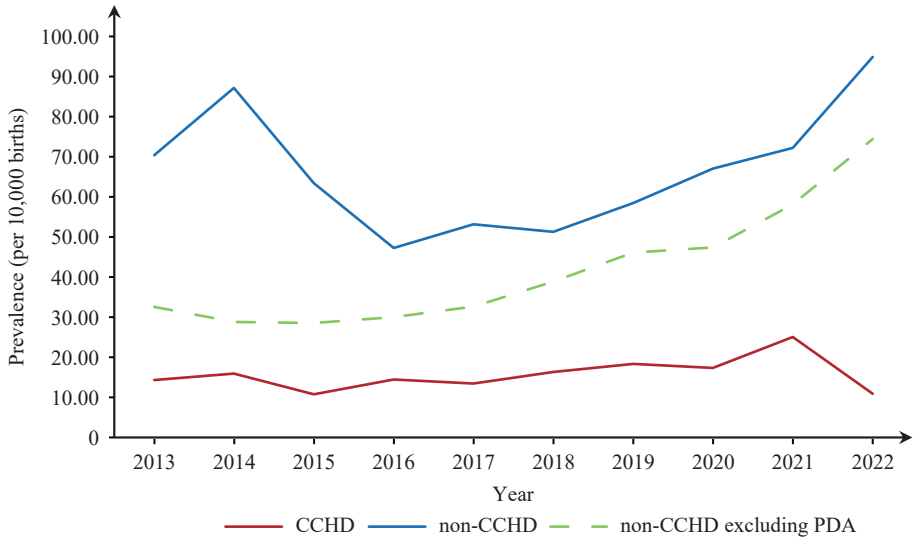

FIGURE 2. Prevalence of critical and non-critical congenital heart defects in Haidian District, Beijing Municipality, China, between 2013 and 2022.
Abbreviation: CCHDs=critical congenital heart defects; non-CCHDs=noncritical congenital heart defects; PDA=patent ductus arteriosus.

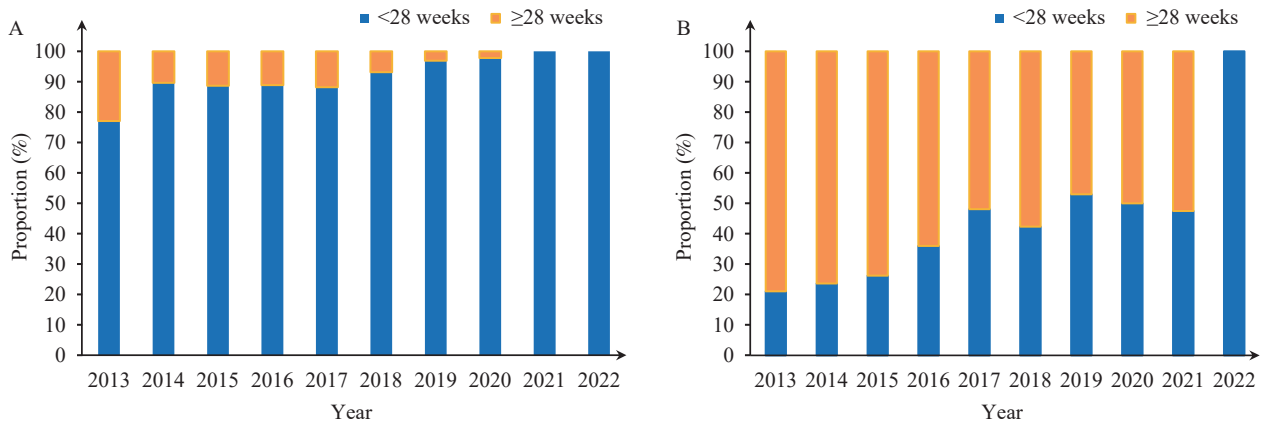

FIGURE 3. Percentage of congenital heart defects diagnosed at less than 28 weeks and greater than or equal to 28 weeks in Haidian District, Beijing Municipality, China, from 2013 to 2022. (A) Percentage of critical congenital heart defects; (B) Percentage of non-critical congenital heart defects.

increase in CCHDs prevalence occurred, from 14.25/10,000 to 25.01/10,000, throughout the period of 2013–2021, while an abrupt drop to 10.86/10,000 was reported in 2022.

Figure 3 illustrates the proportion of CCHDs and non-CCHDs diagnoses for gestational weeks less than 28 and more than 28. The proportion of diagnoses made during gestational weeks less than 28 is demonstrating a significant increase for both. Specifically, the CCHDs diagnoses have been growing by 2.40% annually under 28 gestational weeks (AAPC: 2.40%; 95% *CI*: 1.47% to 3.34%; *P*<0.001). In 2013, the proportion of CCHDs diagnoses made at under 28 gestational weeks was 77.05%, which increased to 100% in 2022 (Figure 3A). Non-CCHDs diagnoses at under 28 gestational weeks have been increasing by 15.08% annually (AAPC: 15.08%; 95% *CI*: 9.70% to 20.72%; *P*<0.001), and significantly, the proportion of non-CCHDs diagnoses at under 28 gestational weeks doubled from 21.03% in 2013 to 47.49% in 2021. Over time, although the proportion of CCHDs diagnoses are notably higher, non-CCHDs diagnoses have shown a more rapid increase (AAPC: 15.08% *vs.* 2.40%). Lastly, by the end of 2022, 100% of non-CCHDs diagnoses are made at under 28 gestational weeks (Figure 3B).

Table 1 illustrates a trend of decreasing survival rates for both CCHDs and non-CCHDs. The AAPC was

TABLE 1. Survival rates for critical and non-critical congenital heart defects in Haidian District, Beijing Municipality, China, from 2013 to 2022.

Year	CCHDs			Non-CCHDs		
	Live birth	Total	Survival rate (%)	Live birth	Total	Survival rate (%)
2013	10	61	16.39	237	271	87.45
2014	7	77	9.09	335	372	90.05
2015	6	44	13.64	214	244	87.70
2016	11	63	17.46	171	203	84.24
2017	12	59	20.34	191	233	81.97
2018	10	58	17.24	157	182	86.26
2019	7	64	10.94	166	204	81.37
2020	4	45	8.89	146	174	83.91
2021	3	62	4.84	147	179	82.12
2022	7	26	26.92	196	227	86.34
Total	77	482	19.01	1960	2289	85.63

Note: AAPC was −2.19% for CCHDs (AAPC: −2.19%, 95% *CI*: −14.35% to 11.70%, *P*=0.71), and −0.62% (AAPC: −0.62%; 95% *CI*: −1.37% to 0.12%; *P*=0.09).
Abbreviation: CCHDs=critical congenital heart defects; non-CCHDs=non-critical congenital heart defects; AAPC=average annual percent change; *CI*=confidence interval.

TABLE 2. Trends in the prevalence of specific coronary heart disease subtypes and proportion diagnosed before 28 weeks in Haidian District, Beijing Municipality from 2003 to 2022, as analyzed by Joinpoint regression.

Variable	Trend	Period	APC (95% *CI*)	*P*	AAPC (95% *CI*)	*P*
Joinpoint trends in Figure 1						
Total	Trend 1	2013–2017	−9.84 (−20.46 to 2.20)	0.087	1.35 (−4.24 to 7.26)	0.643
	Trend 2	2018–2022	11.29 (1.85 to 21.61)	0.027		
Total exclude PDA	Trend 1	2013–2015	−9.43 (−25.97 to 10.82)	0.263	6.93 (2.97 to 11.04)	<0.001
	Trend 2	2016–2022	12.12 (9.14 to 15.18)	<0.001		
PDA	Trend 1	2013–2022	−11.33 (−19.67 to −2.12)	<0.05	−11.33 (−19.67 to −2.12)	<0.05
VSD	Trend 1	2013–2022	7.79 (2.96 to 12.86)	<0.01	7.79 (2.96 to 12.86)	<0.01
ASD	Trend 1	2013–2017	−18.79 (−36.75 to 4.28)	0.085	0.646 (−10.11 to 12.69)	0.911
	Trend 2	2018–2022	19.49 (0.13 to 42.60)	<0.05		
PLSVC	Trend 1	2013–2016	33.12 (4.42 to 69.70)	<0.05	15.13 (6.87 to 24.04)	<0.001
	Trend 2	2017–2022	7.07 (−1.37 to 16.23)	0.085		
TOF	Trend 1	2013–2022	1.66 (−8.34 to 12.76)	0.723	1.66 (−8.34 to 12.76)	0.723
Joinpoint trends in Figure 2						
CCHDs	Trend 1	2013–2022	2.46 (−3.93 to 9.28)	0.409	2.46 (−3.93 to 9.28)	0.409
Non-CCHDs	Trend 1	2013–2018	−6.60 (−15.62 to 3.38)	0.144	3.19 (−3.30 to 10.12)	0.344
	Trend 2	2019–2022	16.87 (1.24 to 34.92)	20.038		
Non-CCHDs excluding PDA	Trend 1	2013–2022	14.55 (10.97 to 18.24)	<0.001	14.55 (10.97 to 18.24)	<0.001
Joinpoint trends in Figure 3						
CHDs diagnosed at <28 weeks	Trend 1	2013–2022	2.40 (1.47 to 3.34)	<0.001	2.40 (1.47 to 3.34)	<0.001
Non-CCHDs diagnosed at <28 weeks	Trend 1	2013–2022	15.08 (9.70 to 20.72)	<0.001	15.08 (9.70 to 20.72)	<0.001

Abbreviation: VSD=ventricular septal defect; PDA=patent ductus arteriosus; ASD=atrial septal defect; PLSVC=persistent left superior vena cava; TOF=tetralogy of Fallot; CHDs=critical congenital heart defects; non-CCHDs=noncritical congenital heart defects; APC=annual percentage change; AAPC=average annual percentage change.

–2.19% for CCHDs (AAPC: –2.19%; 95% *CI*: –14.35% to 11.70%; *P*=0.71) and –0.62% for non-CCHDs (AAPC: –0.62%; 95% *CI*: –1.37% to 0.12%; *P*=0.09), though neither was statistically significant. Within the CCHDs category, the highest survival rate recorded was 26.92% in 2022, while the lowest was 4.84% in 2021. Additionally, survival rates were markedly higher in non-CCHDs than in CCHDs (85.63% *vs.* 19.01%). When reviewing non-CCHDs specifically, the survival rate peaked at 90.05% in 2014 and dipped to a low of 81.37% in 2019. All AAPCs discussed are listed in Table 2.

DISCUSSION

The prevalence of CHDs within Haidian District from 2013–2022 was 80.77 per 10,000 births. This was higher than the rate witnessed in Jinan from 2013–2020 (52.10 per 10,000 births) (*6*), but was modestly lower than figures recorded in Europe from 2013–2021 (82.00 per 10,000 births) (*2* and Shanghai from 2016–2018 (81.00 per 10,000 births) (*3*). It's commonly cited that the worldwide prevalence of CHDs is 80.00 per 10,000 births, mirroring our findings (*1*). The common CHDs variants in Haidian District were — in descending order — VSD, PDA, ASD, PLSVC and TOF. The four most common variants were non-CCHDs, while TOF was the only CCHD presented within the top five. Non-CCHDs were notably more prevalent compared to CCHDs.

The overall prevalence of CHDs from 2013 to 2022 did not display a noteworthy temporal trend. Various countries and regions, such as Asia (1970–2017) and Jinan (2005–2020), have reported a broad upward prevalence trend for CHDs (*4*,*7*). Evidently, the prevalence trend of total CHDs is mainly influenced by non-CCHDs, with PDA and VSD playing key roles. During 2018–2022, non-CCHDs exclude PDA has risen significantly, by 12.93% annually, outpacing CCHDs, which remained comparatively stable. Until 2016, total CHDs were predominated by PDA, exhibiting a progressive increase from 37.88/10,000 to 58.35/10,000 in 2013–2014 and a significant decrease from 58.35/10,000 to 17.19/10,000 in 2014–2016. The implementation of new screening criteria (2015 edition), that came into effect in 2016, led to a precipitous decrease in the prevalence of PDA, as defects smaller than 3 mm were no longer classified. Consequently, VSD emerged as the leading subtype. Over the years, VSD has sustained a steady influx, likely as a result of overdiagnosis due to technological progress or adverse atmospheric conditions, as its steady rise suggests. For other reasons probably, researchers from southern California discovered that a higher exposure to carbon monoxide leads to an increased risk of VSD (*8*). Considering the potential overdiagnosis of PDA prior to the publication of the new diagnostic criteria, we also analyzed the prevalence trend excluding PDA. This evaluation revealed a substantial increasing trend with an annual average growth of 9.36%.

The detection of CHDs at less than 28 weeks of gestation illustrates advancements in diagnostic ultrasound techniques. Both CCHDs and non-CCHDs have continually been better identified through these improved screening methods. More pronounced structural defects make CCHDs easier to diagnose, often necessitating early surgery. Conversely, minor non-CCHDs forms, such as small VSDs and PDAs, even if diagnosed early, may not lead to health complications. They often close on their own over time. Early detection of non-CCHDs has not significantly enhanced survival rates, which may be due to the possible increase in therapeutic abortions. According to the collected data, the rate of therapeutic abortions was 10.98% from 2013–2015, increasing to 13.38% from 2016–2022. European Surveillance of Congenital Anomalies (EUROCAT) data also showed an increasing trend in the termination of pregnancy for congenital anomaly (TOPFA), from 50% in 2013 to 62.5% in 2021 (*2*). Many parents tend to decide on induced abortions upon diagnosis, often without sufficient medical consultation and regardless of prognosis. Moreover, the survival rate for CCHDs in 2022 was extremely high, primarily due to the reduction in the number of CCHDs cases. Yet, these results coincided without any changes in screening criteria, signaling a need for additional investigation into the high survival rate of CCHDs in 2022. In conclusion, there has been an increase in the prevalence of CHDs, specifically non-CCHDs, in the Haidian District of China over the past decades. This increase is likely attributed to the ongoing improvement in diagnostic techniques.

For effective management of CCHDs, it is essential to conduct screenings as early as possible to facilitate timely surgical intervention. Conversely, for non-CCHDs, it's critical to update diagnosis criteria in time to prevent overdiagnosis and unnecessary TOPFA (*9*–*10*). Due to this, we advocate both a graded approach in managing CCHDs and non-CCHDs

conditions and periodic updates to diagnosis criteria to prevent potential overdiagnosis in non-CCHDs cases. Moreover, post-diagnosis medical consultation should be enhanced to minimize unnecessary therapeutic abortions. The lack of comprehensive medical consultation has often resulted in unwarranted inductions in mild non-CCHDs cases, despite them having a high survival possibility.

The present study boasts several key strengths. First, it utilizes a thorough BD surveillance system, established in Beijing, which is characterized by adherence to rigorous detection standards. This guarantees the reliability of the results. Secondly, Haidian District, where the hospital-based surveillance data was collected, boasts a 100% rate of hospitalized deliveries. As a result, the surveillance data provides an accurately representative picture of the broader population. Lastly, the study introduces an expanded classification system for CHDs within the surveillance system, incorporating more detailed subtypes. This facilitates a more nuanced analysis of CHDs prevalence, which will significantly contribute to the enhancement of future classification systems.

This study, however, is not without its limitations. Given the absence of individual-level data for non-CHDs births, we were unable to conduct a multivariate analysis for other factors associated with CHDs. Future research is needed to further explore the potential influence of these factors on CHDs. Moreover, our investigation was constrained to Haidian District in Beijing, which due to its comparatively advanced economy, might limit the generalizability of the findings to other regions.

Conflicts of interest: No conflicts of interest.

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