

Vital Surveillances

Evaluation of Perinatal Prevalence, Geographic Disparities, and Survival of Neural Tube Defects — China, 2006–2024

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ABSTRACT

Introduction: Neural tube defects (NTDs) are a major cause of perinatal mortality and lifelong disability. However, long-term trends in NTD prevalence, regional disparities, and survival patterns in China remain poorly characterized.

Methods: Data from the Chinese Birth Defects Monitoring Network (CBDMN) were analyzed for perinatal NTDs occurring between 2006 and 2024. Bayesian Poisson regression models incorporating subtype, geographic strata, maternal age, calendar year, and interaction effects were applied to estimate long-term trends in perinatal prevalence and survival. Joinpoint analysis was employed to estimate annual percentage changes (APCs).

Results: The estimated perinatal prevalence of NTDs in China declined from 8.84 per 10,000 births in 2006 to 0.77 per 10,000 births in 2024, representing a 91.29% reduction. Joinpoint analysis identified a three-phase decline pattern, with the APC accelerating from −10.43% (2006–2009) to −16.08% (2009–2016), followed by a slower decline of −10.60% (2016–2024). Similar downward trends were observed across all major NTD subtypes, with anencephaly showing the steepest decline. Long-standing nationwide north-south and urban-rural gaps in NTD prevalence were greatly reduced, with no statistically distinguishable differences observed during the late study period. Meanwhile, overall perinatal survival increased from 23.33% to 46.76%, driven primarily by marked improvements in spina bifida and encephalocele survival.

Conclusion: From 2006 to 2024, China demonstrated a remarkable decline in perinatal NTD prevalence, alongside a substantial narrowing of the long-standing national north-south and urban-rural gaps in disease burden. The increasing perinatal survival among nonlethal subtypes highlights the emerging need for long-term pediatric care and rehabilitation.

Neural tube defects (NTDs), one of the most prevalent birth defects, are a major cause of perinatal mortality and lifelong childhood disability worldwide (1). In the 1980s, NTDs had a high perinatal prevalence of 27 per 10,000 births, ranking first among all types of congenital malformations in China, with striking north-south and urban-rural disparities (2). The 1995 promulgation of the Law on Maternal and Infant Health Care of the People's Republic of China legalized national birth defect prevention and control. The Working Committee on Women and Children under the State Council issued the Outline for Chinese Children's Development (2001–2020), which for the first time included "reducing the incidence of birth defects" in government work targets (3). Since 2003, the rapid popularization of prenatal ultrasonography has allowed more NTD cases to be diagnosed prenatally (4). Following the national basic public health service equalization reform initiated in 2008, China implemented key preventive strategies, including free folic acid supplementation (2009) and free pre-pregnancy health screening for rural residents (2011) (5–6). These interventions have substantially reduced the occurrence of NTDs and reshaped their epidemiological profiles nationwide. Previous epidemiological studies have documented a substantial decrease in the perinatal prevalence of NTDs in China over the past decade (7). However, research on the temporal dynamics of north-south variations and urban-rural disparities in NTDs, along with the long-term trends in perinatal survival, remains limited. Herein, data from the Chinese Birth Defects Monitoring Network (CBDMN) was utilized to assess the temporal trends, geographic disparities, and perinatal survival rates of NTDs from 2006 to 2024, with the aim of providing robust epidemiological evidence for optimizing national NTD prevention and control strategies in China.

METHODS

Data were obtained from the CBDMN, a nationwide hospital-based surveillance system covering 786 hospitals across 326 counties or districts in 31 provincial-level administrative divisions (PLADs) in China. The CBDMN routinely collects data on the number of live births and stillbirths from all participating hospitals. All births delivered at monitoring hospitals with birth defects diagnosed during the perinatal period (28 gestational weeks to 7 days after birth) are mandatorily reported and coded according to the Tenth Revision of the International Classification of Diseases (ICD-10). The CBDMN annually monitors approximately 10% of all births in China. The annual numbers of monitored births are listed in [Supplementary Table S1](#) (available at <https://weekly.chinacdc.cn/>). Data were collected using standardized national protocols with multilevel quality control at the hospital, provincial, and national levels (8–9).

NTD cases were classified into three major subtypes: anencephaly (ICD-10: Q00), encephalocele (Q01), and spina bifida (Q05). The urban-rural classification was based on maternal residence; northern and southern China were defined by the Qinling Mountain–Huaihe River Line (10). The original monitoring data were sorted and restructured to establish a dataset for analysis. The variables included in the final dataset were calendar year (variable name: t ; 2006–2024), geographic and urban-rural stratification (x_1 ; north-urban, north-rural, south-urban, and south-rural), NTD subtype (x_2), maternal age group (x_3 ; <20, 20–24, 25–29, 30–34, and ≥ 35 years), number of births (n_{lbs}), number of affected cases (y_1), and number of affected cases surviving within 7 days after birth (y_2).

Perinatal prevalence was defined as the NTD case count per 10,000 perinatal births. Perinatal survival was defined as the 7-day postnatal survival proportion of NTD-affected cases. Bayesian Poisson regression models were applied to estimate the annual perinatal NTD prevalence and survival rates stratified by geography (north *vs.* south) and residence (urban *vs.* rural). For the prevalence estimation model, a log link function was applied for the dependent variable y_1 with an offset term $\exp(n_{lbs})$. Predictors included time t and t^2 ; covariates x_1 , x_2 , and x_3 ; and interaction terms x_1t and x_2t . For the perinatal survival rate estimation model, as several subgroups contained no NTD exposures and thus had zero denominators for

calculating survival rates, cases and survival events were pooled across age groups to ensure reliable model estimation. $\text{Log}(y_2)$ with y_1 as the offset and predictors t , t^2 , x_1 , x_2 , x_1t , and x_2t were used. Interaction terms were incorporated, given the distinct temporal trends in NTD prevalence and perinatal survival across subtypes, regions, and urban-rural settings (11). Bayesian estimates of NTD prevalence and survival rates with 95% uncertainty intervals (UIs) were obtained from 10,000 Markov Chain Monte Carlo posterior samples. Joinpoint regression was applied to identify temporal changes and estimate phase-specific annual percentage changes (APCs).

Bayesian analyses were performed using Stata (version 17.0; StataCorp LLC, College Station, Texas, USA), and Joinpoint regression analyses were conducted using the Joinpoint Regression Program (version 6.0.1; National Cancer Institute, Bethesda, MD, USA).

RESULTS

The estimated perinatal prevalence of NTDs in China declined from 8.84 per 10,000 births in 2006 to 0.77 per 10,000 births in 2024, representing an overall reduction of 91.29% (Figure 1). Joinpoint analysis identified two statistically significant inflection points in 2009 and 2016, defining three consecutive trend segments (2006–2009, 2009–2016, and 2016–2024), with the APC accelerating from –10.43% during 2006–2009 to a peak of –16.08% during 2009–2016, followed by a slower decline of –10.60% during 2016–2024 (Table 1). Similar trends were observed for all major NTD subtypes. Anencephaly consistently demonstrated the steepest annual reduction across all periods. Spina bifida remained the predominant subtype, with its prevalence decreasing from 4.90 to 0.54 per 10,000 births during 2006–2024. The prevalence of anencephaly declined from 2.57 to 0.14 per 10,000 births, while that of encephalocele decreased from 1.39 to 0.09 per 10,000 births.

Marked reductions in north-south and urban-rural disparities in NTD prevalence were observed (Figure 2). In 2006, the prevalence in northern China was higher than that in southern China (12.56 *vs.* 5.43 per 10,000 births), with a corresponding prevalence ratio of 2.31 (95% UI: 1.92, 2.81). By 2024, the prevalence decreased to 0.73 per 10,000 births in the north and 0.80 per 10,000 births in the south, with a prevalence ratio of 0.90 (95% UI: 0.62, 1.28). Similarly, the estimated prevalence in rural areas

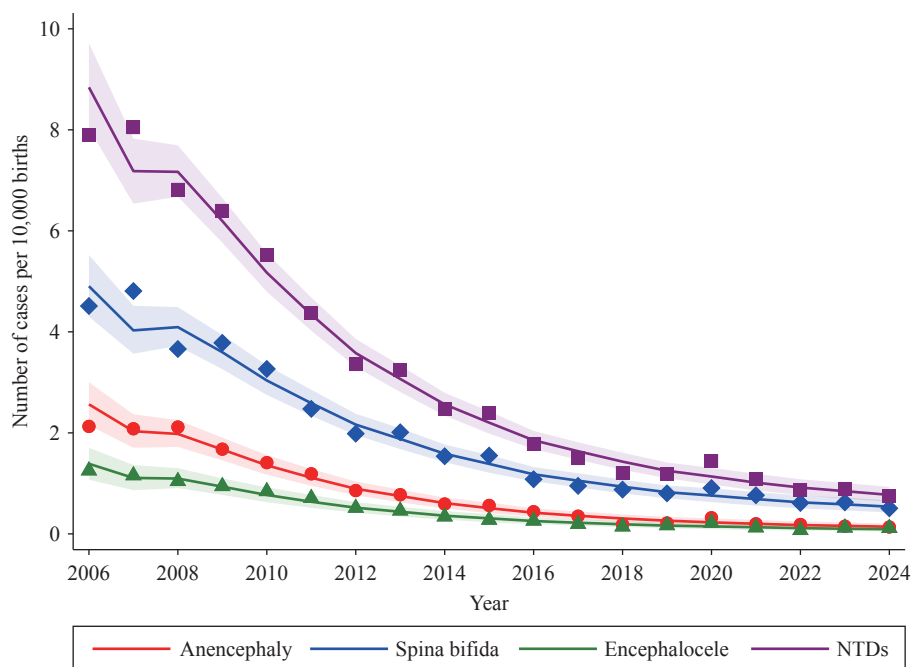


FIGURE 1. Temporal trends in perinatal prevalence of neural tube defects and major subtypes in China, 2006–2024. Note: Dots represent observed rates, and solid lines represent Bayesian posterior median estimates. Abbreviation: NTDs=Neural tube defects.

TABLE 1. Annual percentage change in the perinatal prevalence of all neural tube defects and the major subtypes across three study periods in China, 2006–2024.

Phenotype	Stage 1 (2006–2009)	Stage 2 (2009–2016)	Stage 3 (2016–2024)
Anencephaly	–12.60 (–14.85, –8.78)	–18.17 (–20.65, –17.35)	–13.01 (–14.60, –10.20)
Spina bifida	–9.04 (–11.48, –4.86)	–14.95 (–17.19, –14.14)	–9.55 (–10.89, –7.56)
Encephalocele	–11.59 (–13.95, –7.44)	–17.19 (–19.82, –16.35)	–12.05 (–13.61, –9.35)
Total NTDs	–10.43 (–12.79, –6.54)	–16.08 (–18.35, –15.27)	–10.60 (–12.01, –8.53)

Note: Values in parentheses represent the 95% confidence intervals. Abbreviation: NTDs=Neural tube defects.

(16.27 per 10,000 births) was nearly three times higher than that in urban areas (4.99 per 10,000 births) in 2006. By 2024, the urban-rural prevalence ratio had declined to 1.29 (95% *UI*: 0.89, 1.84), with the 95% *UI* including 1, suggesting no statistically significant urban-rural gap in NTD prevalence.

The estimated NTD perinatal survival rate substantially increased during the study period (Figure 3). By subtype, the perinatal survival rate of anencephaly remained persistently low (<10.00%). In comparison, the survival rate improved markedly for spina bifida (30.43% to 54.84%) and encephalocele (27.71% to 57.14%). The overall NTD perinatal survival rate increased from 23.33% to 46.76% during the study period. Perinatal survival rate improvements were observed in both urban (from 25.46% to 49.40%) and rural (21.82% to 41.07%) settings, with rates being slightly higher in urban *vs.* rural

populations. Given the substantial overlap of the 95% *UIs*, no statistically significant urban-rural differences were observed (Supplementary Figure S1, available at <https://weekly.chinacdc.cn/>).

DISCUSSION

This study extends previous national surveillance studies by applying Bayesian methods to characterize the long-term trends in NTD prevalence, geographic disparities, and perinatal survival (9,12). The results revealed substantial reductions in NTD prevalence and geographic disparities, along with improvements in perinatal survival over time. These findings reflect a shift in public health priorities, transitioning from primary incidence reduction to enhanced clinical management and supportive care for NTD survivors.

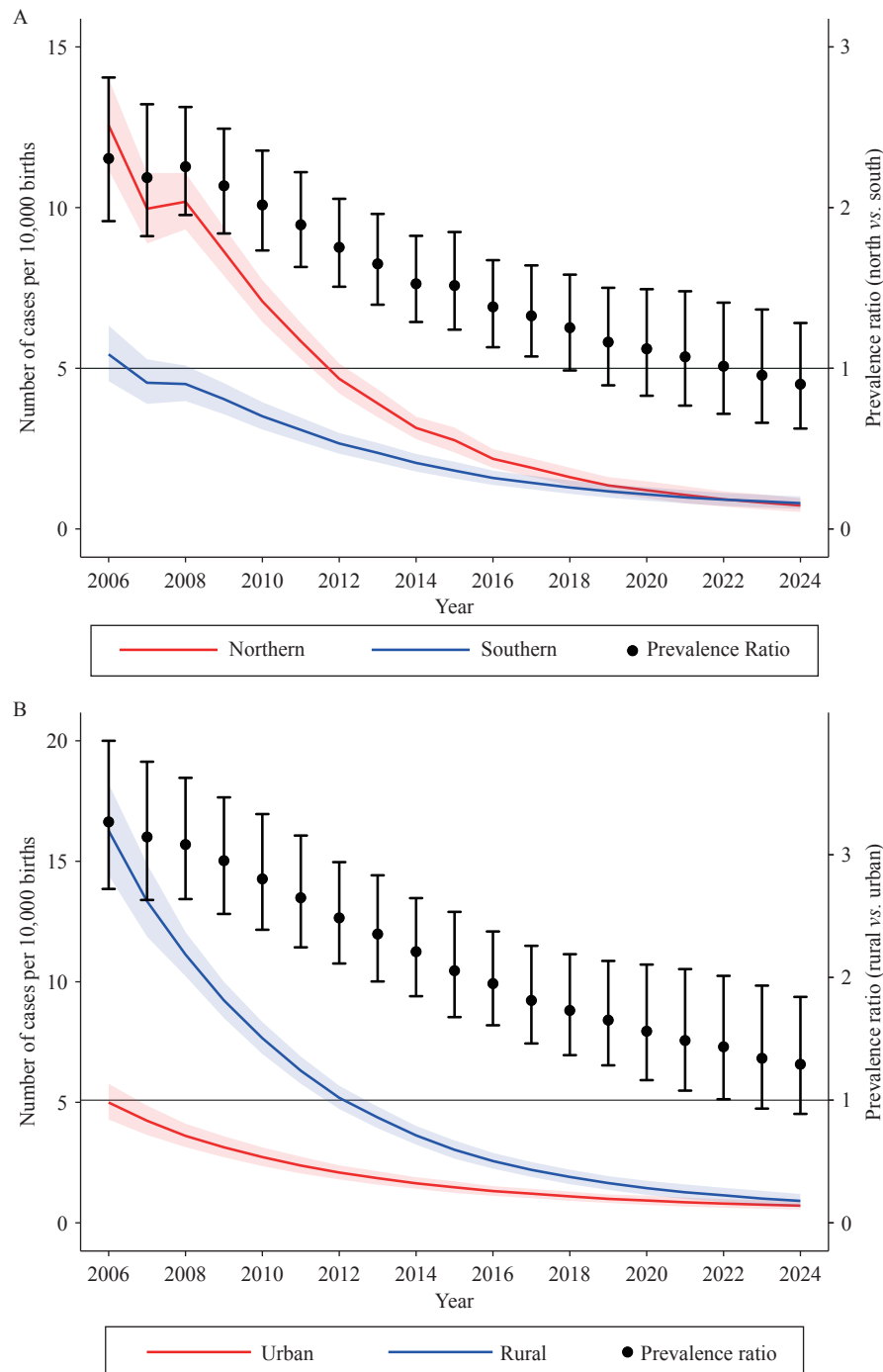


FIGURE 2. Geographic and urban-rural differences in the perinatal neural tube defect prevalence in China, 2006–2024. (A) North-south differences. (B) Urban-rural differences. Abbreviation: NTD=Neural tube defect.

China's rapid decline in perinatal NTD prevalence may have been driven by the nationwide expansion and improvement of birth defect prevention and control measures. Since 2009, nationwide folic acid supplementation programs have progressively expanded from rural to urban areas. From 2000–2004 to 2011–2012, periconceptional folic acid use

increased from 15% to 85% in high-NTD-prevalence areas and from 66% to 92% in low-prevalence areas (13). The free pre-pregnancy health screening program was piloted in 100 counties in 2010. It had expanded to all counties and districts across China by 2013, covering rural couples planning pregnancy with a target population coverage rate of >80%. By 2016, the

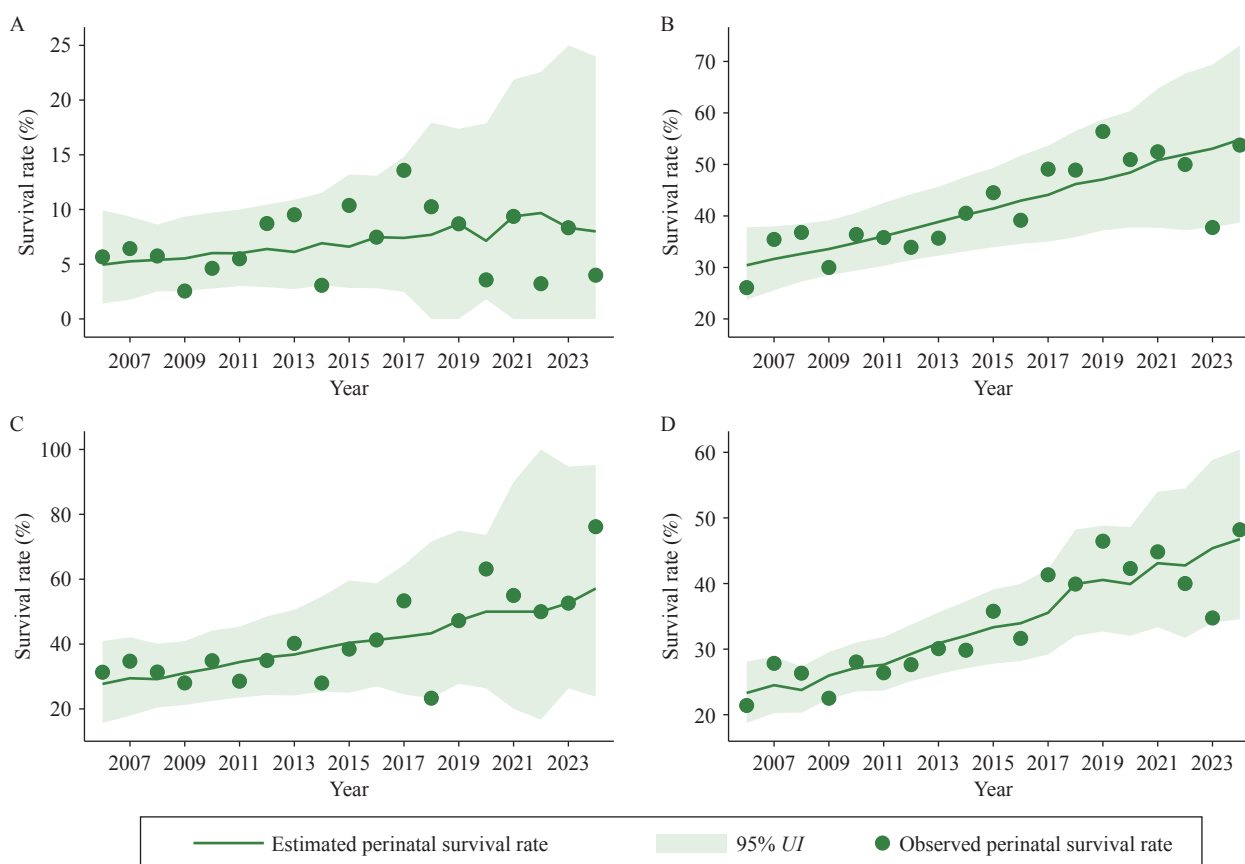


FIGURE 3. Temporal trends in perinatal survival rates of all neural tube defects and the major subtypes in China, 2006–2024. The panels show the survival rates for (A) anencephaly, (B) spina bifida, (C) encephalocele, and (D) NTDs. Note: Dots represent observed rates, and solid lines represent Bayesian posterior median estimates. Abbreviation: NTDs=Neural tube defects; UI=Uncertainty interval.

coverage rate had increased to 93.5%. The quick growth in coverage may explain the rapid decline in NTD prevalence (7). The first National Health Industry Standard for prenatal NTD screening and diagnosis was released in 2010. The 2012 guidelines promoting universal prenatal ultrasound screening, especially for severe anomalies, significantly improved the ability of prenatal screening institutions to detect NTDs. By 2020, second-trimester ultrasound screening coverage exceeded 80%, and maternal serum alpha-fetoprotein screening coverage for NTDs increased from 8.4% (2007) to 65.9% (2020) (14). These interventions were initially implemented between 2009 and 2012, likely explaining the rapid decline in NTD prevalence that was observed during this period.

Globally, the NTD prevalence has declined substantially, particularly in countries implementing folic acid fortification and maternal health interventions. For example, following mandatory folic acid fortification, the United States and Canada

reported marked declines in NTD prevalence, with recent estimates stabilizing at approximately 4–7 per 10,000 births. Beyond these interventions, growing evidence indicates that comprehensive pre-conception care may further reduce the risk of structural birth defects (15–16). However, international comparisons should be interpreted cautiously, because surveillance definitions differ substantially. Most countries report the total birth prevalence across all gestational ages, potentially leading to lower observed prevalence estimates.

Historical NTD disparities in northern and rural China likely reflected underlying biological, health awareness, environmental, nutritional, and healthcare factors, as they predated widespread prenatal screening (10). With socioeconomic progress and ongoing efforts to equalize public health services nationwide, the universal use of folic acid, better nutrition, and improved maternal and child healthcare services have jointly reduced the north-south and urban-rural disparities attributed to uneven dietary conditions and

healthcare accessibility (3,5). Moreover, cross-regional population mobility and population intermixing may have modestly diluted historically localized genetic susceptibilities, although this hypothesis warrants further investigation (17). However, improved prenatal diagnosis and early termination may have contributed to the observed North-South and urban-rural differences in perinatal NTD prevalence in the last decade. Nevertheless, it remains unclear whether these NTD prevalence gaps have been completely eliminated at the economic or provincial level.

The increased survival among non-lethal NTD subtypes reflects a shift in public health priorities from mortality prevention to long-term care. These improvements likely resulted from advances in fetal anomaly screening, prenatal diagnosis, perinatal management, and neonatal surgery (18). As NTD cases become increasingly rare, annual survival estimates become more susceptible to random variations and should be interpreted cautiously.

This study has some limitations. First, potential selection bias may exist owing to the hospital-based surveillance design. Second, the effects of specific prevention policies could not be evaluated quantitatively. Third, the north-south classification may not capture provincial-level heterogeneity.

In conclusion, from 2006 to 2024, China demonstrated substantial reductions in the prevalence of perinatal NTD, with marked reductions in geographic and socioeconomic disparities. Future public health programs may need to focus on addressing residual risk factors while expanding long-term rehabilitation and supportive care.

Conflicts of interest: No conflicts of interest.

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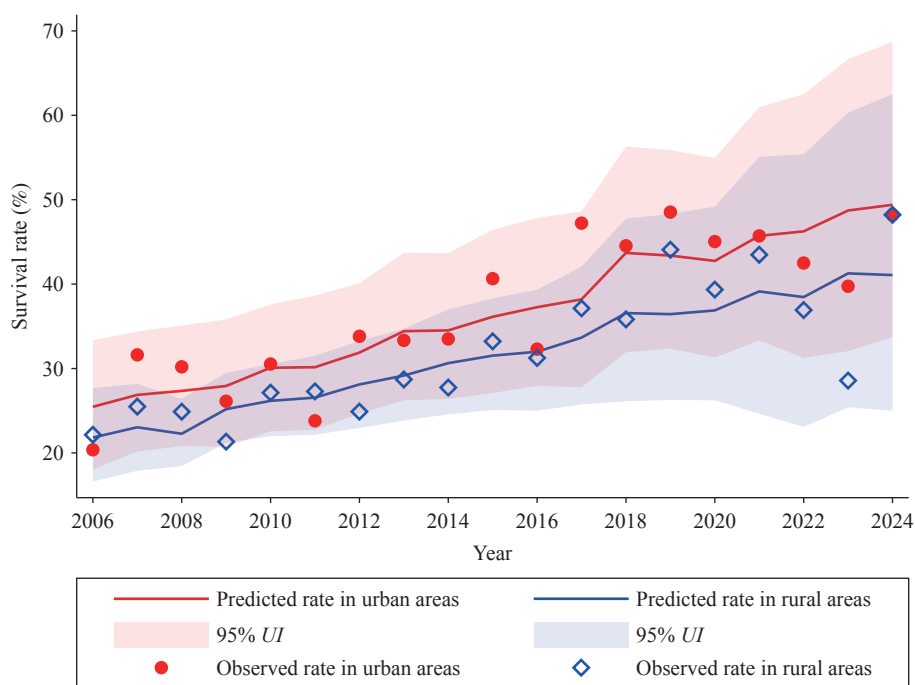
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SUPPLEMENTARY MATERIALS

SUPPLEMENTARY TABLE S1. Annual number of births and NTD cases by geographic region in China, 2006–2024.

Year	Total births	North China births	South China births	Total NTD cases
2006	662,761	316,835	345,926	523
2007	821,468	397,376	424,092	661
2008	1,314,091	615,749	698,342	896
2009	1,401,331	658,900	742,431	897
2010	1,531,143	710,112	821,031	845
2011	1,681,096	766,755	914,341	735
2012	2,005,526	915,846	1,089,680	673
2013	1,893,854	859,802	1,034,052	615
2014	2,198,818	1,026,846	1,171,972	543
2015	1,883,843	760,598	1,123,245	450
2016	2,432,979	1,090,669	1,342,310	433
2017	2,315,621	986,088	1,329,533	346
2018	2,097,800	881,155	1,216,645	253
2019	2,143,629	922,797	1,220,832	254
2020	1,751,281	721,170	1,030,111	253
2021	1,596,171	661,292	934,879	174
2022	1,666,779	692,032	974,747	145
2023	1,572,552	643,425	929,127	141
2024	1,837,817	779,115	1,058,702	139

Abbreviation: NTD=Neural tube defect.



SUPPLEMENTARY FIGURE S1. Urban-rural differences in perinatal survival rates of all neural tube defects in China, 2006–2024.

Abbreviation: NTDs=Neural tube defects; UI=Uncertainty interval.