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The analysis for the neonatal mortality and leading causes of deaths in China from 2014 to 2018

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Abstract

Objective: The present study estimated the national and urban-rural levels and causes of neonatal deaths in China annually between 2014 and 2018 to provide data support for the further end of preventable neonatal deaths for China and other low-and middle-income countries.

Methods: The study was based on data from the National Maternal and Child Health Surveillance System (NMCHSS). All neonates of surveillance districts (gestational week ≥ 28weeks) who died after delivery have been involved in the study. The mortality rate and the leading causes of death for neonates were analyzed.

Results: The NMR of China has steadily decreased from 5.9 deaths per 1000 live births in 2014 to 3.9 deaths per 1000 live births in 2018. The NMR in 2018 of urban and rural areas was 2.2 deaths per 1000 live births and 4.7 deaths per 1000 live births, respectively. The leading preventable death causes of neonatal deaths in 2018 were preterm birth (106.6 deaths per 100,000 live births), intrapartum complications (84.6 deaths per 100,000 live births), and pneumonia (35.0 deaths per 100,000 live births). Mortality rates of these three causes fell significantly between 2014 and 2018, but contributed to a higher proportion of deaths in rural areas than urban areas. The proportion of preventable deaths accounted for 73.9% in 2018.

Conclusions: The NMR of China has decreased steadily from 2014 to 2018. However, the inequality between urban and rural areas still exists. The goal of government interventions

should be to reduce the health inequality of neonates and further take targeted measures to eliminate the preventable neonatal death.

Keywords: neonatal mortality, leading cause, Surveillance, inequality, China

Strengths and limitations of this study

- The study covers the most geographically extensive newborn population in mainland China, the data are from 334 National Maternal and Child Health Surveillance Districts.
- The study provides describes the status of neonatal deaths in China from 2014 to 2018.
- The study has not covered pre-natal assessment due to system design limitation.

Introduction

In 2015, the United Nations (UN) summit on sustainable development formally adopted the 2030 agenda for sustainable development. The UN has proposed 17 sustainable development goals (SDG) from three key economic, social, and environmental dimensions. In SDG3, the goal is to end preventable neonatal and under-five children deaths by 2030[1], with all countries aiming to reduce neonatal mortality to at least as low as 12 deaths per 1,000 live births and under-five mortality to at least as low as 25 deaths per 1,000 live births. The importance of newborn health issues has received global attention. The Chinese government has always attached great importance to the survival, protection, and development of children, and has made great achievements in reducing child mortality.

The MDG4 (Millennium Development Goal 4) was achieved eight years ahead of schedule in 2007[2-7], and it is also rated by the World Health Organization as a country with "high performance in maternal and child health". In 2018, the mortality rate of children under five (U5MR) in China was 8.4‰, which was lower than 25 per 1000 live births by 2030[8]. The biggest challenge for China in the face of the SDGs is to eliminate preventable neonatal and children under 5 deaths. This study will analyze neonatal mortality trends and its mortality of major causes of death in China from 2014 to 2018 to provide data support for the further elimination of key preventable diseases that can cause neonatal deaths.

Materials and Methods

Study subjects

The study covered all the 334 districts of National Maternal and Child Health Surveillance Districts (with 124 urban districts and 210 rural districts) in 31 provinces, autonomous regions, and municipalities of China. Further details about the National Maternal and Child Health Surveillance System (NMCHSS) have been described elsewhere[9].

All neonates of surveillance districts (gestational week ≥ 28weeks) who died after delivery, and had one of the four vital signs would be involved in surveillance subject, including heartbeat, breath, umbilical cord pulsation, and voluntary muscle contraction. The surveillance subject also includes adoption children and children of non-local household residents whose mothers have living in the surveillance districts for more than one year.

Data collection and quality control

After each child died in the surveillance districts, the local village doctor (or community doctor) needs to report to the local township health centers (or community health service centers) within 10 days. Local township health centers (or community health service centers) need to be verified within 7 days after reporting and fill the Child Death Report Card based on the hospital's death diagnosis. If the child died at home or on the way to the health facilities, infer the cause of death would base on 2016 WHO Verbal Autopsy

Standards[10] and then fill the Child Death Report Card. The classification of diseases according to the international classification of diseases-10 (ICD-10).

The children's mortality data was reported level by level, and the data is timely reported through the network direct reporting system. Technical personnel responsible for monitoring work are set up at all levels to complete the collection, review, and operation of surveillance data. The completed child death data would send to the county (or district) level maternal and child health institutions each season. The county (or district) level maternal and child health institutions would report the local child deaths status to prefecture-level and province-level maternal and child health institutions each season, the National Office of Maternal and Child Health would summarize and analyzes the data finally.

For quality control, we have used the regular level-by-level on-site quality control system. At the county (district), city, and provincial levels, following the requirements of the Chinese Maternal and Child Health Surveillance Work Manual, a multi-source data cross-check method is used to complete the on-site quality control work in sampling surveillance districts. The National Office of Maternal and Child Health will select 18 districts in 6 provinces each year for quality inspection[9,11].

Statistical analysis

Results were collected in Microsoft Excel and analyzed using SPSS 22.0 (IBM, Armonk, NY, USA). The neonatal mortality rates (NMR) of different regions and the main cause-specific mortality rates were corrected using the average underreporting rate of the national-level surveillance data quality checks in the past three years. The national NMR and the main cause-specific mortality rate were weighted calculated according to the proportion of the urban and rural population in the census. The diagnostic level composition ratio of the neonate is calculated based on the reported Child Death Report Card, excluding children who died of accidental injuries[11].

The Poisson regression model was used to calculate the average annual rate of decline of NMR, cause-of-death mortality, and its 95% confidence interval in the country, urban and rural areas, respectively. Linear by the linear association in the chi-square test using SPSS software was used to test whether there was a linear downward trend in different regions and causes of death.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of West China Second University Hospital, Sichuan University, China.

Patient and public involvement

Patients and members of the public were not involved in the design of this study.

Data Availability Statement

This study used data from the NMCHSS. This system is co-established by the National Health and Family Planning Commission of the People Republic of China and Sichuan University, and finally owned by National Health and Family Planning Commission of the People Republic of China. The researchers did not obtain consent to publicly share data. The de-identified data set is available upon request to interested researchers. For data requests, please contact the Department of Science and Technology of West China Second University Hospital, Sichuan University, at:fu2yuankjb@163.com.This department is in charge of all the programs in the hospital, including the data management. One staff from the department (named Xian He) monitors this email.

Result

1. The NMR of China from 2014 to 2018

At the national level, the NMR of China has steadily decreased from 5.9 deaths per 1000 live births in 2014 to 3.9 deaths per 1000 live births in 2018（p<0.001）, the average annual rate of decline was 10.7%. The NMR of urban and rural areas have both showed a declining trend in the same period（p<0.001）. The mortality rate of urban areas decreased from 3.5 deaths per 1000 live births to 2.2 deaths per 1000 live births, with the average annual rate of decline was 13.0%. In rural areas, the NMR decreased significantly from 2014 to 2018 (6.9 deaths per 1000 live births to 4.7 deaths per 1000 live births, the average annual rate of decline was 10.6%, p<0.001). The absolute difference between NMR of urban and rural areas has reduced from 3.4 deaths per 1000 live births to 2.5 deaths per 1000 live births, but the relative difference has increased from 2.0 to 2.2. (See **Figure 1**)

2. Cause of neonates mortality in China from 2014 to 2018

Nationwide, compared with 2014, the neonatal deaths caused due to preterm birth, intrapartum complication, and pneumonia in 2018 have sharply decreased. Among the particular diseases, the intrapartum complications have the highest average annual decline rate (AADR) from 2014 to 2018 (with 13.5%, p<0.001). The smallest AADR belonged to Tetanus (with 0.8%, p<0.05). In any given year, preterm birth, intrapartum complication, and pneumonia were the top three leading causes of neonatal death in China, total

accounting for nearly 60%. (See **Table 1**) In 2018, all deaths causes have been divided into preventable diseases and unpreventable diseases to analyses the proportion. The proportion of preventable diseases reached 73.9%. Moreover, the top three diseases at the national level were preterm birth, intrapartum complications, and congenital malformations. (See **Figure 2A**)

Table 1. Leading causes of death in neonates in China from 2014 to 2018

Causes of death	Cause-specific mortality (per 100,000 livebirths)							Proportion (%)				
	2014	2015	2016	2017	2018	Average annual decline rate (%)	P value	2014	2015	2016	2017	2018
National wide												
Preterm birth	170.7	167.2	139.8	144.4	106.6	9.7 (7.4, 11.9)	<0.001	29.1	30.8	28.7	32.2	27.3
Intrapartum complications	141.7	138.5	103.9	92.5	84.6	13.5 (11.0, 15.9)	<0.001	24.2	25.5	21.4	20.6	21.7
Pneumonia	66.1	46.7	55.7	49.1	35.0	11.0 (7.1, 14.7)	<0.001	11.3	8.6	11.4	11	9
Diarrhea	2.2	2.8	1.4	0.2	1.7	20.1 (-2.0, 37.4)	>0.05	0.4	0.5	0.3	0	0.4
Tetanus	0.8	0	0	0	0	N/A	<0.05	0.1	0	0	0	0
HIV	0	0	0	0	0	N/A		0	0	0	0	0
Neonatal sepsis/meningitis	14.5	14.3	19.3	15	19.6	-6.5 (-14.7, 1.2)	>0.05	2.5	2.6	4	3.3	5
Other infectious diseases	1.8	1.1	1.4	0.9	0	33.1 (7.9, 51.4)	<0.05	0.3	0.2	0.3	0.2	0
Congenital malformations	101.7	82.3	91.9	82.8	78.5	5.1 (2.0, 8.1)	<0.01	17.4	15.2	18.9	18.5	20.2
Other diseases	86.1	90	73	63.4	63.8	9.2 (5.9, 12.3)	<0.001	14.7	16.6	15	14.2	16.4
Urban area												
Preterm birth	111.2	92.9	74.5	84.3	63.3	11.4 (7.1, 15.5)	<0.001	31.4	28.6	25.5	31.8	28.8

Intrapartum complications	92	80.2	63.6	61.4	41.2	16.4 (11.8, 20.7)	<0.001	25.9	24.6	21.8	23.2	18.7
Pneumonia	28.8	26.1	34.9	22.9	13.5	12.4 (4.5, 19.7)	<0.01	8.1	8	12	8.6	6.1
Diarrhea	0.6	0.7	0	0.5	0.6	2.7 (-96.6, 51.8)	>0.05	0.2	0.2	0	0.2	0.3
Tetanus	0	0	0	0	0	N/A	N/A	0	0	0	0	0
HIV	0	0	0	0	0	N/A	N/A	0	0	0	0	0
Neonatal sepsis/meningitis	10.2	12.7	16.6	17.5	20.9	2.7 (-96.6, 51.8)	<0.01	2.9	3.9	5.7	6.6	9.5
Other infectious diseases	1.9	2	1.7	1.5	0	25.2 (-7.7, 48.1)	>0.05	0.5	0.6	0.6	0.5	0
Congenital malformations	72.9	64.2	57.3	46.3	41.2	13.6 (8.4, 18.5)	<0.001	20.5	19.7	19.6	17.5	18.7
Other diseases	37.1	46.8	43.5	30.7	39.3	3.2 (-3.7, 9.7)	>0.05	10.5	14.4	14.9	11.6	17.9
Rural area												
Preterm birth	197.2	200.3	168.9	171.3	125.9	9.2 (6.3, 12.1)	<0.001	28.6	31.3	29.5	32.3	27
Intrapartum complications	163.8	164.5	121.9	106.5	104	12.8 (9.5, 15.9)	<0.001	23.8	25.7	21.3	20.1	22.3
Pneumonia	82.8	55.9	64.9	60.8	44.7	10.8 (5.9, 15.5)	<0.001	12	8.7	11.3	11.5	9.6
Diarrhea	2.9	3.8	2	0	2.2	25.5 (-0.3, 44.6)	<0.05	0.4	0.6	0.3	0	0.5
Tetanus	1.2	0	0	0	0	N/A	<0.05	0.2	0	0	0	0
HIV	0	0	0	0	0	N/A	N/A	0	0	0	0	0
Neonatal sepsis/meningitis	16.4	15.1	20.5	13.9	19	-2.3 (-13.2, 7.7)	>0.05	2.4	2.4	3.6	2.6	4.1
Other infectious diseases	1.8	0.6	1.3	0.7	0	29.7 (-13.7, 56.6)	>0.05	0.3	0.1	0.2	0.1	0
Congenital malformations	114.5	90.4	107.3	99.2	95.2	3.0 (-1.2, 6.9)	>0.05	16.6	14.1	18.7	18.7	20.4
Other diseases	108	109.3	86.1	78	74.7	10.3 (6.3, 14.2)	<0.001	15.7	17.1	15	14.7	16.1

The death cause distribution and AADR were also significantly different among regions.

In urban areas, preterm birth, intrapartum complication, and congenital anomalies also accounting the largest proportion of all deaths cause from 2014 to 2018. Moreover, the AADR of preterm birth, intrapartum complications, pneumonia, and congenital malformations in urban areas were all larger than that of the national level. In rural areas, the mortality rate of preterm birth, intrapartum complication, and congenital anomalies significantly decreased. Additionally, the NMR of diarrhea have sharply decreased, with AADR was 25.5% ($p<0.001$). (See **Table 1**)

In contrast, the urban-rural gap still existed. The contribution of tetanus among neonates in urban areas remains zero during the study period, while the rate in rural areas has eliminated until 2015. (See Table 1) In the disease proportion aspect, the proportion of intrapartum complications and pneumonia in rural areas significantly higher than that of urban areas. (See Figure 2B&C) According to the data analysis, causes of neonatal death varied between urban and rural areas ($P<0.05$), but the correlation between neonatal mortality and whether the newborn lived in urban or rural areas was weak (Cramer's $V=0.129$).

3. Neonate Diagnosis Facilities Level in China between 2014 and 2018

The children's diagnosis facilities level has also be included in surveillance. Nationwide, from 2014 to 2018, the proportion of neonate diagnosis at the provincial (or municipal) level health facilities has significantly increased, and the proportion of the district (or

county) level has decreased. Moreover, the proportion of township level and village level have both fluctuating declined during this period. In 2018, the proportion of neonate who has not to seek any medical care has minimized, which declined to 3.9% in 2018. (See **Figure 3**)

In an urban aspect, from 2014 to 2018, the majority of children (accounted for over 80%) in urban areas have been diagnosed at provincial (or municipal) level medical facilities. The proportion of the district (or county) level and township -level both have a slight rise between 2014 and 2018. As a result, the percentage of children who have not to seek medical has declined, with 1.9% in 2014 and 1.1% in 2018. (See **Figure 3**)

On the contract, the diagnosis contribution figure of rural areas was different. Although the proportion of provincial (or municipal) level have shown growth trend from 2014 to 2018, the proportion in rural areas have only half of that in urban areas. Moreover, the proportion of street-level diagnoses in the urban area is reduced to 1.4% in 2018, while this proportion in rural areas fluctuated and remained at 3.7% in the same year. Another significant contributor is the proportion of children who have not sought medical care. The proportion of neonate who has not to seek medical care has decreased, and still, 5.5% of children have not sought any medical advice. (See **Figure 3**)

Discussion

Globally, there were 5.3 million deaths occurred on children under 5 in 2018, 47% of them died during their first month of life. The vast majority of neonatal deaths occur in low - and middle-income countries. Approximately 73,000 neonates died in China in 2018, accounting for about 3.0% of the total newborn deaths worldwide, ranking sixth in the world[12]. Moreover, the global decline in neonatal mortality rate (NMR) has been slower than the decline in the under-five mortality rate (U5MR)[6]. Global U5MR declined from 93 per 1,000 live births in 1990 to 39 per 1,000 live births in 2018, while that of NMR only declined from 37 per 1,000 live births to 18 per 1,000 live births during the same time period. Additionally, a great many studies have shown that neonatal deaths amounting a large proportion of total mortality of children under 5[13-15]. Furthermore, SDGs (Sustainable Development Goals) have targeted specifically for reducing neonatal mortality and eliminating preventable child deaths in 2015[1].

The results of this study show that the NMR in urban and rural areas of China have decreased significantly between 2014 and 2018. According to the NMR data from World Bank in 2018[14], although Chinese NMR (3.9 deaths per 1000 live births in 2018) is at a low level in developing countries (such as the NMR in Brazil was 8.1 deaths per 1000 live births, and Thailand was 5.0 deaths per 1000 live births), it still lags behind that in

developed countries (such as the NMR in Australia was 2.3 deaths per 1000 live births, and Germany was 2.2 deaths per 1000 live births). In order to further shorten the gap with developed countries, there is still room for improvement in neonatal deaths in China. In addition, there were significant differences in NMR between urban and rural areas, which were consistent with significant differences in NMR between countries and regions globally[16,17].

From 2014 to 2018, Chinese NMR continued to decline, and it was dropped quickly. This is closely related to the rapid growth of China's economy[18], the continuous improvement of transportation, and the improvement of the educational level of women at reproductive age[19]. Moreover, it also benefits from the improvement of medical treatment at all levels of health facilities, and all levels of government attached great importance to strengthen the construction of the pediatric institution, raise pediatricians' payment, and continue to implement neonatal asphyxia recovery training program[20]. As a result, neonatal deaths from pneumonia and infectious diseases, intrapartum complications, and premature delivery were significantly reduced.

China has implemented the Safe Maternal Initiative and the National Program to Reduce Maternal Mortality and Eliminate Tetanus, China has officially eliminated neonatal tetanus in 2012[21], and from 2015 to 2018, the NMR of neonatal tetanus remained 0. Moreover,

through the success of the Prevention of Mother-to-child Transmission of HIV, Syphilis, and Hepatitis B Program, the HIV/AIDS mortality rate has also been 0 from 2014 to 2018[22,23]. In 2018 the national neonatal mortality, although already less than 12 deaths per 1000 live births, but the preventable deaths still accounted for 73.9%. Among those preventable diseases, mainly pneumonia, intrapartum complication, premature birth. Among these diseases, the proportion of preterm birth was highest in both nationwide, urban areas, and rural areas. In the recent two decades, the prevalence of preterm birth has significantly increased[9], especially after the Two-child Policy[24] was implemented In China. The mortality rate among preterm birth infants was apparently higher than the full-term infant, and the risk of mortality increases proportionally with decreasing gestational age[25]. Furthermore, with the widespread development of assisted reproductive technique (ART), the incidence of monozygotic twins has increased significantly[26]. The risk of premature birth is significantly higher in ART infants than in infants conceived naturally[27], and the NMR of twins is several times higher than that of singletons[28].

Addressing the issue of preterm birth may require different priorities in rural and urban areas. Because of the good management of many curable neonatal complications (such as pneumonia), the proportion of preterm birth in urban areas is obviously larger than that of rural areas[29]. Hence, for urban areas, it is suggested that urban areas need to pay more attention to the prevention of the death of premature infants less than 32 weeks age. For

rural areas, the local government needs to focus on the prevention of premature infants at 32-36 weeks and continue to invest in medical services to improve medical services accessibility for women and children in rural areas.

In addition, the neonatal mortality rate of preterm birth, intrapartum complication, and pneumonia in rural areas were over doubled than urban areas。 Hence, the government needs to implement the interventions in preterm birth, intrapartum complications, and root, especially in rural areas.

For neonates, surviving from preterm birth, intrapartum complication and pneumonia are close linking to accessibility to health care, local hospitals' obstetrics and neonates departments' treatment level, and rescue skills[30,31]. Therefore, the issue can be addressed from the following four aspects.

Firstly, the local governments need to strengthen the construction of RNTN (Regional Neonatal Transport Network), carry out the transport plan according to the Guidelines for the Construction and Management of Critical Neonatal Treatment Center[32], and ensure the applying of professional medical staff and newborn rescue equipment for neonatal transport. Secondly, one study in Japan has pointed out that the medical care resources

(including Neonatal Intensive Care Unit (NICU), midwives, emergency physicians, and emergency medical care centers) would impact on the NMR decline[33]. Therefore, the local governments may base on the Administration guide (proposal) of the Neonatal Physician Branch of the Chinese Physician Association[34] to grading neonatal wards, and establishing NICU after analyses local medical establishment plan and newborn medical treatment needs. Thirdly, local health departments can regularly organize multi-level，especially provincial, prefecture-level and district-level) newborn health training programs. In rural areas, with the policies support of the New Rural Construction and the Targeted Poverty Alleviation[35,36], the improved rural transport and higher incomes have prompted the enhanced accessibility of health services in rural areas, and the proportion of rural children receiving medical treatment in provincial and municipal hospitals has significantly increased. The proportion of rural neonate diagnosis at the provincial (or municipal) level health facilities has significantly increased from 39.2% to 47.6% from 2014 to 2018. Set training objectives for medical staff in health facilities of different levels, and strengthen the newborn treatment technology in each level of health facilities. Especially for the health workers in rural areas, the newborn resuscitation training needs to be specifically strengthened. Fourthly, the local communities can strengthen publicity to encourage caregivers to take children to attend to the health facilities for treatment. As for poor households, local governments can set up special subsidies for them to reduce the economic cost of medical treatment.

Conclusion

With the joint efforts of the economic development and the governmental policies and strategies, the neonatal mortality rate of China has significantly decreased from 2014 to 2018. The gap between neonatal mortality and cause-of-death distribution still existed between urban and rural areas. The goal of government interventions should be to narrow the urban-rural gap, reduce the health inequality of neonates, and further take targeted measures to eliminate the preventable death of neonates, especially premature births, so as to achieve the SDGs goal.

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Conflicts of interest

The authors declare no conflicts of interest.

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Figure 1. The national and urban-rural neonatal mortality rates (per 1,000 live births) in China between 2014 and 2018

Figure 2A. The proportion of cause-specific neonatal diseases of China in 2018

Figure 2B. The proportion of cause-specific neonatal diseases of urban China in 2018

Figure 2C. The proportion of cause-specific neonatal diseases of rural China in 2018

Figure 3. The proportion of neonatal diagnose level in China from 2014 to 2018

Figure 1. The national and urban–rural neonatal mortality rates (per 1,000 live births) in China between 2014 and 2018

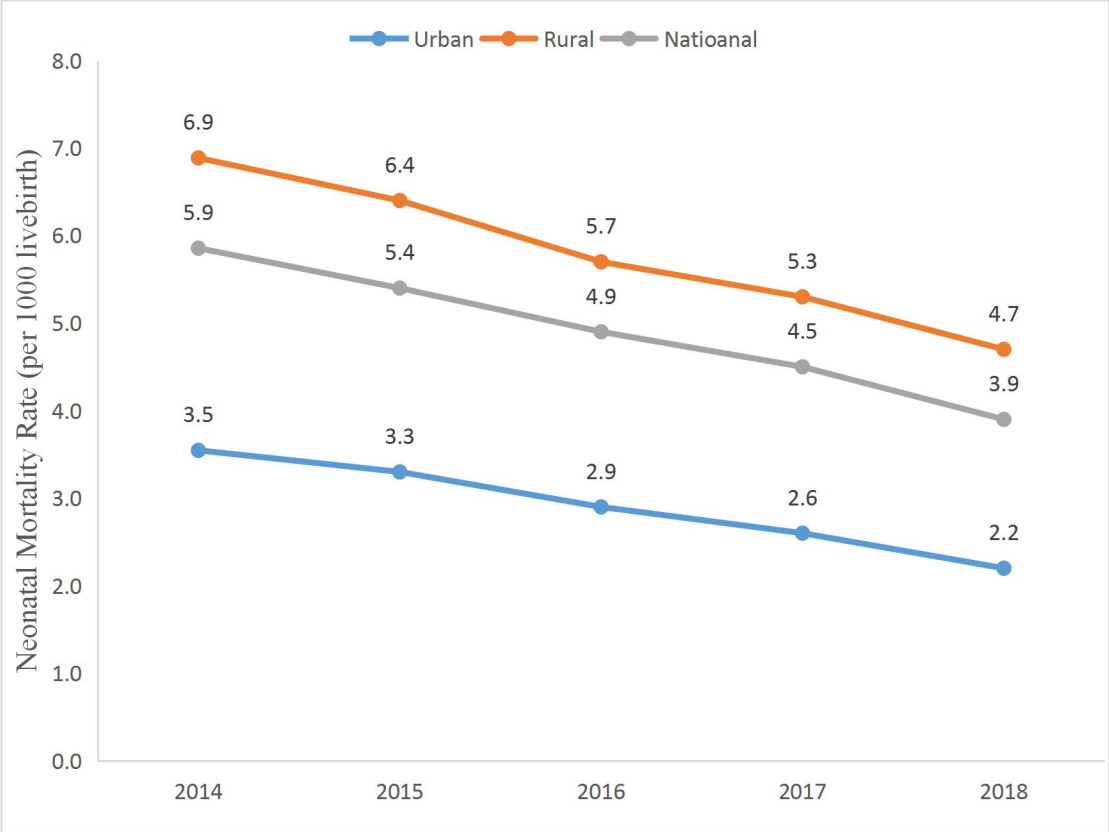


Figure 2A. The proportion of cause-specific neonatal diseases of China in 2018

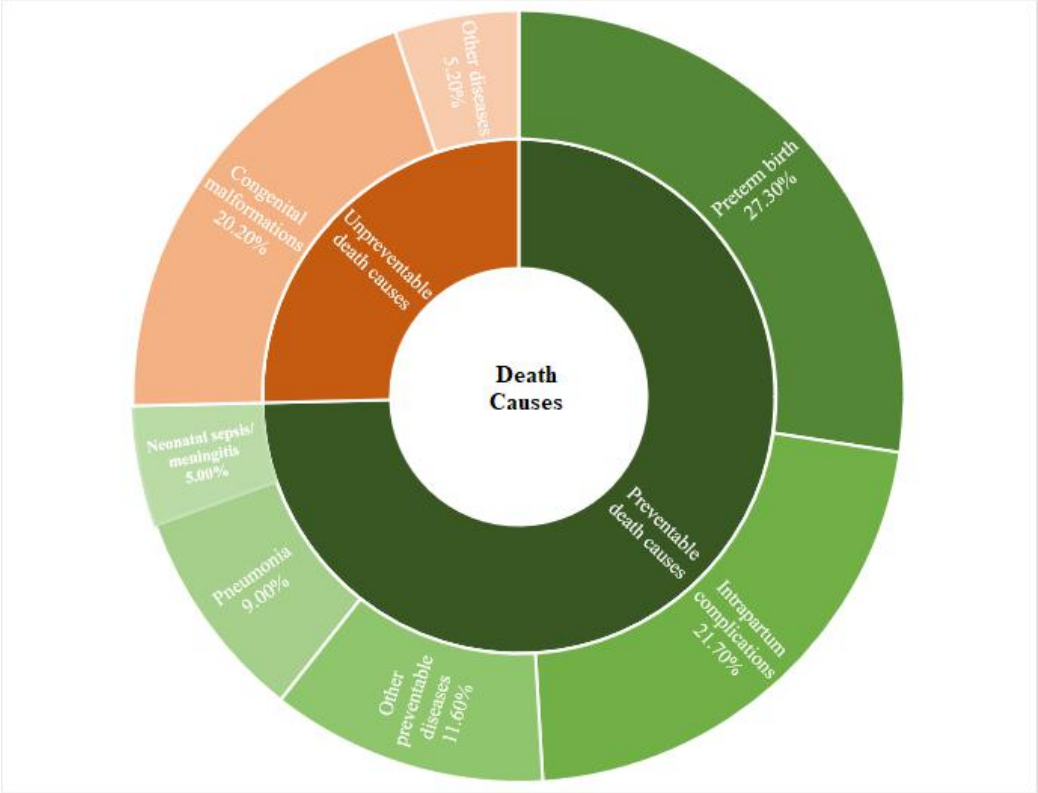


Figure 2B. The proportion of cause-specific neonatal diseases of urban China in 2018

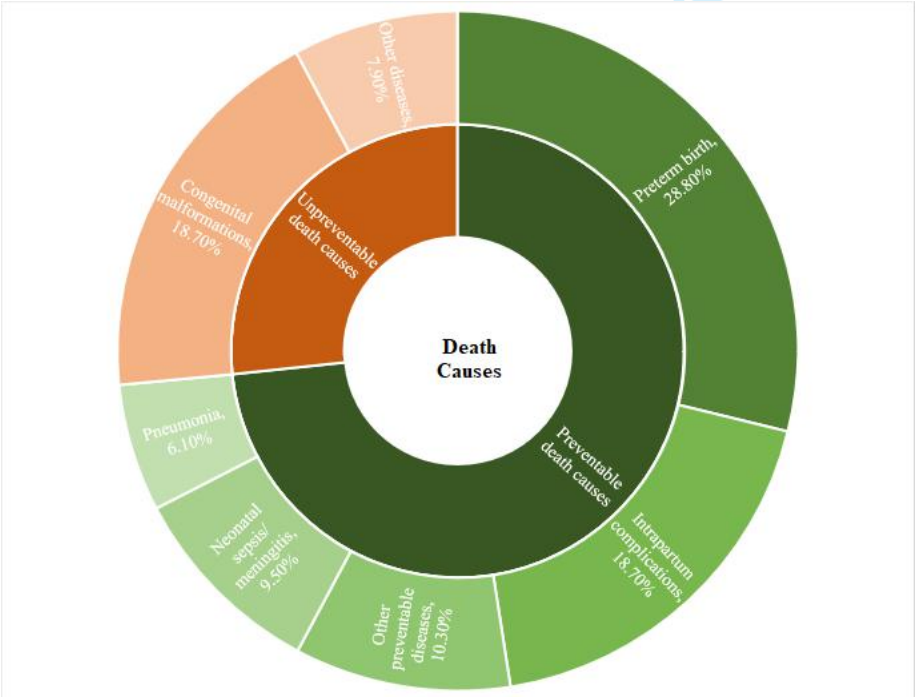


Figure 2C. The proportion of cause-specific neonatal diseases of rural China in 2018

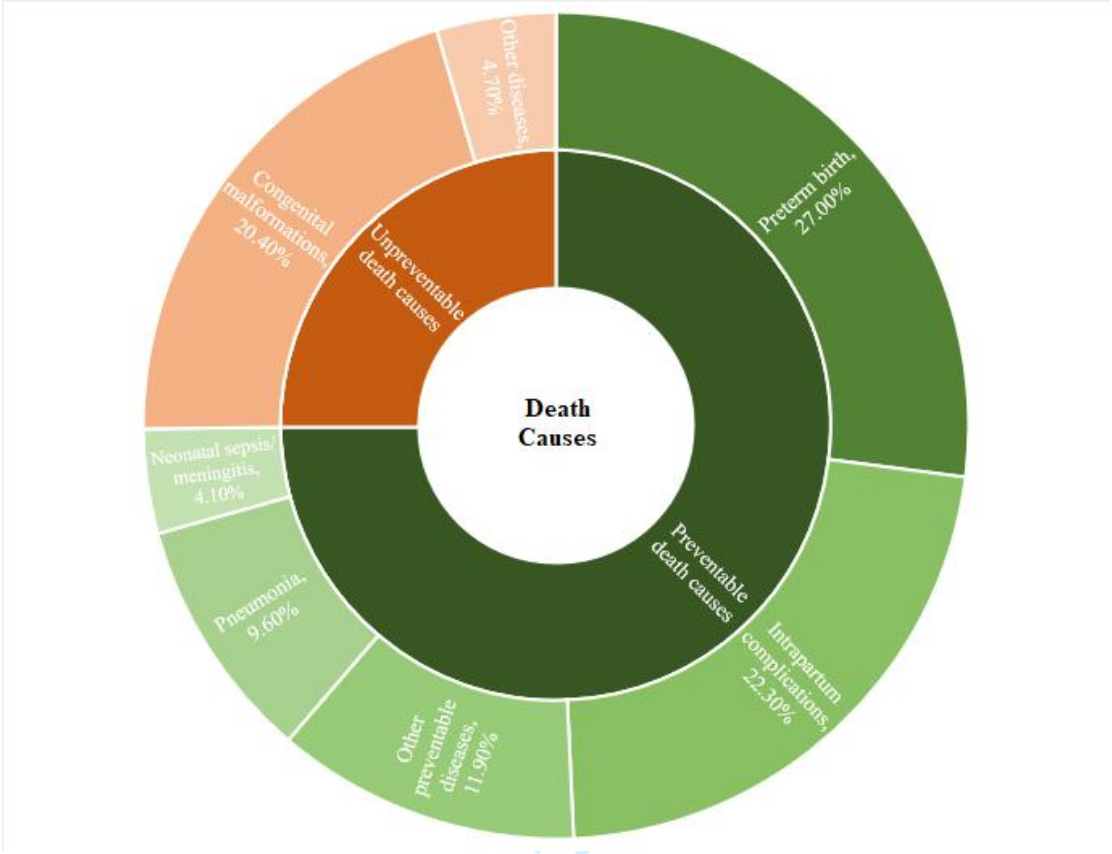
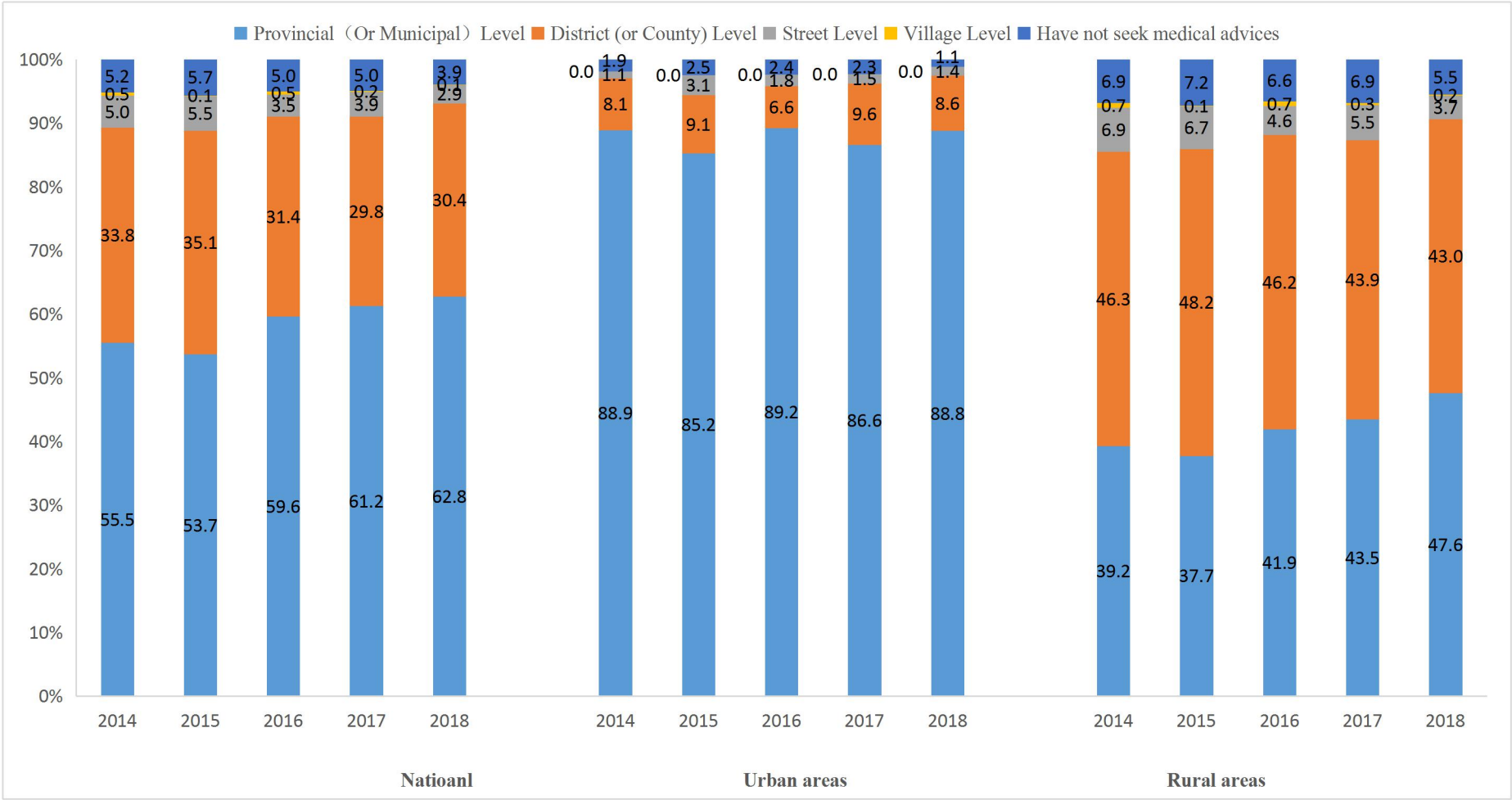


Figure 3. The proportion of neonatal diagnose level in China from 2014 to 2018



STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	a descriptive study
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3	The present study estimated the national and urban-rural levels and causes of neonatal deaths in China annually between 2014 and 2018. The Poisson regression model was used to calculate the average annual rate of decline of NMR, cause-of-death mortality, and its 95% confidence interval in the country, urban and rural areas, respectively. The neonatal mortality rate in China has significantly decreased from 2014 to 2018. The gap between neonatal mortality and cause-of-death distribution still existed between urban and rural areas. The further goal of government interventions need to focus on be to narrow the urban-rural gap and reduce the health inequality of neonates.
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5	Paragraphs 1 to 2 in the introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	5	Paragraphs 2 in the introduction
Methods				
Study design	4	Present key elements of study design early in the paper	6	The data in this study were extracted from National Maternal and Child Health Surveillance System (NMCHSS). **(first paragraph in Study subjects section)**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6	Data used in this study were obtained from NMCHSS, a well-established population-based under-5 child death registry system. The 334 surveillance districts covering 124 urban districts and 210 rural districts in 31 provinces, autonomous regions, and municipalities of China. According to the women's residence, the surveillance sites can be classified into urban areas or rural areas. More details about data collection and quality control have been described elsewhere. **(Study subjects section)**
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and	6-7	After each child died in the surveillance districts, the local village doctor (or community doctor) needs to report to the local township health centers (or community health service centers) within 10 days. Local township health centers (or community health service centers) need to be verified within 7 days after reporting and fill the Child Death Report Card based on the hospital's death diagnosis. The classification of diseases according to the international classification of diseases-10 (ICD-10). **(Data collection and quality control section)**

		the sources and methods of selection of participants		
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6	All neonates of surveillance districts (gestational week ⩾ 28weeks) who died after delivery, and had one of the four vital signs would be involved in surveillance subject, including heartbeat, breath, umbilical cord pulsation, and voluntary muscle contraction. **(Study subjects section)**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6	The data in this study were extracted from National Maternal and Child Health Surveillance System (NMCHSS). **(First paragraph in Study subjects section)**
Bias	9	Describe any efforts to address potential sources of bias	-	-
Study size	10	Explain how the study size was arrived at	6	The data in this study were extracted from National Maternal and Child Health Surveillance System (NMCHSS). **(First paragraph in Study subjects section)**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	-	-
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding		
		(*b*) Describe any methods used to examine subgroups and interactions	8	**Statistical analysis section**
		(*c*) Explain how missing data were addressed		
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy		
		(*e*) Describe any sensitivity analyses		

Continued on next page

Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg	10	During 2014 to 2018, the NMR of China has steadily decreased from 5.9 deaths per 1000 live births in 2014 to 3.9 deaths per 1000 live births in 2018（p<0.001）, the

		numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed		average annual rate of decline was 10.7%. The mortality rate of urban areas decreased from 3.5 deaths per 1000 live births to 2.2 deaths per 1000 live births, with the average annual rate of decline was 13.0%. In rural areas, the NMR decreased significantly from 2014 to 2018 (6.9 deaths per 1000 live births to 4.7 deaths per 1000 live births, the average annual rate of decline was 10.6%, p<0.001). **(the first paragraph in The NMR of China from 2014 to 2018 section)**
		(b) Give reasons for non-participation at each stage	-	-
		(c) Consider use of a flow diagram	-	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10	**Results section**
		(b) Indicate number of participants with missing data for each variable of interest	-	-
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	-	-
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time		
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures	10-14	**Results section**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-14	**Results section**
		(*b*) Report category boundaries when continuous variables were categorized	-	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-	-
Discussion				
Key results	18	Summarise key results with reference to study objectives	15	**Discussion section**
Limitations	19	Discuss limitations of the study, taking into account sources of	-	-

		potential bias or imprecision. Discuss both direction and magnitude of any potential bias		
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-19	**Discussion section**
Generalisability	21	Discuss the generalisability (external validity) of the study results	15-19	**Discussion section**
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	20	This study was supported by the Department of Women and Children of the National Health Commission of China, and UNICEF.

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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

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Neonatal mortality and leading causes of deaths: a descriptive study in China, 2014-2018

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, NEONATOLOGY

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Neonatal mortality and leading causes of deaths: a descriptive study in China, 2014-2018

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Abstract

Objective: The present study estimated the national and urban-rural levels and causes of neonatal deaths in China annually between 2014 and 2018 to provide data support for the further end of preventable neonatal deaths for China and other low-and middle-income countries.

Methods: The study was based on data from the National Maternal and Child Health Surveillance System (NMCHSS). All neonates of surveillance districts (gestational week ≥ 28weeks) who died after delivery have been involved in the study. The mortality rate and the leading causes of death for neonates were analyzed.

Results: The NMR of China has steadily decreased from 5.9 deaths per 1000 live births in 2014 to 3.9 deaths per 1000 live births in 2018. The NMR in 2018 of urban and rural areas was 2.2 deaths per 1000 live births and 4.7 deaths per 1000 live births, respectively. The leading preventable causes of neonatal deaths are the same in the urban and rural areas were same, which were preterm birth, intrapartum complications, and pneumonia. Mortality rates of these three causes fell significantly between 2014 and 2018 but contributed to a higher proportion of deaths in rural areas than urban areas. The proportion of preventable deaths accounted for 73.9% in 2018.

Conclusions: The NMR of China has decreased steadily from 2014 to 2018. However, the inequality between urban and rural areas still exists. The goal of government interventions

should be to reduce the health inequality of neonates and further take targeted measures to eliminate preventable neonatal death.

Keywords: neonatal mortality, leading cause, Surveillance, inequality, China

Strengths and limitations of this study

- This is the first study to show the status of neonatal deaths in China from 2014 to 2018.
- The study covers the most geographically extensive newborn population in mainland China.
- The data from the National Maternal and Child Health Surveillance System used in this study have been shown to be representative of mainland China and to be of high quality for the recording of death causes of children under 5.
- The system has not covered the pre-natal assessment due to design limitations.

Introduction

In 2015, the United Nations (UN) summit on sustainable development formally adopted the 2030 agenda for sustainable development. In SDG3, the goal is to end preventable neonatal and under-five child deaths by 2030[1], with all countries aiming to reduce neonatal mortality to at least as low as 12 deaths per 1,000 live births and under-five mortality to at least as low as 25 deaths per 1,000 live births. The importance of newborn health issues has received global attention. The Chinese government has always attached great importance to the survival, protection, and development of children, and has made great achievements in reducing child mortality. Professional institutions for maternal and child health care began to be established in 1950[2]. Moreover, the Chinese government has taken U5MR, IMR, and other indicators of children's health as assessment targets for provincial governments, and has promulgated the National Program of Action for Child Development in China every decade since 1990s[2,3].

Globally, there were 5.3 million deaths occurred on children under 5 in 2018, 47% of them died during their first month of life. The vast majority of neonatal deaths occur in low - and middle-income countries. Approximately 73,000 neonates died in China in 2018, accounting for about 3.0% of the total newborn deaths worldwide, ranking sixth in the world[4]. Moreover, the global decline in neonatal mortality rate (NMR) has been slower than the decline in the under-five mortality rate (U5MR)[6]. Global U5MR declined from 93 per 1,000 live births in 1990 to 39 per 1,000 live births in 2018, while that of NMR only

declined from 37 per 1,000 live births to 18 per 1,000 live births during the same period. Additionally, a great many studies have shown that neonatal deaths amounting to a large proportion of total mortality of children under 5[5-7]. Therefore, reducing preventable neonatal deaths is important to further reduce the U5MR.

China has achieved the MDG4 (Millennium Development Goal 4) eight years ahead of schedule in 2007[8-13], and it is also rated by the World Health Organization as a country with "high performance in maternal and child health". In 2018, the NMR of China was 3.9 deaths per 1000 live births, which was lower than the target of SDG3[14]. However, according to the NMR data from World Bank in 2018, the NMR of China is at a low level in developing countries (such as the NMR in Brazil was 8.1 deaths per 1000 live births, and Thailand was 5.0 deaths per 1000 live births), it still lags behind that in developed countries (such as the NMR in Australia was 2.3 deaths per 1000 live births, and Germany was 2.2 deaths per 1000 live births)[15]. Moreover, since urban areas generally have better economic development than rural areas, resulting in better health service infrastructure and health service infrastructures[16], there is an urban-rural inequity in neonatal mortality in China[17]. To further shorten the gap with developed countries, and reduce the difference in neonatal mortality between urban and rural areas, there is still room for improvement in neonatal deaths in China. This study will analyze neonatal mortality trends and its mortality of major causes of death in China from 2014 to 2018 to provide data support for the further elimination of key preventable diseases that can cause neonatal deaths.

Materials and Methods

Study subjects

The study covered all the 327 districts of the National Maternal and Child Health Surveillance Districts (with 124 urban districts and 203 rural districts) in 31 provinces, autonomous regions, and municipalities of China. Further details about the National Maternal and Child Health Surveillance System (NMCHSS) have been described elsewhere[18].

All neonates of surveillance districts (gestational week ≥ 28weeks) who died after delivery, and had one of the four vital signs would be involved in surveillance subject, including heartbeat, breath, umbilical cord pulsation, and voluntary muscle contraction. The surveillance subject also includes adoption children and children of non-local household residents whose mothers have living in the surveillance districts for more than one year.

Data collection and quality control

After each child died in the surveillance districts, the local village doctor (or community doctor) needs to report to the local township health centers (or community health service centers) within 10 days. Local township health centers (or community health service

centers) need to be verified within 7 days after reporting and fill the Child Death Report Card based on the hospital's death diagnosis. If the child died at home or on the way to the health facilities, infer the cause of death would base on the 2016 WHO Verbal Autopsy Standards[19] and then fill the Child Death Report Card. The classification of diseases according to the international classification of diseases-10 (ICD-10).

The children's mortality data was reported level by level, and the data is timely reported through the network direct reporting system. Technical personnel responsible for monitoring work are set up at all levels to complete the collection, review, and operation of surveillance data. The completed child death data would send to the county (or district) level maternal and child health institutions each season. The county (or district) level maternal and child health institutions would report the local child deaths status to prefecture-level and province-level maternal and child health institutions each season, the National Office of Maternal and Child Health would summarize and analyzes the data finally.

For quality control, we have used the regular level-by-level on-site quality control system. At the county (district), city, and provincial levels, following the requirements of the Chinese Maternal and Child Health Surveillance Work Manual, a multi-source data cross-check method is used to complete the on-site quality control work in sampling surveillance

districts. The National Office of Maternal and Child Health will select 18 districts in 6 provinces each year for quality inspection[17,18].

Statistical analysis

Results were collected in Microsoft Excel and analyzed using SPSS 22.0 (IBM, Armonk, NY, USA). The neonatal mortality rates (NMR) of different areas (urban areas & rural areas) and stages (early neonates & late neonates), and the main cause-specific mortality rates were corrected using the average underreporting rate of the national-level surveillance data quality checks in the past three years. The national NMR and the main cause-specific mortality rate were weighted calculated according to the proportion of the urban and rural population in the census. The diagnostic level composition ratio of the neonate is calculated based on the reported Child Death Report Card, excluding children who died of accidental injuries[17].

The Poisson regression model was used to calculate the average annual rate of decline of NMR, cause-of-death mortality, and its 95% confidence interval in the country, urban and rural areas, and its 95% confidence interval in early and late neonates, respectively. Linear by the linear association in the chi-square test using SPSS software was used to test whether there was a linear downward trend in different regions and causes of death.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of West China Second University Hospital, Sichuan University, China.

Patient and public involvement

Patients and members of the public were not involved in the design of this study.

Result

1. The NMR of China from 2014 to 2018

At the national level, the NMR of China has steadily decreased from 5.9 deaths per 1000 live births in 2014 to 3.9 deaths per 1000 live births in 2018（$p<0.001$）, the average annual rate of decline was 10.7%. The NMR of urban and rural areas have both showed a declining trend in the same period（$p<0.001$）. The mortality rate of urban areas decreased from 3.5 deaths per 1000 live births to 2.2 deaths per 1000 live births, with the average annual rate of decline was 13.0%. In rural areas, the NMR decreased significantly from 2014 to 2018 (6.9 deaths per 1000 live births to 4.7 deaths per 1000 live births, the average annual rate of decline was 10.6%, $p<0.001$). The absolute difference between

NMR of urban and rural areas has reduced from 3.4 deaths per 1000 live births to 2.5 deaths per 1000 live births, but the relative difference has increased from 2.0 to 2.2. (See **Figure 1**)

2. Cause of neonates mortality in China from 2014 to 2018

Nationwide, compared with 2014, the neonatal deaths caused due to preterm birth, intrapartum complication, and pneumonia in 2018 have sharply decreased. Among the particular diseases, the intrapartum complications have the highest average annual decline rate (AADR) from 2014 to 2018 (with 13.5%, $p<0.001$). The smallest AADR belonged to Tetanus (with 0.8%, $p<0.05$). In any given year, preterm birth, intrapartum complication, and pneumonia were the top three leading causes of neonatal death in China, total accounting for nearly 60%. (See **Table 1**) In 2018, all deaths causes have been divided into preventable diseases and unpreventable diseases to analyze the proportion. The proportion of preventable diseases reached 73.9%. Moreover, the top three diseases at the national level were preterm birth, intrapartum complications, and congenital malformations. (See **Figure 2A**)

Table 1. The proportion of cause-specific neonatal mortality in China from 2014 to 2018

Causes of death	0-6 days					7-28 days					0-28 days				
	2014	2015	2016	2017	2018	2014	2015	2016	2017	2018	2014	2015	2016	2017	2018
Nationalwide															
Preterm birth	32.3	33.1	32.0	36.2	26.7	19	24.2	19.9	22.3	28.8	29.1	30.8	28.7	32.2	27.3
Intrapartum complications	29.0	31.9	27.0	26.4	28.5	8.4	7.1	6	6.2	5.6	24.2	25.5	21.4	20.6	21.7
Pneumonia	9.5	6.9	9.0	8.0	7.9	17.3	13.5	18	18.2	11.5	11.3	8.6	11.4	11	9
Diarrhea	0.1	0.0	0.0	0.0	0.2	1.3	2	1.1	0.2	1	0.4	0.5	0.3	0	0.4
Tetanus	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.1	0	0	0	0
HIV	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0	0	0	0	0
Neonatal sepsis/meningitis	1.6	2.1	2.7	2.4	3.0	5.3	4.3	7.5	5.8	9.8	2.5	2.6	4	3.3	5
Other infectious diseases	0.3	0.3	0.2	0.3	0.0	0.3	0.0	0.4	0.0	0.0	0.3	0.2	0.3	0.2	0
Congenital malformations	15.5	12.5	16.1	16.7	19.0	23.4	22.8	26.4	22.7	22.8	17.4	15.2	18.9	18.5	20.2
Other diseases	11.7	13.2	12.9	9.9	14.7	24.4	26.1	20.7	24.6	20.5	14.7	16.6	15	14.2	16.4
Urban area															
Preterm birth	35.5	30	26.6	36.5	29.1	15.5	24.6	22.8	19.8	27.9	31.4	28.6	25.5	31.8	28.8
Intrapartum complications	28	30	28.2	27.8	24.3	18.1	10.4	5.5	11.2	6.4	25.9	24.6	21.8	23.2	18.7
Pneumonia	7.3	7.9	10.7	6.4	5.3	11.3	8.2	15.1	14.5	8.1	8.1	8	12	8.6	6.1
Diarrhea	0.0	0.0	0.0	0.0	0.0	0.8	0.8	0.0	0.7	0.9	0.2	0.2	0	0.2	0.3
Tetanus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0	0	0	0	0
HIV	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0	0	0	0	0

Neonatal sepsis/meningitis	2.7	2.5	4.7	4.3	8.1	3.4	7.5	8.3	12.4	12.6	2.9	3.9	5.7	6.6	9.5
Other infectious diseases	0.7	0.9	0.5	0.8	0.0	0.0	0.0	0.7	0.0	0	0.5	0.6	0.6	0.5	0
Congenital malformations	17.3	16.4	17.8	16.3	15.4	32.8	28.4	24.2	20.4	26.2	20.5	19.7	19.6	17.5	18.7
Other diseases	8.4	12.2	11.5	7.9	17.8	18.1	20.1	23.4	21.0	17.9	10.5	14.4	14.9	11.6	17.9
Rural area															
Preterm birth	31.5	33.7	33.2	36.1	26.2	19.6	24.1	19.1	22.9	29	28.6	31.3	29.5	32.3	27
Intrapartum complications	29.2	32.3	26.8	26.1	29.3	6.4	6.2	6.1	5.2	5.4	23.8	25.7	21.3	20.1	22.3
Pneumonia	10.0	6.7	8.7	8.4	8.4	18.6	14.8	18.7	18.9	12.4	12	8.7	11.3	11.5	9.6
Diarrhea	0.1	0.0	0.0	0.0	0.2	1.4	2.4	1.3	0.0	1.1	0.4	0.6	0.3	0	0.5
Tetanus	0.0	0.0	0.0	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.2	0	0	0	0
HIV	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0	0	0	0	0
Neonatal sepsis/meningitis	1.3	2.0	2.2	1.9	2.0	5.7	3.5	7.4	4.3	9.1	2.4	2.4	3.6	2.6	4.1
Other infectious diseases	0.2	0.1	0.2	0.2	0.0	0.4	0.0	0.4	0.0	0.0	0.3	0.1	0.2	0.1	0
Congenital malformations	15.1	11.7	15.7	16.8	19.8	21.4	21.4	27.0	23.3	22.0	16.6	14.1	18.7	18.7	20.4
Other diseases	12.5	13.5	13.2	10.4	14.0	25.7	27.6	20.0	25.4	21.0	15.7	17.1	15	14.7	16.1

222 Table 2. Leading causes of death in neonates in China from 2014 to 2018

Causes of death	Cause-specific mortality (per 100,000livebirths)																	
	0-6 (<7) days newborns						7-27 days newborns						0-27 (<28) days newborns					
	2014	2015	2016	2017	2018	Average annual decline rate (%)	2014	2015	2016	2017	2018	Average annual decline rate (%)	2014	2015	2016	2017	2018	Average annual decline rate (%)
Nationalwide																		
Preterm birth	144.8	133.5	113.8	115.7	73.4	12.7 (15.1,10.2) **	25.9	33.7	26.0	28.7	33.2	-3.2 (2.4,-9.1) △	170.7	167.2	139.8	144.4	106.6	9.7 (7.4, 11.9) **
Intrapartum complications	130.2	128.7	96.1	84.5	78.2	13.5 (16.1,10.9) **	11.5	9.8	7.8	8.0	6.4	12.7 (21.3,3.3) **	141.7	138.5	103.9	92.5	84.6	13.5 (11.0, 15.9) **
Pneumonia	42.4	27.9	32.1	25.7	21.7	13.6 (18.3,8.7) **	23.7	18.8	23.6	23.4	13.3	7.2 (13.1,0.8) *	66.1	46.7	55.7	49.1	35	11.0 (7.1, 14.7) **
Diarrhea	0.4	0.0	0.0	0.0	0.5	-	1.8	2.8	1.4	0.2	1.2	24.5 (41.7,2.1) △	2.2	2.8	1.4	0.2	1.7	20.1 (-2.0, 37.4) △
Tetanus	0.0	0.0	0.0	0.0	0.0	-	0.8	0.0	0.0	0.0	0.0	-	0.8	0	0	0	0	-
HIV	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-	0	0	0	0	0	-
Neonatal sepsis/meningitis	7.2	8.4	9.4	7.6	8.3	-2 (8.2,-13.3) △	7.3	5.9	9.9	7.4	11.3	-12.1 (-0.9,-24.5) *	14.5	14.3	19.3	15	19.6	-6.5 (-14.7, 1.2) △
Other infectious	1.4	1.1	0.8	0.9	0.0	30.1	0.4	0.0	0.6	0.0	0.0	35.6 (68,-	1.8	1.1	1.4	0.9	0	33.1

diseases						(51,0.3) △						29.5) △						(7.9, 51.4) *
Congenital malformations	69.8	50.6	57.3	53.5	52.3	5.6 (9.3,1.8) **	31.9	31.7	34.6	29.3	26.2	4.3 (9.4,-1) △	101.7	82.3	91.9	82.8	78.5	5.1 (2.0, 8.1) **
Other diseases	52.8	53.6	45.9	31.6	40.2	10.4 (14.3,6.2) **	33.3	36.4	27.1	31.8	23.6	7.4 (12.3,2.2) **	86.1	90	73	63.4	63.8	9.2 (5.9, 12.3) **
Urban area																		
Preterm birth	99.7	70.9	55.6	69.6	44.2	15 (19.4,10.4) **	11.5	22.0	18.9	14.7	19.1	-4.2 (6.2,-15.7) △	111.2	92.9	74.5	84.3	63.3	11.4 (7.1, 15.5) **
Intrapartum complications	78.6	70.9	59.0	53.1	36.9	15.8 (20.5,10.9) **	13.4	9.3	4.6	8.3	4.3	21.2 (32.7,7.9) *	92	80.2	63.6	61.4	41.2	16.4 (11.8, 20.7) **
Pneumonia	20.4	18.7	22.3	12.2	8.0	18 (26.5,8.5) **	8.4	7.4	12.6	10.7	5.5	2.7 (15.8,-12.4) △	28.8	26.1	34.9	22.9	13.5	12.4 (4.5, 19.7) **
Diarrhea	0.0	0.0	0.0	0.0	0.0	-	0.6	0.7	0.0	0.5	0.6	2.7 (51.8,-96.6) △	0.6	0.7	0	0.5	0.6	2.7 (-96.6, 51.8) △
Tetanus	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-	0	0	0	0	0	-
HIV	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-	0	0	0	0	0	-
Neonatal sepsis/meningitis	7.7	6.0	9.7	8.3	12.3	-13.8 (1.9,-32.1) △	2.5	6.7	6.9	9.2	8.6	-25.5 (-5.7,-49.1)**	10.2	12.7	16.6	17.5	20.9	2.7 (-96.6, 51.8) **
Other infectious diseases	1.9	2.0	1.1	1.5	0.0	33 (56,-1.9) △	0.0	0.0	0.6	0.0	0.0	2.7 (76.2,-297.1)△	1.9	2	1.7	1.5	0	25.2 (-7.7, 48.1) △

Congenital malformations	48.6	38.8	37.2	31.2	23.3	14.9 (20.9,8.4) **	24.3	25.4	20.1	15.1	17.9	10.8 (19,1.8) *	72.9	64.2	57.3	46.3	41.2	13.6 (8.4, 18.5) **
Other diseases	23.6	28.7	24.1	15.1	27.0	3.5 (11.8,-5.5)△	13.5	18.1	19.4	15.6	12.3	3.3 (13.3,-7.8)△	37.1	46.8	43.5	30.7	39.3	3.2 (-3.7, 9.7) △
Rural area																		
Preterm birth	165.0	161.4	139.8	136.2	86.4	12 (15.2,8.8) **	32.2	38.9	29.1	35.1	39.5	-4.1 (2.9,-11.7)△	197.2	200.3	168.9	171.3	125.9	9.2 (6.3, 12.1) **
Intrapartum complications	153.2	154.5	112.6	98.5	96.6	13.1 (16.3,9.7)**	10.6	10.0	9.3	8.0	7.4	8.2 (20.2,-5.5)△	163.8	164.5	121.9	106.5	104	12.8 (9.5, 15.9) **
Pneumonia	52.3	32.0	36.4	31.7	27.8	12.9 (18.8,6.5) **	30.5	23.9	28.5	29.1	16.9	7.6 (14.9,-0.4)△	82.8	55.9	64.9	60.8	44.7	10.8 (5.9, 15.5) **
Diarrhea	0.6	0.0	0.0	0.0	0.7	-	2.3	3.8	2.0	0.0	1.5	25.1 (45.4,-2.8)△	2.9	3.8	2	0	2.2	25.5 (-0.3, 44.6) *
Tetanus	0.0	0.0	0.0	0.0	0.0	-	1.2	0.0	0.0	0.0	0.0	-	1.2	0	0	0	0	-
HIV	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-	0	0	0	0	0	-
Neonatal sepsis/meningitis	7.0	9.4	9.3	7.3	6.6	3.3 (16.7,-12.4)△	9.4	5.7	11.2	6.6	12.4	-7.3 (6.7,-23.5)△	16.4	15.1	20.5	13.9	19	-2.3 (-13.2, 7.7)△
Other infectious diseases	1.2	0.6	0.7	0.7	0.0	30.3 (60.9,-24)△	0.6	0.0	0.6	0.0	0.0	42.4 (82.5,-89.3)△	1.8	0.6	1.3	0.7	0	29.7 (-13.7, 56.6)△
Congenital	79.3	55.9	66.2	63.5	65.2	3.3 (8.2,-	35.2	34.5	41.1	35.7	30.0	2.5 (9.1,-4.6)	114.5	90.4	107.3	99.2	95.2	3.0 (-

malformations						1.8)△						△						1.2, 6.9) △
Other diseases	65.8	64.7	55.6	39.0	46.1	11.6 (16.5,6.4) **	42.2	44.6	30.5	39.0	28.6	8.5 (14.6,1.9) *	108	109.3	86.1	78	74.7	10.3 (6.3, 14.2) **

(** means p value<0.01, * means p value<0.05, △ means p value≥0.05)

The death cause distribution and AADR were also significantly different among urban-rural areas. In urban areas, preterm birth, intrapartum complication, and congenital anomalies also accounting the largest proportion of all deaths cause from 2014 to 2018. Moreover, the AADR of preterm birth, intrapartum complications, pneumonia, and congenital malformations in urban areas were all larger than that of the national level. In rural areas, the mortality rate of preterm birth, intrapartum complication, and congenital anomalies significantly decreased. Additionally, the NMR of diarrhea have sharply decreased, with AADR was 25.5% ($p<0.001$). (See **Table 2**)

In contrast, the urban-rural gap still existed. The contribution of tetanus among neonates in urban areas remains zero during the study period, while the rate in rural areas has been eliminated until 2015. In 2018, the neonatal mortality in rural areas was almost twice as high as in urban areas due to preterm birth, intrapartum complications, and congenital malformations. Moreover, during the study period, the largest number of neonatal deaths in the urban and rural areas was pneumonia, increased from 2.9 times (82.8 per 100,000 live births in rural areas VS 28.8 per 100,000 live births in urban areas) in 2014 to 3.3 times (44.7 per 100,000 live births in rural areas VS 13.5 per 1000 live births in urban areas) in 2018. (See **Table 2**) In the disease proportion aspect, the proportion of intrapartum complications and pneumonia in rural areas significantly higher than that of urban areas. (See Figure 2B&C) According to the data analysis, causes of neonatal death varied between urban and rural areas ($P<0.05$), but the correlation between neonatal mortality and whether

the newborn lived in urban or rural areas was weak (Cramer's V=0.129).

The mortality rates have also shown difference when divided neonates into early neonates (0-6 days) and late neonates (7-28 days). Nationwide, except for neonatal sepsis (or meningitis) and diarrhea, the mortality rate of other causes of death of early neonates was significantly higher than that of late neonates, with the biggest difference being intrapartum complications, preterm birth, and congenital malformations. In 2018, the mortality rate of preterm birth was 73.4 per 100,000 livebirth in early neonates and 33.2 per 100,000 livebirth in late neonates. In the same year, the mortality rate of congenital malformations was 52.3 per 100,000 livebirth in early neonates and 26.2 per 100,000 livebirth in late neonates. It is worth noting that intrapartum complications were the second leading cause of death among 0-28 days newborns in China from 2014 to 2018, with the mortality rate of 78.2 per 100,000 livebirth in early neonates and only 6.4 per 100,000 livebirth in late neonates (See **Table 2**).

3. Neonate Diagnosis Facilities Level in China between 2014 and 2018

The children's diagnosis facilities level has also be included in surveillance. Nationwide, from 2014 to 2018, the proportion of neonate diagnosis at the provincial (or municipal) level health facilities has significantly increased, and the proportion of the district (or county) level has decreased. Moreover, the proportion of township level and village level

have both fluctuating declined during this period. In 2018, the proportion of neonate who has not to seek any medical care has minimized, which declined to 3.9% in 2018. (See **Figure 3**)

In an urban aspect, from 2014 to 2018, the majority of children (accounted for over 80%) in urban areas have been diagnosed at provincial (or municipal) level medical facilities. The proportion of the district (or county) level and township -level both have a slight rise between 2014 and 2018. As a result, the percentage of children who have not to seek medical care has declined, with 1.9% in 2014 and 1.1% in 2018. (See **Figure 3**)

On the contract, the diagnosis contribution figure of rural areas was different. Although the proportion of provincial (or municipal) level has shown a growth trend from 2014 to 2018, the proportion in rural areas have only half of that in urban areas. Moreover, the proportion of street-level diagnoses in the urban area is reduced to 1.4% in 2018, while this proportion in rural areas fluctuated and remained at 3.7% in the same year. Another significant contributor is the proportion of children who have not sought medical care. The proportion of neonate who has not to seek medical care has decreased, and still, 5.5% of children have not sought any medical advice. (See **Figure 3**)

Discussion

The results of this study show that the NMR in urban and rural areas of China have decreased significantly between 2014 and 2018. In addition, there were significant differences in NMR between urban and rural areas, which were consistent with significant differences in NMR between countries and regions globally[20,21].

From 2014 to 2018, Chinese NMR continued to decline, and it was dropped quickly. It benefits from the improvement of medical treatment at all levels of health facilities, and all levels of government attached great importance to strengthen the construction of the pediatric institution, raise pediatricians' payment, and continue to implement neonatal asphyxia recovery training program[22]. As a result, neonatal deaths from pneumonia and infectious diseases, intrapartum complications, and premature delivery were significantly reduced.

China has implemented the Safe Maternal Initiative and the National Program to Reduce Maternal Mortality and Eliminate Tetanus, China has officially eliminated neonatal tetanus in 2012[23], and from 2015 to 2018, the NMR of neonatal tetanus remained 0. Moreover, through the success of the Prevention of Mother-to-child Transmission of HIV, Syphilis, and Hepatitis B Program, the HIV/AIDS mortality rate has also been 0 from 2014 to

2018[24,25]. Although the national neonatal mortality in 2018 was already less than 12 deaths per 1000 live births, the preventable deaths still accounted for 73.9%, mainly were pneumonia, intrapartum complication, premature birth. Among these diseases, the proportion of preterm birth was highest in both nationwide, urban areas, and rural areas. In the recent two decades, the prevalence of preterm birth has significantly increased[18], especially after the Two-child Policy[26] was implemented in China. The mortality rate among preterm birth infants was apparently higher than the full-term infant, and the risk of mortality increases proportionally with decreasing gestational age[27]. Furthermore, with the widespread development of assisted reproductive technique (ART), the incidence of monozygotic twins has increased significantly[28]. The NMR of twins is several times higher than that of singletons[29-31].

Addressing the issue of preterm birth may require different priorities in rural and urban areas. Because of the good management of many curable neonatal complications (such as pneumonia), the proportion of preterm birth in urban areas is obviously larger than that of rural areas[32]. Hence, urban areas need to pay more attention to preventing premature deaths less than 32 weeks of gestation. For rural areas, the local government needs to focus on the prevention of premature infants at 32-36 weeks and continue to invest in medical services to improve medical services accessibility for women and children in rural areas.

In addition, from 2014 to 2018, the neonatal mortality rate in rural areas due to preterm birth, intrapartum complications, pneumonia, and congenital malformations was decreasing in rural areas but was still significantly higher than in urban areas. (See **Table 2**) The higher mortality rate may be linked to the relatively poorer economy, lower quality of health care, and lack of accessibility to health care in rural China. The average median net income per capita was ¥39251 (about US $6000) in urban China, but ¥14617 (about the US $2234) in rural China in 2018[33]. The annual spending on health care per capita accounted for 7.8% in urban China, but 10.2% in rural China in 2018[34]. The average health care personnel were 4.0 per 1000 people in urban China and 1.8 per 1000 people in rural China in 2018[34]. The number of beds in medical institutions per 1,000 people in urban areas was 8.70, compared with 4.56 in rural areas in 2018[34].

Not only markedly difference the NMR of urban and rural areas has shown, but also significantly difference in early and late neonates. The results of this study showed that the range of cause-specific mortality of late neonates was significantly less than that of early neonates, both nationwide and urban-rural areas. (See **Table 2**) Therefore, for preventable neonatal diseases, the focus should be on early neonates, especially for early neonates in rural areas.

For neonates, surviving from preterm birth, intrapartum complication and pneumonia are close linking to accessibility to health care, local hospitals' obstetrics and neonates departments' treatment level, and rescue skills[35,36]. Therefore, the issue can be addressed from the following four aspects.

Firstly, the local governments need to strengthen the construction of RNTN (Regional Neonatal Transport Network), carry out the transport plan according to the Guidelines for the Construction and Management of Critical Neonatal Treatment Center[37], and ensure the applying of professional medical staff and newborn rescue equipment for neonatal transport. Secondly, one study in Japan has pointed out that the medical care resources (including Neonatal Intensive Care Unit (NICU), midwives, emergency physicians, and emergency medical care centers) would impact the NMR decline[38]. Therefore, the local governments may base on the Administration guide (proposal) of the Neonatal Physician Branch of the Chinese Physician Association[39] to grading neonatal wards and establishing NICU after analyzing local medical establishment plan and newborn medical treatment needs. Thirdly, local health departments can regularly organize multi-level， especially provincial, prefecture-level and district-level) newborn health training programs. In rural areas, with the policies support of the New Rural Construction and the Targeted Poverty Alleviation[40,41], the improved rural transport and higher incomes have prompted the enhanced accessibility of health services, and the proportion of rural children receiving

medical treatment in provincial and municipal hospitals has significantly increased. The proportion of rural neonate diagnosis at the provincial (or municipal) level health facilities has significantly increased from 39.2% to 47.6% from 2014 to 2018. Set training objectives for medical staff in health facilities of different levels, and strengthen the newborn treatment technology in each level of health facilities. Especially for the health workers in rural areas, the newborn resuscitation training needs to be specifically strengthened. Fourthly, the local communities can strengthen publicity to encourage caregivers to take children to attend the health facilities for treatment. As for poor households, local governments can set up special subsidies for them to reduce the economic cost of medical treatment.

Conclusion

With the joint efforts of the economic development and the governmental policies and strategies, the neonatal mortality rate of China has significantly decreased from 2014 to 2018. The gap between neonatal mortality and cause-of-death distribution still existed between urban and rural areas. The goal of government interventions should be to narrow the urban-rural gap, reduce the health inequality of neonates, and further take targeted measures to eliminate the preventable death of neonates, especially premature births, to achieve the SDGs goal.

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Conflicts of interest

The authors declare no conflicts of interest.

Data Availability Statement

This study used data from the NMCHSS. This system is co-established by the National Health and Family Planning Commission of the People Republic of China and Sichuan University and finally owned by the National Health and Family Planning Commission of the People Republic of China. The researchers did not obtain consent to publicly share data. The de-identified data set is available upon request to interested researchers. For data requests, please contact the Department of Science and Technology of West China Second University Hospital, Sichuan University, at: fu2yuankjb@163.com. This department is in charge of all the programs in the hospital, including the data management. One staff from the department monitors this email.

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Figure 1. The national and urban-rural neonatal mortality rates (per 1,000 live births) in China between 2014 and 2018

Figure 2A. Causes of deaths in neonates in China, 2018

Figure 2B. Causes of deaths in neonates in urban China, 2018

Figure 2C. Causes of deaths in neonates in rural China, 2018

Figure 3. The proportion of neonatal diagnose level in China from 2014 to 2018

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Figure 1. The national and urban–rural neonatal mortality rates (per 1,000 live births) in China between 2014 and 2018

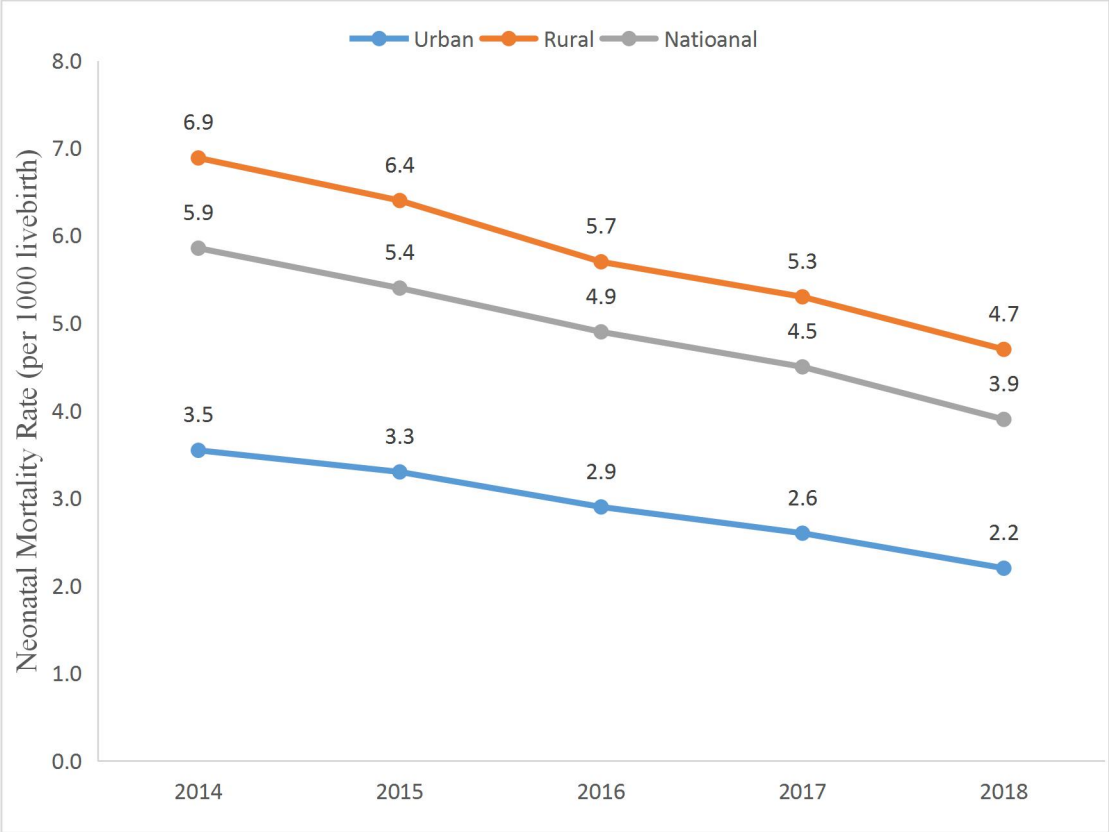


Figure 3. The proportion of neonatal diagnose level in China from 2014 to 2018

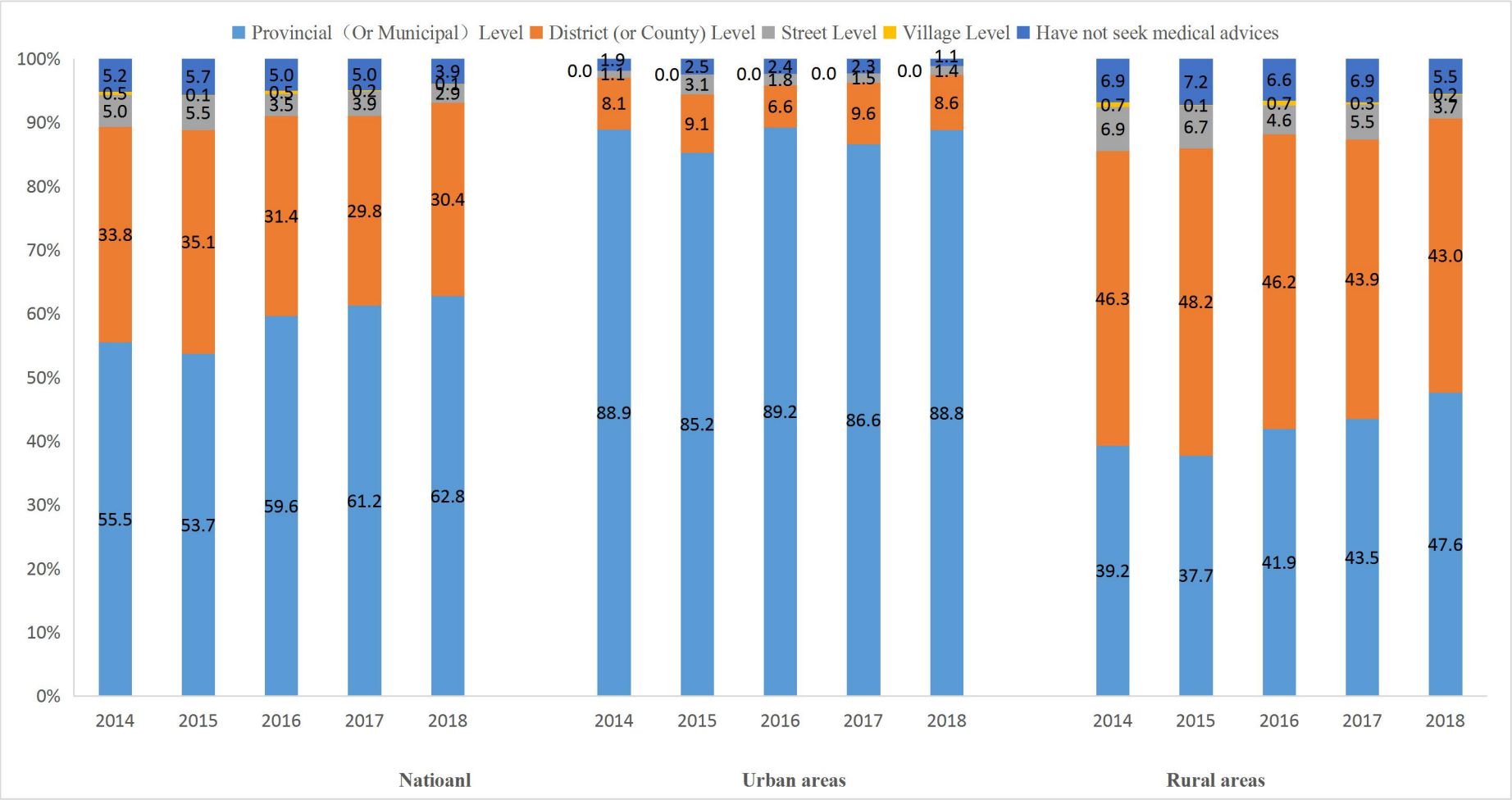


Figure 2A. Causes of deaths in neonates in China, 2018

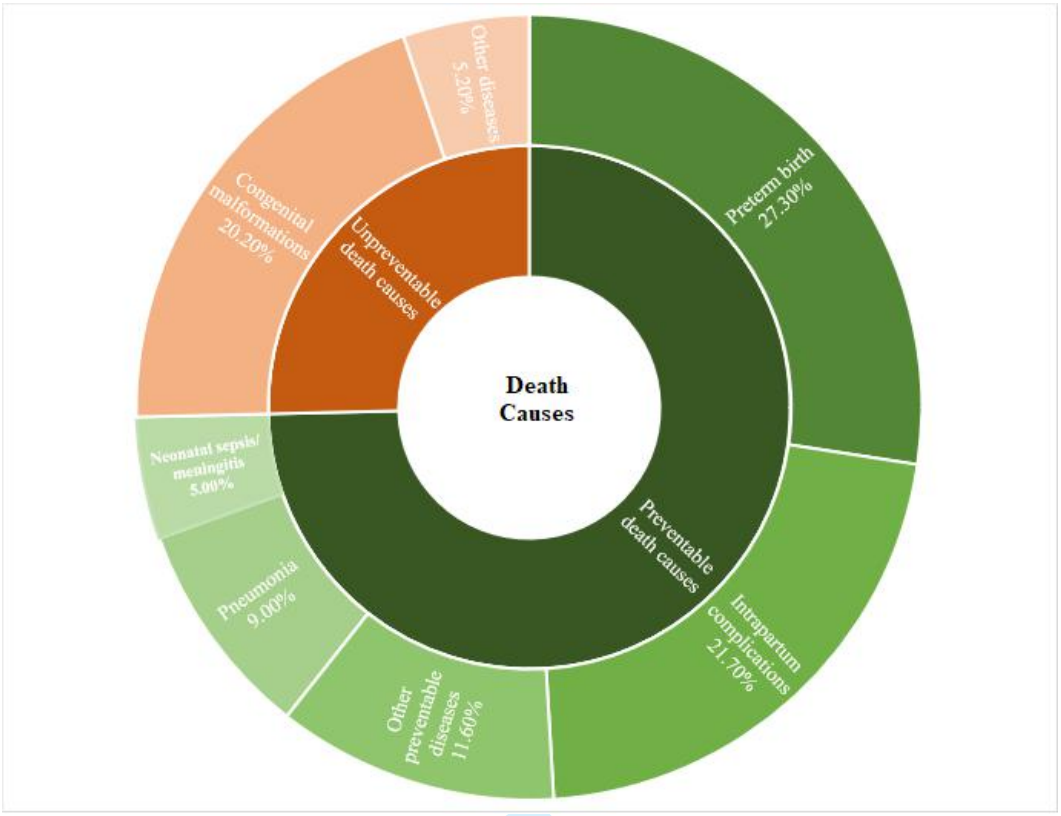


Figure 2B. Causes of deaths in neonates in urban China, 2018

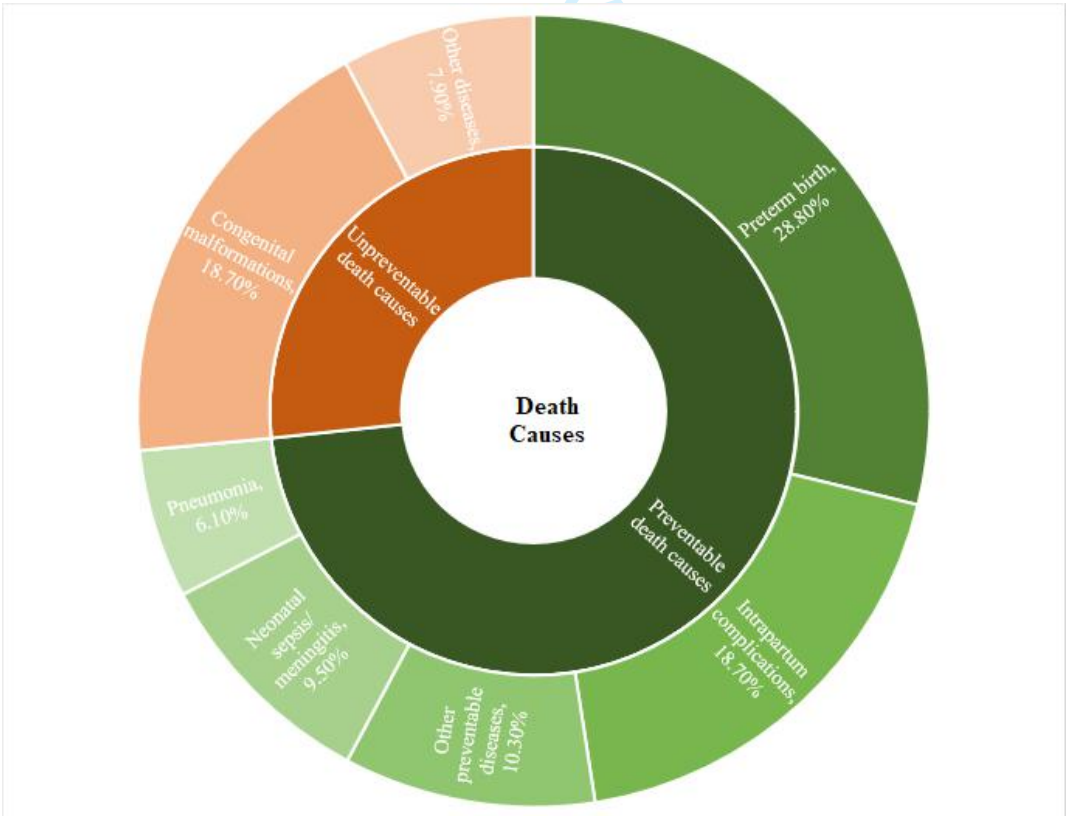
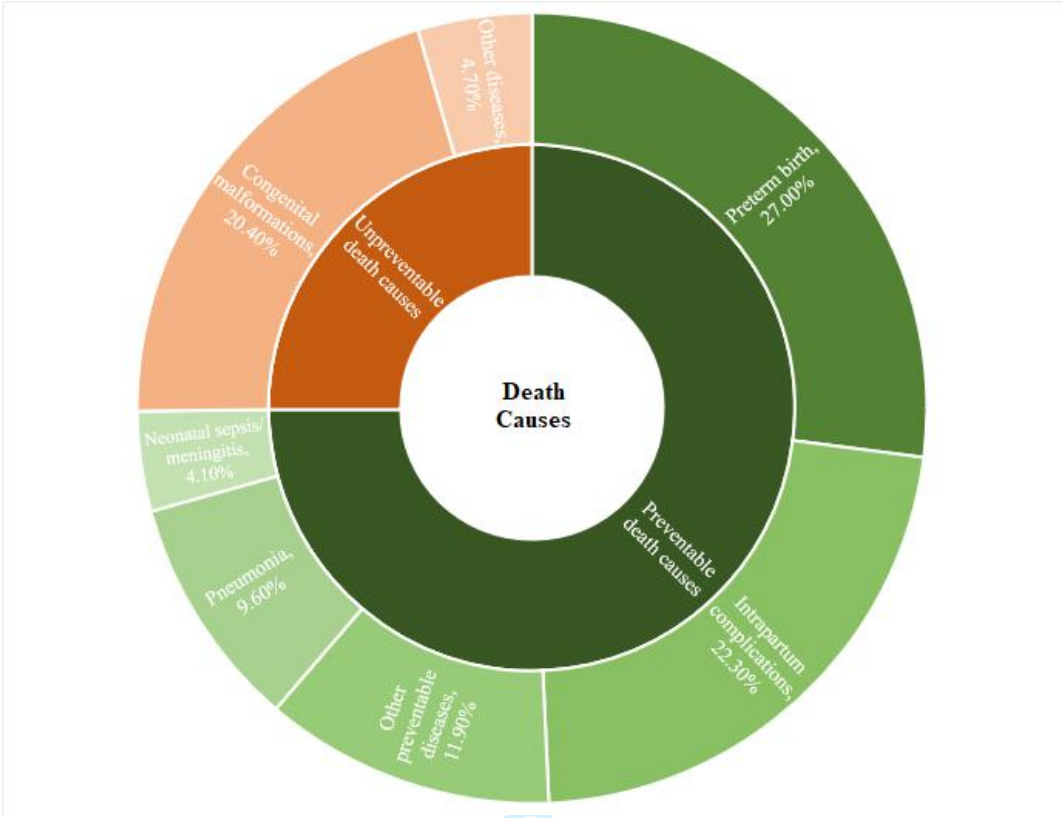


Figure 2C. Causes of deaths in neonates in rural China, 2018



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Neonatal mortality and leading causes of deaths: a descriptive study in China, 2014-2018

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Abstract

Objective: The present study estimated the national and urban-rural levels and causes of neonatal deaths in China annually between 2014 and 2018 to provide data support for the further end of preventable neonatal deaths for China and other low-and middle-income countries.

Methods: The study was based on data from the National Maternal and Child Health Surveillance System (NMCHSS). All neonates of surveillance districts (gestational week ≥ 28weeks) who died after delivery have been involved in the study. The mortality rate and

the leading causes of death for neonates were analyzed.

Results: The NMR (Neonatal Mortality Rate) of China has steadily decreased from 5.9 deaths per 1000 live births in 2014 to 3.9 deaths per 1000 live births in 2018. The NMR in 2018 of urban and rural areas was 2.2 deaths per 1000 live births and 4.7 deaths per 1000 live births, respectively. The leading preventable causes of neonatal deaths are the same in the urban and rural areas were same, which were preterm birth, intrapartum complications, and pneumonia. Mortality rates of these three causes fell significantly between 2014 and 2018 but contributed to a higher proportion of deaths in rural areas than urban areas. The proportion of preventable deaths accounted for 73.9% in 2018.

Conclusions: The NMR of China has decreased steadily from 2014 to 2018. However, the inequality between urban and rural areas still exists. The goal of government interventions should be to reduce the health inequality of neonates and further take targeted measures to eliminate preventable neonatal death.

Keywords: neonatal mortality, leading cause, Surveillance, inequality, China

Strengths and limitations of this study

- This is the first study to show the status of neonatal deaths in China from 2014 to 2018.

- The study covers the most geographically extensive newborn population in mainland China.
- The data from the National Maternal and Child Health Surveillance System used in this study have been shown to be representative of mainland China and to be of high quality for the recording of death causes of children under 5.
- The system has not covered the pre-natal assessment due to design limitations.

Introduction

In 2015, the United Nations (UN) summit on sustainable development formally adopted the 2030 agenda for sustainable development. In the Sustainable Development Goals 3

(SDGs3), the goal is to end preventable neonatal and under-five child deaths by 2030[1], with all countries aiming to reduce neonatal mortality to at least as low as 12 deaths per 1,000 live births and under-five mortality to at least as low as 25 deaths per 1,000 live births. The importance of newborn health issues has received global attention. The Chinese government has always attached great importance to the survival, protection, and development of children, and has made great achievements in reducing child mortality. Professional institutions for maternal and child health care began to be established in 1950[2]. Moreover, the Chinese government has taken the under-five mortality rate (U5MR), the infant mortality rate (IMR), and other indicators of children's health as assessment targets for provincial governments, and has promulgated the National Program of Action for Child Development in China every decade since 1990s[2,3].

Globally, there were 5.3 million deaths occurred on children under 5 in 2018, 47% of them died during their first month of life. The vast majority of neonatal deaths occur in low - and middle-income countries. Approximately 73,000 neonates died in China in 2018, accounting for about 3.0% of the total newborn deaths worldwide, ranking sixth in the world[4]. Moreover, the global decline in neonatal mortality rate (NMR) has been slower than the decline in the U5MR[5]. Global U5MR declined from 93 per 1,000 live births in 1990 to 39 per 1,000 live births in 2018, while that of NMR only declined from 37 per

1,000 live births to 18 per 1,000 live births during the same period. Additionally, a great many studies have shown that neonatal deaths amounting to a large proportion of total mortality of children under 5[5-7]. Therefore, reducing preventable neonatal deaths is important to further reduce the U5MR.

China has achieved the MDG4 (Millennium Development Goal 4) eight years ahead of schedule in 2007[8-13], and it is also rated by the World Health Organization as a country with "high performance in maternal and child health". In 2018, the NMR of China was 3.9 deaths per 1000 live births, which was lower than the target of SDG3[14]. However, according to the NMR data from World Bank in 2018, the NMR of China is at a low level in developing countries (such as the NMR in Brazil was 8.1 deaths per 1000 live births, and Thailand was 5.0 deaths per 1000 live births), it still lags behind that in developed countries (such as the NMR in Australia was 2.3 deaths per 1000 live births, and Germany was 2.2 deaths per 1000 live births)[15]. Moreover, since urban areas generally have better economic development than rural areas, resulting in better health service infrastructure and health service infrastructures[16], there is an urban-rural inequity in neonatal mortality in China[17]. To further shorten the gap with developed countries, and reduce the difference in neonatal mortality between urban and rural areas, there is still room for improvement in neonatal deaths in China. This study will analyze neonatal mortality trends and its mortality

of major causes of death in China from 2014 to 2018 to provide data support for the further elimination of key preventable diseases that can cause neonatal deaths.

Materials and Methods

Study subjects

The study covered all the 327 districts of the National Maternal and Child Health Surveillance Districts (with 124 urban districts and 203 rural districts) in 31 provinces, autonomous regions, and municipalities of China. Further details about the National Maternal and Child Health Surveillance System (NMCHSS) have been described elsewhere[18].

All neonates of surveillance districts (gestational week ≥ 28weeks) who died after delivery, and had one of the four vital signs would be involved in surveillance subject, including heartbeat, breath, umbilical cord pulsation, and voluntary muscle contraction. The surveillance subject also includes adoption children and children of non-local household residents whose mothers have living in the surveillance districts for more than one year.

Data collection and quality control

After each child died in the surveillance districts, the local village doctor (or community doctor) needs to report to the local township health centers (or community health service centers) within 10 days. Local township health centers (or community health service centers) need to be verified within 7 days after reporting and fill the Child Death Report Card based on the hospital's death diagnosis. If the child died at home or on the way to the health facilities, infer the cause of death would base on the 2016 WHO Verbal Autopsy Standards[19] and then fill the Child Death Report Card. The classification of diseases according to the international classification of diseases-10 (ICD-10).

The children's mortality data was reported level by level, and the data is timely reported through the network direct reporting system. Technical personnel responsible for monitoring work are set up at all levels to complete the collection, review, and operation of surveillance data. The completed child death data would send to the county (or district) level maternal and child health institutions each season. The county (or district) level maternal and child health institutions would report the local child deaths status to prefecture-level and province-level maternal and child health institutions each season, the

National Office of Maternal and Child Health would summarize and analyzes the data finally.

For quality control, we have used the regular level-by-level on-site quality control system. At the county (district), city, and provincial levels, following the requirements of the Chinese Maternal and Child Health Surveillance Work Manual, a multi-source data cross-check method is used to complete the on-site quality control work in sampling surveillance districts. The National Office of Maternal and Child Health will select 18 districts in 6 provinces each year for quality inspection[17,18].

Statistical analysis

Results were collected in Microsoft Excel and analyzed using SPSS 22.0 (IBM, Armonk, NY, USA). The neonatal mortality rates (NMR) of different areas (urban areas & rural areas) and stages (early neonates & late neonates), and the main cause-specific mortality rates were corrected using the average underreporting rate of the national-level surveillance data quality checks in the past three years. The national NMR and the main cause-specific mortality rate were weighted calculated according to the proportion of the urban and rural population in the census. The diagnostic level composition ratio of the neonate is calculated

based on the reported Child Death Report Card, excluding children who died of accidental injuries[17].

The Poisson regression model was used to calculate the average annual rate of decline of NMR, cause-of-death mortality, and its 95% confidence interval in the country, urban and rural areas, and its 95% confidence interval in early and late neonates, respectively. Linear by the linear association in the chi-square test using SPSS software was used to test whether there was a linear downward trend in different regions and causes of death.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of West China Second University Hospital, Sichuan University, China.

Patient and public involvement

Patients and members of the public were not involved in the design of this study.

Result

1. The NMR of China from 2014 to 2018

At the national level, the NMR of China has steadily decreased from 5.9 deaths per 1000 live births in 2014 to 3.9 deaths per 1000 live births in 2018（p<0.001）, the average annual rate of decline was 10.7%. The NMR of urban and rural areas have both showed a declining trend in the same period（p<0.001）. The mortality rate of urban areas decreased from 3.5 deaths per 1000 live births to 2.2 deaths per 1000 live births, with the average annual rate of decline was 13.0%. In rural areas, the NMR decreased significantly from 2014 to 2018 (6.9 deaths per 1000 live births to 4.7 deaths per 1000 live births, the average annual rate of decline was 10.6%, p<0.001). The absolute difference between NMR of urban and rural areas has reduced from 3.4 deaths per 1000 live births to 2.5 deaths per 1000 live births, but the relative difference has increased from 2.0 to 2.2. (See **Figure 1**)

2. Cause of neonates mortality in China from 2014 to 2018

Nationwide, compared with 2014, the neonatal deaths caused due to preterm birth, intrapartum complication, and pneumonia in 2018 have sharply decreased. Among the particular diseases, the intrapartum complications have the highest average annual decline rate (AADR) from 2014 to 2018 (with 13.5%, p<0.001). The smallest AADR belonged to Tetanus (with 0.8%, p<0.05). In any given year, preterm birth, intrapartum complication,

and pneumonia were the top three leading causes of neonatal death in China, total accounting for nearly 60%. (See **Table 1**) In 2018, all deaths causes have been divided into preventable diseases and unpreventable diseases to analyze the proportion. The proportion of preventable diseases reached 73.9%. Moreover, the top three diseases at the national level were preterm birth, intrapartum complications, and congenital malformations. (See **Figure 2A**)

Table 1. The proportion of cause-specific neonatal mortality in China from 2014 to 2018

Causes of death	0-6 days					7-28 days					0-28 days				
	2014	2015	2016	2017	2018	2014	2015	2016	2017	2018	2014	2015	2016	2017	2018
Nationalwide															
Preterm birth	32.3	33.1	32.0	36.2	26.7	19	24.2	19.9	22.3	28.8	29.1	30.8	28.7	32.2	27.3
Intrapartum complications	29.0	31.9	27.0	26.4	28.5	8.4	7.1	6	6.2	5.6	24.2	25.5	21.4	20.6	21.7
Pneumonia	9.5	6.9	9.0	8.0	7.9	17.3	13.5	18	18.2	11.5	11.3	8.6	11.4	11	9
Diarrhea	0.1	0.0	0.0	0.0	0.2	1.3	2	1.1	0.2	1	0.4	0.5	0.3	0	0.4
Tetanus	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.1	0	0	0	0
HIV	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0	0	0	0	0
Neonatal sepsis/meningitis	1.6	2.1	2.7	2.4	3.0	5.3	4.3	7.5	5.8	9.8	2.5	2.6	4	3.3	5
Other infectious diseases	0.3	0.3	0.2	0.3	0.0	0.3	0.0	0.4	0.0	0.0	0.3	0.2	0.3	0.2	0
Congenital	15.5	12.5	16.1	16.7	19.0	23.4	22.8	26.4	22.7	22.8	17.4	15.2	18.9	18.5	20.2

malformations															
Other diseases	11.7	13.2	12.9	9.9	14.7	24.4	26.1	20.7	24.6	20.5	14.7	16.6	15	14.2	16.4
Urban area															
Preterm birth	35.5	30	26.6	36.5	29.1	15.5	24.6	22.8	19.8	27.9	31.4	28.6	25.5	31.8	28.8
Intrapartum complications	28	30	28.2	27.8	24.3	18.1	10.4	5.5	11.2	6.4	25.9	24.6	21.8	23.2	18.7
Pneumonia	7.3	7.9	10.7	6.4	5.3	11.3	8.2	15.1	14.5	8.1	8.1	8	12	8.6	6.1
Diarrhea	0.0	0.0	0.0	0.0	0.0	0.8	0.8	0.0	0.7	0.9	0.2	0.2	0	0.2	0.3
Tetanus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0	0	0	0	0
HIV	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0	0	0	0	0
Neonatal sepsis/meningitis	2.7	2.5	4.7	4.3	8.1	3.4	7.5	8.3	12.4	12.6	2.9	3.9	5.7	6.6	9.5
Other infectious diseases	0.7	0.9	0.5	0.8	0.0	0.0	0.0	0.7	0.0	0	0.5	0.6	0.6	0.5	0
Congenital malformations	17.3	16.4	17.8	16.3	15.4	32.8	28.4	24.2	20.4	26.2	20.5	19.7	19.6	17.5	18.7

Other diseases	8.4	12.2	11.5	7.9	17.8	18.1	20.1	23.4	21.0	17.9	10.5	14.4	14.9	11.6	17.9
Rural area															
Preterm birth	31.5	33.7	33.2	36.1	26.2	19.6	24.1	19.1	22.9	29	28.6	31.3	29.5	32.3	27
Intrapartum complications	29.2	32.3	26.8	26.1	29.3	6.4	6.2	6.1	5.2	5.4	23.8	25.7	21.3	20.1	22.3
Pneumonia	10.0	6.7	8.7	8.4	8.4	18.6	14.8	18.7	18.9	12.4	12	8.7	11.3	11.5	9.6
Diarrhea	0.1	0.0	0.0	0.0	0.2	1.4	2.4	1.3	0.0	1.1	0.4	0.6	0.3	0	0.5
Tetanus	0.0	0.0	0.0	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.2	0	0	0	0
HIV	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0	0	0	0	0
Neonatal sepsis/meningitis	1.3	2.0	2.2	1.9	2.0	5.7	3.5	7.4	4.3	9.1	2.4	2.4	3.6	2.6	4.1
Other infectious diseases	0.2	0.1	0.2	0.2	0.0	0.4	0.0	0.4	0.0	0.0	0.3	0.1	0.2	0.1	0
Congenital malformations	15.1	11.7	15.7	16.8	19.8	21.4	21.4	27.0	23.3	22.0	16.6	14.1	18.7	18.7	20.4
Other diseases	12.5	13.5	13.2	10.4	14.0	25.7	27.6	20.0	25.4	21.0	15.7	17.1	15	14.7	16.1

Table 2. Leading causes of death in neonates in China from 2014 to 2018

Causes of death	Cause-specific mortality (per 100,000livebirths)																	
	0-6 (<7) days newborns						7-27 days newborns						0-27 (<28) days newborns					
	2014	2015	2016	2017	2018	Average annual decline rate (%)	2014	2015	2016	2017	2018	Average annual decline rate (%)	2014	2015	2016	2017	2018	Average annual decline rate (%)
Nationalwide																		
Preterm birth	144.8	133.5	113.8	115.7	73.4	12.7 (15.1,10.2)**	25.9	33.7	26.0	28.7	33.2	-3.2 (2.4,-9.1) △	170.7	167.2	139.8	144.4	106.6	9.7 (7.4, 11.9)**
Intrapartum	130.2	128.7	96.1	84.5	78.2	13.5	11.5	9.8	7.8	8.0	6.4	12.7	141.7	138.5	103.9	92.5	84.6	13.5 (11.0,

complications						(16.1,10.9) **						(21.3,3.3) **						15.9) **
Pneumonia	42.4	27.9	32.1	25.7	21.7	13.6 (18.3,8.7) **	23.7	18.8	23.6	23.4	13.3	7.2 (13.1,0.8) *	66.1	46.7	55.7	49.1	35	11.0 (7.1, 14.7) **
Diarrhea	0.4	0.0	0.0	0.0	0.5	-	1.8	2.8	1.4	0.2	1.2	24.5 (41.7,2.1) △	2.2	2.8	1.4	0.2	1.7	20.1 (-2.0, 37.4) △
Tetanus	0.0	0.0	0.0	0.0	0.0	-	0.8	0.0	0.0	0.0	0.0	-	0.8	0	0	0	0	-
HIV	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-	0	0	0	0	0	-
Neonatal sepsis/meningitis	7.2	8.4	9.4	7.6	8.3	-2 (8.2,-13.3) △	7.3	5.9	9.9	7.4	11.3	-12.1 (-0.9,-24.5) *	14.5	14.3	19.3	15	19.6	-6.5 (-14.7, 1.2) △
Other infectious diseases	1.4	1.1	0.8	0.9	0.0	30.1 (51,0.3) △	0.4	0.0	0.6	0.0	0.0	35.6 (68,-29.5) △	1.8	1.1	1.4	0.9	0	33.1 (7.9, 51.4) *
Congenital malformations	69.8	50.6	57.3	53.5	52.3	5.6 (9.3,1.8) **	31.9	31.7	34.6	29.3	26.2	4.3 (9.4,-1) △	101.7	82.3	91.9	82.8	78.5	5.1 (2.0, 8.1) **
Other diseases	52.8	53.6	45.9	31.6	40.2	10.4	33.3	36.4	27.1	31.8	23.6	7.4 (12.3,2.2)	86.1	90	73	63.4	63.8	9.2 (5.9,

						(14.3,6.2) **						**					12.3) **
Urban area																	
Preterm birth	99.7	70.9	55.6	69.6	44.2	15 (19.4,10.4) **	11.5	22.0	18.9	14.7	19.1	-4.2 (6.2,-15.7) △	111.2	92.9	74.5	84.3	63.3	11.4 (7.1, 15.5) **
Intrapartum complications	78.6	70.9	59.0	53.1	36.9	15.8 (20.5,10.9) **	13.4	9.3	4.6	8.3	4.3	21.2 (32.7,7.9) *	92	80.2	63.6	61.4	41.2	16.4 (11.8, 20.7) **
Pneumonia	20.4	18.7	22.3	12.2	8.0	18 (26.5,8.5) **	8.4	7.4	12.6	10.7	5.5	2.7 (15.8,-12.4) △	28.8	26.1	34.9	22.9	13.5	12.4 (4.5, 19.7) **
Diarrhea	0.0	0.0	0.0	0.0	0.0	-	0.6	0.7	0.0	0.5	0.6	2.7 (51.8,-96.6) △	0.6	0.7	0	0.5	0.6	2.7 (-96.6, 51.8) △
Tetanus	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-	0	0	0	0	0	-
HIV	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-	0	0	0	0	0	-
Neonatal sepsis/meningitis	7.7	6.0	9.7	8.3	12.3	-13.8 (1.9,-32.1) △	2.5	6.7	6.9	9.2	8.6	-25.5 (-5.7,-49.1)**	10.2	12.7	16.6	17.5	20.9	2.7 (-96.6,

																	51.8) **
Other infectious diseases	1.9	2.0	1.1	1.5	0.0	33 (56,-1.9) △	0.0	0.0	0.6	0.0	0.0	2.7 (76.2,-297.1)△	1.9	2	1.7	1.5	0	25.2 (-7.7, 48.1) △
Congenital malformations	48.6	38.8	37.2	31.2	23.3	14.9 (20.9,8.4) **	24.3	25.4	20.1	15.1	17.9	10.8 (19,1.8) *	72.9	64.2	57.3	46.3	41.2	13.6 (8.4, 18.5) **
Other diseases	23.6	28.7	24.1	15.1	27.0	3.5 (11.8,-5.5)△	13.5	18.1	19.4	15.6	12.3	3.3 (13.3,-7.8) △	37.1	46.8	43.5	30.7	39.3	3.2 (-3.7, 9.7) △
Rural area																		
Preterm birth	165.0	161.4	139.8	136.2	86.4	12 (15.2,8.8) **	32.2	38.9	29.1	35.1	39.5	-4.1 (2.9,-11.7)△	197.2	200.3	168.9	171.3	125.9	9.2 (6.3, 12.1) **
Intrapartum complications	153.2	154.5	112.6	98.5	96.6	13.1 (16.3,9.7)**	10.6	10.0	9.3	8.0	7.4	8.2 (20.2,-5.5) △	163.8	164.5	121.9	106.5	104	12.8 (9.5, 15.9) **
Pneumonia	52.3	32.0	36.4	31.7	27.8	12.9 (18.8,6.5) **	30.5	23.9	28.5	29.1	16.9	7.6 (14.9,-0.4) △	82.8	55.9	64.9	60.8	44.7	10.8 (5.9, 15.5) **

Diarrhea	0.6	0.0	0.0	0.0	0.7	-	2.3	3.8	2.0	0.0	1.5	25.1 (45.4,-2.8)△	2.9	3.8	2	0	2.2	25.5 (-0.3, 44.6)*
Tetanus	0.0	0.0	0.0	0.0	0.0	-	1.2	0.0	0.0	0.0	0.0	-	1.2	0	0	0	0	-
HIV	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-	0	0	0	0	0	-
Neonatal sepsis/meningitis	7.0	9.4	9.3	7.3	6.6	3.3 (16.7,-12.4)△	9.4	5.7	11.2	6.6	12.4	-7.3 (6.7,-23.5)△	16.4	15.1	20.5	13.9	19	-2.3 (-13.2, 7.7)△
Other infectious diseases	1.2	0.6	0.7	0.7	0.0	30.3 (60.9,-24)△	0.6	0.0	0.6	0.0	0.0	42.4 (82.5,-89.3)△	1.8	0.6	1.3	0.7	0	29.7 (-13.7, 56.6)△
Congenital malformations	79.3	55.9	66.2	63.5	65.2	3.3 (8.2,-1.8) △	35.2	34.5	41.1	35.7	30.0	2.5 (9.1,-4.6) △	114.5	90.4	107.3	99.2	95.2	3.0 (-1.2, 6.9) △
Other diseases	65.8	64.7	55.6	39.0	46.1	11.6 (16.5,6.4)**	42.2	44.6	30.5	39.0	28.6	8.5 (14.6,1.9)*	108	109.3	86.1	78	74.7	10.3 (6.3, 14.2)**

(** means p value<0.01, * means p value<0.05, △ means p value≥0.05)

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The death cause distribution and AADR were also significantly different among urban-rural areas. In urban areas, preterm birth, intrapartum complication, and congenital anomalies also accounting the largest proportion of all deaths cause from 2014 to 2018. Moreover, the AADR of preterm birth, intrapartum complications, pneumonia, and congenital malformations in urban areas were all larger than that of the national level. In rural areas, the mortality rate of preterm birth, intrapartum complication, and congenital anomalies significantly decreased. Additionally, the NMR of diarrhea have sharply decreased, with AADR was 25.5% ($p<0.001$). (See **Table 2**)

In contrast, the urban-rural gap still existed. The contribution of tetanus among neonates in urban areas remains zero during the study period, while the rate in rural areas has been eliminated until 2015. In 2018, the neonatal mortality in rural areas was almost twice as high as in urban areas due to preterm birth, intrapartum complications, and congenital malformations. Moreover, during the study period, the largest number of neonatal deaths in the urban and rural areas was pneumonia, increased from 2.9 times (82.8 per 100,000 live births in rural areas VS 28.8 per 100,000 live births in urban areas) in 2014 to 3.3 times (44.7 per 100,000 live births in rural areas VS 13.5 per 1000 live births in urban areas) in 2018. (See **Table 2**) In the disease proportion aspect, the proportion of intrapartum complications and pneumonia in rural areas significantly higher than that of urban areas. (See Figure 2B&C) According to the data analysis, causes of neonatal death varied between

urban and rural areas (P<0.05), but the correlation between neonatal mortality and whether the newborn lived in urban or rural areas was weak (Cramer's V=0.129).

The mortality rates have also shown difference when divided neonates into early neonates (0-6 days) and late neonates (7-28 days). Nationwide, except for neonatal sepsis (or meningitis) and diarrhea, the mortality rate of other causes of death of early neonates was significantly higher than that of late neonates, with the biggest difference being intrapartum complications, preterm birth, and congenital malformations. In 2018, the mortality rate of preterm birth was 73.4 per 100,000 livebirth in early neonates and 33.2 per 100,000 livebirth in late neonates. In the same year, the mortality rate of congenital malformations was 52.3 per 100,000 livebirth in early neonates and 26.2 per 100,000 livebirth in late neonates. It is worth noting that intrapartum complications were the second leading cause of death among 0-28 days newborns in China from 2014 to 2018, with the mortality rate of 78.2 per 100,000 livebirth in early neonates and only 6.4 per 100,000 livebirth in late neonates (See **Table 2**).

3. Neonate Diagnosis Facilities Level in China between 2014 and 2018

The children's diagnosis facilities level has also be included in surveillance. Nationwide, from 2014 to 2018, the proportion of neonate diagnosis at the provincial (or municipal) level health facilities has significantly increased, and the proportion of the district (or county) level has decreased. Moreover, the proportion of township level and village level have both fluctuating declined during this period. In 2018, the proportion of neonate who has not to seek any medical care has minimized, which declined to 3.9% in 2018. (See **Figure 3**)

In an urban aspect, from 2014 to 2018, the majority of children (accounted for over 80%) in urban areas have been diagnosed at provincial (or municipal) level medical facilities. The proportion of the district (or county) level and township -level both have a slight rise between 2014 and 2018. As a result, the percentage of children who have not to seek medical care has declined, with 1.9% in 2014 and 1.1% in 2018. (See **Figure 3**)

On the contract, the diagnosis contribution figure of rural areas was different. Although the proportion of provincial (or municipal) level has shown a growth trend from 2014 to 2018, the proportion in rural areas have only half of that in urban areas. Moreover, the proportion of street-level diagnoses in the urban area is reduced to 1.4% in 2018, while this proportion in rural areas fluctuated and remained at 3.7% in the same year. Another significant

contributor is the proportion of children who have not sought medical care. The proportion of neonate who has not to seek medical care has decreased, and still, 5.5% of children have not sought any medical advice. (See **Figure 3**)

Discussion

The results of this study show that the NMR in urban and rural areas of China have decreased significantly between 2014 and 2018. In addition, there were significant differences in NMR between urban and rural areas, which were consistent with significant differences in NMR between countries and regions globally[20,21].

From 2014 to 2018, Chinese NMR continued to decline, and it was dropped quickly. It benefits from the improvement of medical treatment at all levels of health facilities, and all levels of government attached great importance to strengthen the construction of the pediatric institution, raise pediatricians' payment, and continue to implement neonatal asphyxia recovery training program[22]. As a result, neonatal deaths from pneumonia and infectious diseases, intrapartum complications, and premature delivery were significantly reduced.

China has implemented the Safe Maternal Initiative and the National Program to Reduce Maternal Mortality and Eliminate Tetanus, China has officially eliminated neonatal tetanus in 2012[23], and from 2015 to 2018, the NMR of neonatal tetanus remained 0. Moreover, through the success of the Prevention of Mother-to-child Transmission of HIV, Syphilis, and Hepatitis B Program, the HIV/AIDS mortality rate has also been 0 from 2014 to 2018[24,25]. Although the national neonatal mortality in 2018 was already less than 12 deaths per 1000 live births, the preventable deaths still accounted for 73.9%, mainly were pneumonia, intrapartum complication, premature birth. Among these diseases, the proportion of preterm birth was highest in both nationwide, urban areas, and rural areas. In the recent two decades, the prevalence of preterm birth has significantly increased[18], especially after the Two-child Policy[26] was implemented in China. The mortality rate among preterm birth infants was apparently higher than the full-term infant, and the risk of mortality increases proportionally with decreasing gestational age[27]. Furthermore, with the widespread development of assisted reproductive technique (ART), the incidence of monozygotic twins has increased significantly[28]. The NMR of twins is several times higher than that of singletons[29-31].

Addressing the issue of preterm birth may require different priorities in rural and urban

areas. Because of the good management of many curable neonatal complications (such as pneumonia), the proportion of preterm birth in urban areas is obviously larger than that of rural areas[32]. Hence, urban areas need to pay more attention to preventing premature deaths less than 32 weeks of gestation. For rural areas, the local government needs to focus on the prevention of premature infants at 32-36 weeks and continue to invest in medical services to improve medical services accessibility for women and children in rural areas.

In addition, from 2014 to 2018, the neonatal mortality rate in rural areas due to preterm birth, intrapartum complications, pneumonia, and congenital malformations was decreasing in rural areas but was still significantly higher than in urban areas. (See **Table 2**) The higher mortality rate may be linked to the relatively poorer economy, lower quality of health care, and lack of accessibility to health care in rural China. The average median net income per capita was ¥39251 (about US $6000) in urban China, but ¥14617 (about the US $2234) in rural China in 2018[33]. The annual spending on health care per capita accounted for 7.8% in urban China, but 10.2% in rural China in 2018[34]. The average health care personnel were 4.0 per 1000 people in urban China and 1.8 per 1000 people in rural China in 2018[34]. The number of beds in medical institutions per 1,000 people in urban areas was 8.70, compared with 4.56 in rural areas in 2018[34].

Not only markedly difference the NMR of urban and rural areas has shown, but also significantly difference in early and late neonates. The results of this study showed that the range of cause-specific mortality of late neonates was significantly less than that of early neonates, both nationwide and urban-rural areas. (See **Table 2**) Therefore, for preventable neonatal diseases, the focus should be on early neonates, especially for early neonates in rural areas.

For neonates, surviving from preterm birth, intrapartum complication and pneumonia are close linking to accessibility to health care, local hospitals' obstetrics and neonates departments' treatment level, and rescue skills[35,36]. Therefore, the issue can be addressed from the following four aspects.

Firstly, the local governments need to strengthen the construction of RNTN (Regional Neonatal Transport Network), carry out the transport plan according to the Guidelines for the Construction and Management of Critical Neonatal Treatment Center[37], and ensure the applying of professional medical staff and newborn rescue equipment for neonatal transport. Secondly, one study in Japan has pointed out that the medical care resources (including Neonatal Intensive Care Unit (NICU), midwives, emergency physicians, and emergency medical care centers) would impact the NMR decline[38]. Therefore, the local

governments may base on the Administration guide (proposal) of the Neonatal Physician Branch of the Chinese Physician Association[39] to grading neonatal wards and establishing NICU after analyzing local medical establishment plan and newborn medical treatment needs. Thirdly, local health departments can regularly organize multi-level， especially provincial, prefecture-level and district-level) newborn health training programs. In rural areas, with the policies support of the New Rural Construction and the Targeted Poverty Alleviation[40,41], the improved rural transport and higher incomes have prompted the enhanced accessibility of health services, and the proportion of rural children receiving medical treatment in provincial and municipal hospitals has significantly increased. The proportion of rural neonate diagnosis at the provincial (or municipal) level health facilities has significantly increased from 39.2% to 47.6% from 2014 to 2018 (See **Figure 3**). Set training objectives for medical staff in health facilities of different levels, and strengthen the newborn treatment technology in each level of health facilities. Especially for the health workers in rural areas, the newborn resuscitation training needs to be specifically strengthened. Fourthly, the local communities can strengthen publicity to encourage caregivers to take children to attend the health facilities for treatment. As for poor households, local governments can set up special subsidies for them to reduce the economic cost of medical treatment.

Conclusion

With the joint efforts of the economic development and the governmental policies and strategies, the neonatal mortality rate of China has significantly decreased from 2014 to 2018. The gap between neonatal mortality and cause-of-death distribution still existed between urban and rural areas. The goal of government interventions should be to narrow the urban-rural gap, reduce the health inequality of neonates, and further take targeted measures to eliminate the preventable death of neonates, especially premature births, to achieve the SDGs goal.

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Conflicts of interest

The authors declare no conflicts of interest.

Data Availability Statement

This study used data from the NMCHSS. This system is co-established by the National Health and Family Planning Commission of the People Republic of China and Sichuan University and finally owned by the National Health and Family Planning Commission of

the People Republic of China. The researchers did not obtain consent to publicly share data. The de-identified data set is available upon request to interested researchers. For data requests, please contact the Department of Science and Technology of West China Second University Hospital, Sichuan University, at: fu2yuankjb@163.com. This department is in charge of all the programs in the hospital, including the data management. One staff from the department monitors this email.

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Figure 1. The national and urban-rural neonatal mortality rates (per 1,000 live births) in China between 2014 and 2018

Figure 2A. Causes of deaths in neonates in China, 2018

Figure 2B. Causes of deaths in neonates in urban China, 2018

Figure 2C. Causes of deaths in neonates in rural China, 2018

Figure 3. The proportion of neonatal diagnose level in China from 2014 to 2018

Figure 1. The national and urban–rural neonatal mortality rates (per 1,000 live births) in China between 2014 and 2018

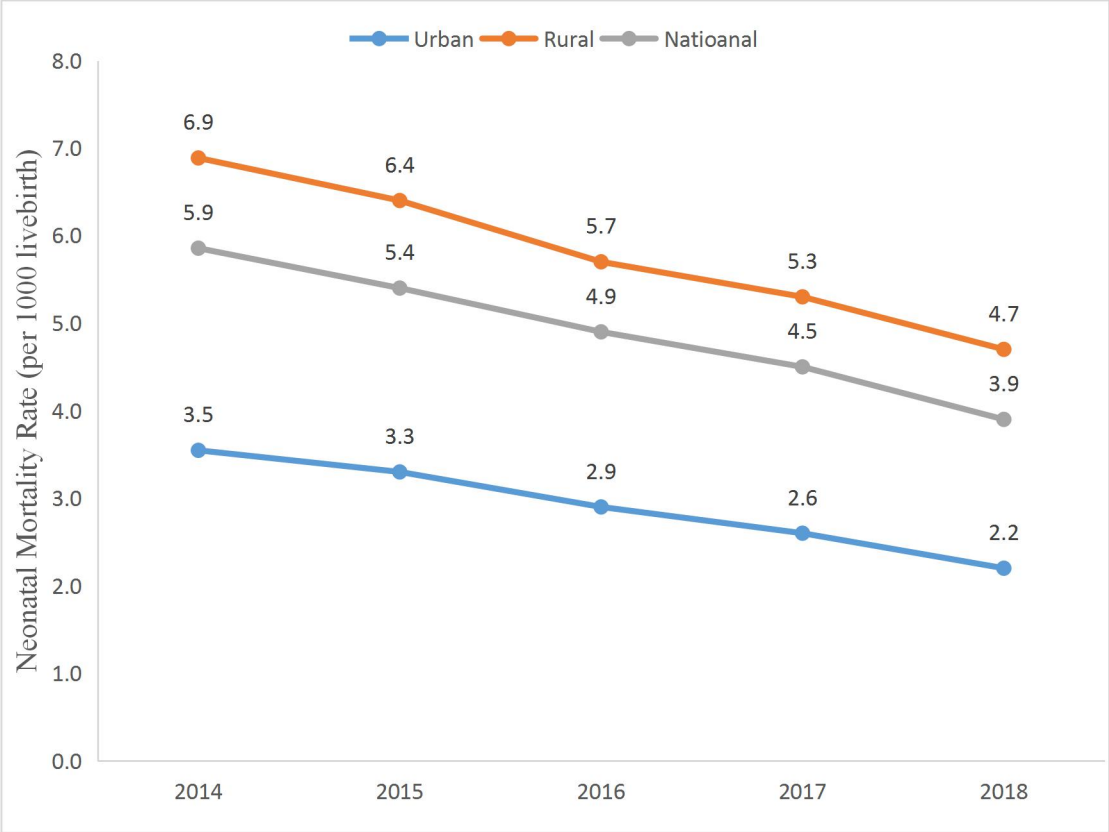
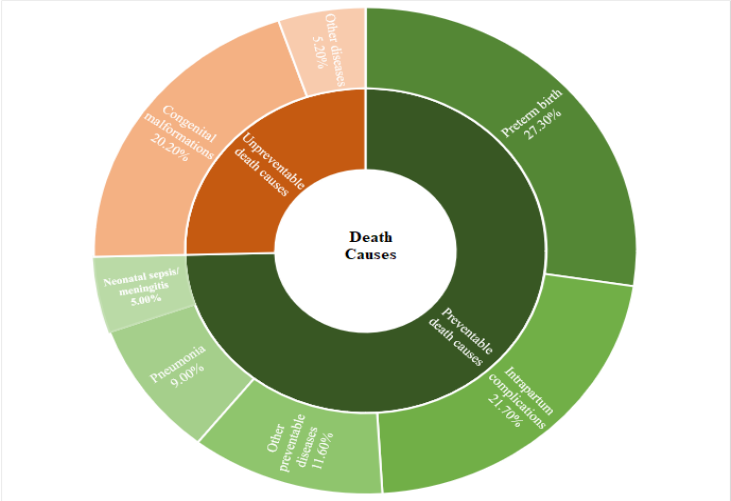


Figure 2A. Causes of deaths in neonates in China, 2018



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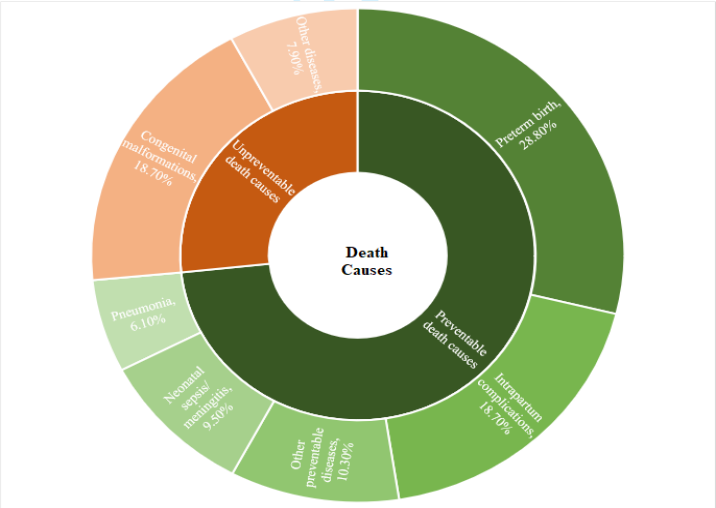

Figure 2C. Causes of deaths in neonates in rural China, 2018

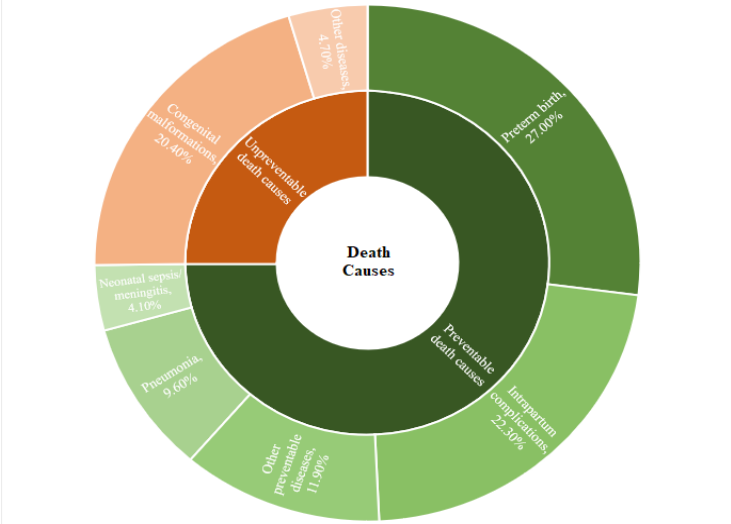

Figure 3. The proportion of neonatal diagnose level in China from 2014 to 2018