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Preplanned Studies

National Alveolar Echinococcosis Distribution — China, 2012–2016 01

Analysis of Early Essential Newborn Care Capacities of Rural Health Facilities — Four Provinces in Western China, 2016 08

Co-Administration of Multiple Childhood Vaccines — Guangdong Province, 2019 13

Notifiable Infectious Diseases Reports

Reported Cases and Deaths of National Notifiable Infectious Diseases — China, November, 2019 16

ISSN 2096-7071

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Cover Photo: Alveolar Echinococcosis Epidemiological Survey in Dalong Village, Shigatse, Tibet Autonomous Region, China, 2016. (Photographer: Shangdong Provincial Medical Team for Tibet)

Preplanned Studies

National Alveolar Echinococcosis Distribution — China, 2012–2016

Canjun Zheng[1,&]; Chuizhao Xue[2,&]; Shuai Han[2,&]; Zhongjie Li[1]; Hu Wang[3]; Liying Wang[2]; Ying Wang[2]; Qian Wang[4]; Yu Feng[5]; Yanyan Hou[6]; Xiao Ma[7]; Junying Ma[7]; Xiumin Han[8]; Gongsang Quzhen[9]; Xiaofeng Jiang[10]; Weidong Guo[10]; Xianglin Wu[11]; Yaming Yang[12]; Lei Cao[13]; Fanka Li[14]; Weiqi Chen[15]; Xinliu Yan[12]; Shicheng Yu[16]; Meihua Fu[2]; Qing Yu[2]; Ning Xiao[2]; Jiangping Cao[2]; Jun Yan[17]; Weiping Wu[2,#]; Xiao-nong Zhou[2,#]

Summary

What is already known about this topic?

Both alveolar echinococcosis (AE) and cystic echinococcosis are endemic in China, among which alveolar echinococcosis has a very high mortality rate.

What is added by this report?

The survey results showed the prevalence and scope of AE in China and identified high-risk groups including children, monks, herdsmen and illiterate people. At the same time, all the cases found in the survey (more than 90% of the patients did not go to the hospital for diagnosis and treatment before survey) were promptly diagnosed and treated.

What are the implications for public health practice?

This study provides information for the development of a plan for AE prevention and control and for the implementation of interventions targeted to high-risk populations.

Alveolar echinococcosis (AE) is a potentially lethal, zoonotic, parasitic disease caused by the larvae of *Echinococcus multilocularis* (*E. multilocularis*) and is designated by the WHO as neglected tropical disease. To comprehensively understand the prevalence and scope of AE in China, China CDC organized the relevant provincial and county-level centers for disease control and prevention to conduct the epidemiological survey on echinococcosis in 409 counties in 9 provincial-level administrative divisions from 2012 to 2016. In total, 1,208,944 people were examined by B-ultrasonography and estimated an overall prevalence in the population of the 6 provincial-level administrative divisions to be 0.27% (95% CI*: 0.25%–0.30%). Using results from this survey, a national plan to address echinococcosis has been formulated, and all detected cases during this study were treated with drugs or surgery. In addition, counties where AE was detected carried out deworming for dogs and wild animals, rat extermination around villages, and large-scale health education initiatives.

The *E. multilocularis* life cycle takes place primarily between wild canids (e.g. foxes, wolves, dogs, etc.) as definitive hosts and their prey (e.g. rodents) as intermediate hosts. Humans can become accidentally infected while consuming parasite eggs that are excreted in the feces of the definitive hosts, but otherwise does not transmit infections as part of the natural cycle. AE can infect the liver in humans and resemble a cancer-like malignant growth and is primarily endemic in the northern hemisphere including Asia, Europe, and North America. The resulting growth in the liver is characterized by slow development of metacestode stage and a prolonged duration of infection. Early stages are often absent of noticeable symptoms, but if left untreated, AE may lead to death in 90% of cases within 10–15 years of diagnosis (*1*).

AE cases have been reported continuously by hospitals in Western China. However, AE endemic areas in Western China, especially Qinghai-Tibet Plateau, often have cases that have not been diagnosed and reported to hospitals, potentially due to factors such as poor economic conditions, inconvenient transportation, and poor access to health services. In addition, undiagnosed cases frequently result in fatal outcomes, so reported hospital cases alone have difficulty capturing the full situation of the epidemic in China.

With the support of the National Health Commission of the People's Republic of China, China CDC organized the relevant provincial and county-level CDCs to conduct an epidemiological survey on

* CI=Confidence Interval.

echinococcosis from 2012 to 2016. Based on the conditions for transmission of echinococcosis in each county and the presence of reported cases of local echinococcosis infection in the Infectious Disease Reporting System of the China CDC, China CDC determined that 409 counties in 9 provincial-level administrative divisions across the country would be investigated.

A stratified and proportionate sampling method was adopted. In the criteria-meeting counties of Sichuan, Gansu, Qinghai provinces, and Xinjiang, Ningxia, and Tibet autonomous regions, all villages were classified by the mode of production of their local residents into four categories.[†] The number of villages, sampled randomly in each layer, was determined based on the proportion of the population in each layer of the county's population,[§] and 16 villages were sampled in each county.[¶]

An investigation team composed of epidemiologists and B-ultrasound doctors conducted B-ultrasound screening on survey subjects, recorded basic information for each subject and lesion information for each case, and then diagnosed and classified cases according to China's "Diagnostic Criteria for Echinococcosis" (WS 257–2006). Before the field survey, all investigators involved in the survey were trained for B-ultrasonography diagnosis and the use of Epi Info software. The same survey plan was used in each county, and all the cases diagnosed in the field survey were reviewed by B-ultrasonography experts at the provincial level.

The positive rate of AE in humans was defined as the number of diagnosed patients out of the total number of people examined. The prevalence of the population was calculated according to the following equation:

$$p = \sum_{j=1} \frac{njwj}{Nj} = \sum_{j=1} pjwj$$

where "p" is the prevalence of the population in the surveyed area, "n" is the number of cases detected in this layer, "N" is the total number of surveyed people in this layer, "j" is the rank of stratification, and "w" is the weight of the stratification (the proportion of the population in the layer to the total population of the region). All data were inputted using double entry in the Epi Info 3.5.4 (US CDC) database, with error correction using double-entry comparison. Statistical analysis was processed using SPSS 21.0 (IBM, New York, USA).

From 2012 to 2016, 1,208,944 people were examined by B-ultrasonography in 409 counties among 9 provincial-level administrative divisions including Qinghai, Sichuan, Gansu, Yunnan, and Shaanxi provinces, and Ningxia, Xinjiang, Tibet, and Inner Mongolia autonomous regions; 52.39% were male and 47.61% were female. No cases of AE were detected in Inner Mongolia, Yunnan, and Shaanxi. In 99 counties of the remaining 6 provincial-level administrative divisions, 1,243 cases of alveolar echinococcosis were diagnosed.

The overall prevalence in the population at risk in 6 endemic provincial-level administrative divisions was 0.27% (95% CI: 0.25%–0.30%), of which the prevalence rate in the population at risk in Qinghai province was the highest 0.73% (95% CI: 0.64%–0.81%). At the county level, the prevalence of 8 counties among 99 AE endemic counties nationwide exceeded 1% and were distributed in Qinghai, Sichuan, and Tibet, and the highest of which was Dari County in Qinghai with a prevalence of 10.95% (95% CI: 9.95%–11.95%) (Figure 1, Table 1).

Among 9,007,094 people at risk in 99 AE-endemic counties, 94,687 men and 106,636 women ranging from 1 to 99 years old were examined by B-ultrasonography, of which 524 and 719 cases of AE were diagnosed, respectively. The positive rate of AE among males was 0.55% (524/94,687, 95% CI: 0.51%–0.60%), and lower than that among females, 0.67% (719/106,636, 95% CI: 0.63%–0.72%), and the difference in positive rate between men and women was statistically significant (χ^2_{person} = 11.71, p<0.01). The youngest case of AE was 3 years old, and the oldest was 82 years old. Among both male and female groups, the positive rate was highest in the 10–14 age group with a positive rate of 1.47% (95% CI: 1.15%–1.78%) among males and 1.70% (95% CI: 1.35%–2.06%) among females. From age groups

[†] Pastoral areas (animal husbandry only), semi-pastoral/semi-farm areas (animal husbandry and farming both), farm areas (farming only), and urban areas (live in urban).

[§] For the surveyed villages, if the population of the administrative village was too large, a smaller group of villages within the administrative village was selected as the surveyed area. If the population of the administrative village was too small and could not meet the minimum requirement of 200 people, people from adjacent villages were added as survey subjects.

[¶] Due to the small population of some counties in Tibet autonomous region, in counties with a population of more than 100,000, 50,000-100,000, 10,000-50,000, and below 10,000, we selected 16 villages, 8 villages, 4 villages, and 2 villages, respectively. In Yunnan and Shaanxi provinces, 12 villages and 15 villages were sampled in each county by simple random sampling, respectively.

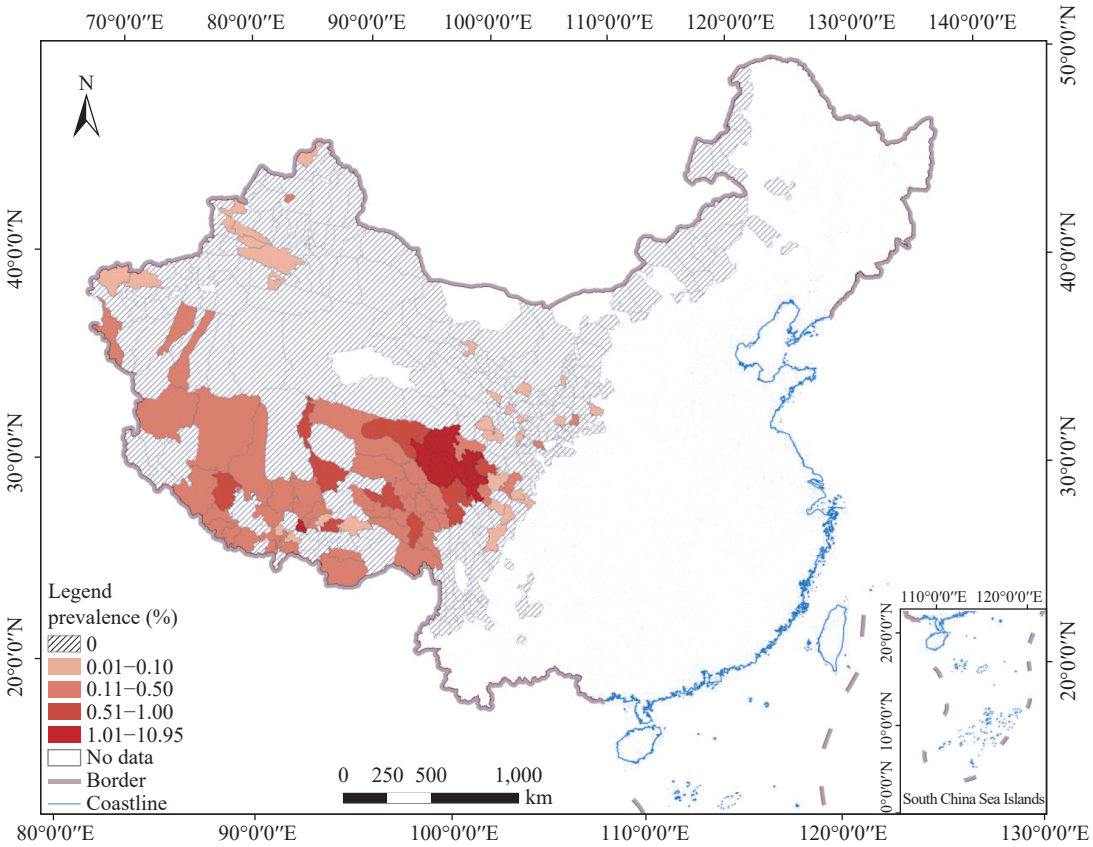

FIGURE 1. Prevalence distribution by county of alveolar echinococcosis in China, 2012–2016.

TABLE 1. Fifteen counties with the highest prevalence of alveolar echinococcosis in China, 2012−2016.

Province/Autonomous Region	County	Population at risk	Surveyed population	Number of cases	Prevalence % (95% CI)
Qinghai	Dari	28,002	3,719	388	10.95(9.95–11.95)
Qinghai	Chengduo	51,136	2,462	105	5.32(4.43–6.20)
Qinghai	Maduo	13,780	143	8	5.19(1.56–8.83)
Sichuan	Siqu	70,100	3,223	150	4.82(4.08–5.56)
Qinghai	Banma	27,206	2,476	109	3.73(2.98–4.48)
Sichuan	Seda	44,820	3,202	65	1.87(1.40–2.34)
Qinghai	Gande	28,815	3,325	42	1.33(0.94–1.72)
Tibet	Nimu	29,228	853	7	1.04(0.36–1.72)
Tibet	Baqing	39,416	823	8	0.97(0.30–1.64)
Tibet	Cuoqin	12,978	824	8	0.97(0.30-1.64)
Qinghai	Qumalai	27,778	995	11	0.95(0.35–1.55)
Sichuan	Dege	78,773	3,208	21	0.94(0.60–1.27)
Tibet	Suoxian	42,398	812	7	0.86(0.23–1.50)
Sichuan	Ganzi	67,780	3,202	27	0.86(0.54–1.18)
Qinghai	Jiuzi	24,965	3,242	28	0.86(0.54–1.17)

ranged 20 to 79, the positive rate of the population remained at about 0.5% without significant changes, but the rate drops sharply for age groups over 80 years old (Figure 2).

Among the 8 occupational groups, the highest positive rate of AE was found among monks (2.09%; 95% CI: 1.34%–2.58%), followed by herdsmen (1.36%; 95% CI: 1.26%–1.45%) and students

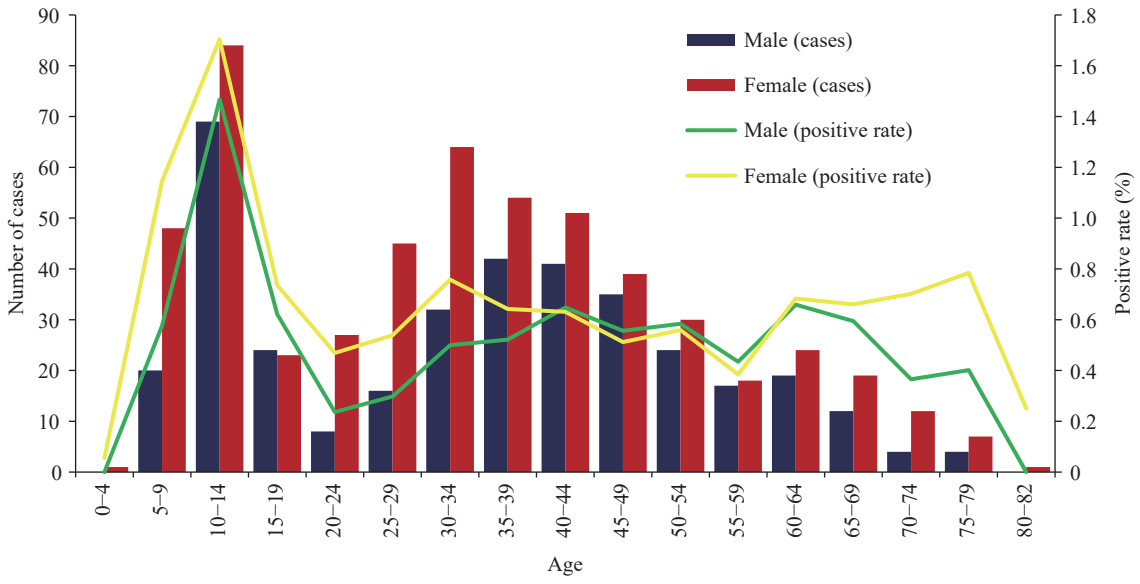

FIGURE 2. Distribution of alveolar echinococcosis across different gender and age groups.

(1.36%; 95% CI: 1.19%–1.53%) (Table 2). The positive rates across different occupational groups showed statistical significance (χ^2_{person} = 1195.62, p<0.001). Among different educational level groups, the positive rate of AE among illiterate people was the highest (0.90%; 95% CI: 0.83%–0.97%). As education increases, the positive rate has a downward trend ($\chi^2_{Linear\text{-}by\text{-}Linear\ Association}$ = 194.85, p<0.001).

Based on the mode of production of their local residents in western China, the survey regions were divided into pastoral areas, pastoral and farm areas, farm areas, and urban areas, and the positive rate of AE of residents living in different areas showed statistical significance (χ^2_{person} = 1316.46, p<0.001), with the positive rate among people living in pastoral areas being the highest (1.53%; 95% CI: 1.43%–1.62%). Because some herdsmen in the Qinghai-Tibet Plateau need to travel far to pasture and live in tents from May to October every year before returning to their settlement for winter, we compared the prevalence in those people to that of settlers who resided at their settlement for the year. The positive rate among those who were nomadic during the summer and settled in the winter (1.56%; 95% CI: 1.44%–1.68%) was significantly higher than that of settlers (χ^2_{person} = 809.75, p<0.001).

Discussion

The results of this survey showed that AE was endemic in 99 counties in 6 provincial-level administrative divisions in China including Qinghai, Sichuan, Gansu, Tibet, Xinjiang, and Ningxia. These counties are concentrated in the Qinghai-Tibet Plateau, especially in the border area between Qinghai and Sichuan provinces, as well as the Tibet Autonomous Region where 13 of the 15 counties with the highest prevalence of AE are located. The Qinghai-Tibet Plateau has a large landscape with a wide variety and large population of wild canids, rodents, and other wild animals, and most of the residents are herdsman so the natural transmission cycle of AE is widespread. There are also many domestic and stray dogs in the Qinghai-Tibet Plateau, which can be considered an important source of infection as terminal hosts (*2*). These natural features may be important determinants for AE in the Qinghai-Tibet Plateau. However, the prevalence at the junctions of the three provincial-level administrative divisions is much higher than that of the other Qinghai-Tibet Plateau regions. For example, residents in areas of Tibet autonomous region that have similar lifestyle habits, modes of production, socioeconomic conditions, and cultural traditions to residents of the junctions have lower prevalence. There may be other factors at work, and further investigation is needed.

In Qinghai, Sichuan, Gansu, Ningxia and other provinces or regions, some sporadic small-scale population surveys of AE conducted in the past showed positive rates varying from 0.2%–10% (*3*), but these survey results used different methods and choice of survey subjects and have difficulty accurately

TABLE 2. Positive rates of alveolar echinococcosis among genders, occupations, education levels, and modes of production, and types of residence in China, 2012−2016.

	Surveyed population	No. of cases	Proportion %	Positive rate % (95% CI)
Gender				
Male	94,687	524	42.16	0.55(0.51–0.60)
Female	106,636	719	57.84	0.67(0.63–0.72)
Occupations				
Herdsmen	56,176	762	62.15	1.36(1.26–1.45)
Farmers/herdsmen	14,679	53	4.32	0.36(0.26–0.46)
Monks	1,385	29	2.37	2.09(1.34–2.58)
Students	17,600	240	19.58	1.36(1.19–1.53)
House workers	1,819	10	0.82	0.55(0.21–0.89)
Public officers	6,195	26	2.12	0.42(0.26–0.58)
Farmers	93,995	95	7.75	0.10(0.08–0.12)
Others	9,477	11	0.90	0.12(0.05–0.18)
Educational level				
Illiterate	69,485	626	51.06	0.90(0.83–0.97)
Elementary school	81,276	532	43.39	0.65(0.60–0.71)
Junior high school	32,007	37	3.02	0.12(0.08–0.15)
High school	7,098	9	0.73	0.13(0.04–0.21)
College and above	5,215	20	1.63	0.38(0.22–0.55)
Local residents' modes of production				
Pastoral area	62,871	961	78.38	1.53(1.43–1.62)
Pastoral and farm area	53,966	120	9.79	0.22(0.18–0.26)
Farm area	64,138	61	4.98	0.10(0.07–0.12)
Urban area	20,343	84	6.85	0.41(0.32–0.50)
Types of residence				
Settled	159,599	575	46.90	0.36(0.33–0.39)
Settled in summer and nomadic in winter	41,581	649	52.94	1.56(1.44–1.68)
Others	13,416	174	14.19	1.30(1.11–1.49)

reflecting the overall AE epidemic situation in China. Following a consistent investigation plan, this survey conducted stratified cluster sampling to examine more than 1.2 million people and showed a 0.27% AE prevalence in 99 counties in 6 provincial-level administrative divisions nationwide. Directly comparing the results of this large population-based sampling survey in China to that of other countries in Europe, Asia, North America, and other regions is difficult because most existing data outside of China are based on hospital reports (*4*), and only one study, based on the population of Sary Mogol in South Kyrgyzstan (*5*) which shows the prevalence of AE to be 4.2%(68/1,617), has been found outside China.

Torgerson PR et al. used the previous sporadic survey results in China and the number of cases reported by hospitals in other endemic countries to estimate that the burden of AE in China accounted for more than 91% of the world (*6*). Applying the calculation method outlined by Torgerson PR et al. to this new survey data, the results still show that China has the most severe AE burden around the world. Apart from the natural factors of the Qinghai-Tibet Plateau, the severity of the AE epidemic in China may be related to poor economic conditions, lack of education in the endemic areas, lack of knowledge on AE, and poor sanitation habits such as insufficient hand washing caused by lack of convenient access to water (*7*).

For the age distribution of AE, this survey found two distinct, novel characteristics, of which no similar findings have been found in the literature because

previous studies in other countries depend on hospital reporting and can only estimate age composition. The first is that the prevalence among children aged 10–14 years is the highest, and the second is that prevalence of the population in the 20–79 age groups is relatively stable. This feature is significantly different from the age distribution of cystic echinococcosis (CE) cases. Population-based surveys in Sichuan, Gansu, Tibet, and other places show that the prevalence of CE increases with age and did not show that the positive rate is higher in the younger age groups (*8*).

The high prevalence of AE in China in the group aged 10–14 may be related to frequent contact with dogs and poor hand washing habits among young people in the Qinghai-Tibet Plateau. Although the source of AE is generally considered to be predominantly wild canids, some surveys on the Qinghai-Tibet Plateau have shown that dogs have a higher rate of infection with *E. multilocularis*, indicating frequent contact with dogs is still an important risk factor for children in the region. In comparison to AE, CE has a long course, which can last several decades, and a low mortality rate, so as age increases, cases gradually accumulate and lead to an increase in the prevalence with age. However, AE often has a high mortality rate, which can exceed 90% over 10 years, so the accumulation of cases is less likely. Therefore, the prevalence of people in the age group of 20–79 years is relatively stable.

This survey shows that the prevalence of women is significantly higher than that of men. Surveys in other countries and regions have also shown this result. When reviewing relevant literature, some scholars found that the odds ratio for women was 1.66 (95% CI: 1.31–2.10) (*9*). This may be a result of women having higher risk of exposure due to taking on more household work, having higher contact with cow dung fuel that may be polluted with worm eggs, and feeding domestic dogs, though a higher biological susceptibility of women to AE should be further investigated.

Most Tibetan residents in the Qinghai-Tibet Plateau region practice Tibetan Buddhism and an important teaching of Buddhism is to not end life, so many stray dogs often gather around the temples to be fed by monks. Therefore, the prevalence of AE among monks is very high in this survey. Herdsmen and illiterate people having higher AE prevalence follows results of surveys in other countries (*10*) and may be due to the natural cycle of AE being widespread in the grasslands where herdsmen reside, and hygiene practices such as hand washing are poor due to the limitations of the living environment. Similarly, lack of knowledge about the disease is also a risk factor among illiterate people with high prevalence of AE.

This survey was carried out using portable B-ultrasonography in the field. Only abdominal lesions of AE could be found, whereas lesions in the lungs, brain, and other areas outside the abdomen could not be detected. Because the study sampled residents, we cannot exclude the possibility of AE epidemics in other counties of the Qinghai-Tibet Plateau. In Inner Mongolia, Heilongjiang, and Jilin where AE cases have been reported previously, further investigation should be carried out to determine whether they are also endemic areas.

Acknowledgments

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[#] Corresponding authors: Weiping Wu, wuwp@nipd.chinacdc.cn; Xiao-nong Zhou, zhouxn1@chinacdc.cn.

[1] Division of Infectious Diseases, Chinese Center for Disease Control and Prevention, Beijing, China; [2] National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention; Chinese Center for Tropical Diseases Research; WHO Collaborating Centre for Tropical Diseases; National Center for International Research on Tropical Diseases, Ministry of Science and Technology; Key Laboratory of Parasite and Vector Biology, Ministry of Health, Shanghai, China; [3] Health Commission of Qinghai Province, Xining, Qinghai, China; [4] Sichuan Provincial Center for Disease Control and Prevention, Chengdu, Sichuan, China; [5] Gansu Provincial Center for Disease Control and Prevention, Lanzhou, Gansu, China; [6] Xingjiang Uyghur Autonomous Region Center for Disease Control and Prevention, Urumqi, Xinjiang, China; [7] Qinhai Institute for Endemic Disease Prevention and Control, Xining, Qinghai, China; [8] Qinghai Provincial People's Hospital, Xining, Qinghai, China; [9] Tibet Center for Diseases Control and Prevention, Lhasa, Tibet, China; [10] Inner Mongolia Autonomous Region Center for Diseases Control and Prevention, Hohhot, Inner Mongolia, China; [11] Ningxia Center for Disease Control and Prevention, Yinchuan, Ningxia, China; [12] Yunnan Institute of Parasitic Diseases, Puer, Yunnan, China; [13] Shaanxi Provincial Center for Disease Control and Prevention, Xi'an, Shaanxi, China; [14] Xinjiang Production and Construction Corps Center for Disease Control and Prevention, Urumqi, Xinjiang, China; [15] Henan Provincial Center for Disease Control and Prevention, Zhengzhou, Henan, China; [16] Office of epidemiology, Chinese Center for Disease Control and Prevention, Beijing, China; [17] National Health Commission of the People's Republic of China, Beijing, China.
[&] Joint first authors.

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Preplanned Studies

Analysis of Early Essential Newborn Care Capacities of Rural Health Facilities — Four Provinces in Western China, 2016

Tao Xu[1,#]; Wen Qu[1]; Yan Wang[1]; Qing Yue[1]; Xiaona Huang[2]; Xiaobo Tian[2]

Summary

What is already known about this topic?

The Early Essential Newborn Care (EENC) intervention package recommended by World Health Organization (WHO) is shown to prevent and treat the leading causes of newborn illness and death. China has begun widespread implementation of the EENC.

What is added by this report?

Among the 14 core interventions, including using antibiotics for mothers with premature rupture of membranes, immediate skin-to-skin contact of mother and baby, delayed umbilical cord clamping, kangaroo mother care for preterm newborn, and neonatal sepsis and pneumonia management, were not sufficiently implemented in health facilities in western China.

What are the implications for public health practice?

There are gaps between the implementation situation and WHO recommendations in terms of EENC capacities in western China. Targeted interventions developed accordingly can ensure quality child health care and decrease newborn mortality in China.

China has achieved remarkable results in reducing under-five mortality rates, but the proportion of neonatal deaths remains high. In order to explore a pattern of early newborn health care service in China, the National Health Commission of the People's Republic of China (China NHC) cooperated with the United Nations International Children's Emergency Fund (UNICEF) to implement the "Safe Neonatal Project" in four western provinces in 2017. The purpose of this study was to understand the gaps between the implementation situation of project areas and the World Health Organization (WHO) recommendations in terms of early newborn health care capacities. A mail survey method was used to collect information of 233 midwifery hospitals in the 21 project counties of 4 western provinces. Descriptive statistical analysis was used to compare the implementation coverage of the 14 core early newborn health care interventions recommended by the WHO. The results indicated that some core interventions were not well implemented, such as using antibiotics for mothers with premature rupture of membranes, immediate skin-to-skin contact between mother and baby, delayed umbilical cord clamping, kangaroo mother care for preterm newborn, and neonatal sepsis and pneumonia management. These results could provide a basis for developing targeted interventions and assessing the project impacts.

In 2017, the national neonatal mortality rate was 4.5‰ in China, accounting for 50% of deaths among children under five years old (*1*). The time of childbirth and the three days after birth is a critical period for neonatal survival and health. Early interventions in this period can effectively reduce neonatal mortality and improve long-term health outcomes (*2*). In 2014, the WHO published the "Action plan for healthy newborn infants in the Western Pacific Region (2014–2020)" and set targets for ending preventable neonatal deaths by 2020. Member States are recommended to implement the Early Essential Newborn Care (EENC), a package of evidence-based interventions shown to prevent and treat the leading causes of newborn illness and death (*3–4*). In 2017, China NHC and UNICEF jointly launched the three-year "Safe Neonatal Project" in four western provinces and introduced EENC. The purpose of this study was to evaluate the baseline situation of project areas in terms of early newborn health care capacities, understand the gaps between existing conditions and the recommendations, and provide a basis for developing targeted interventions.

This study was part of the baseline survey of the "Safe Neonatal Project". From June 2017 to September 2018, all midwifery hospitals in 21 project counties of Guizhou, Qinghai, and Sichuan provinces and Ningxia Autonomous Region participated in a mail survey to collect data. The questionnaire was

focused on the 14-core newborn health care interventionsrecommendedbytheWHOEENCguideline (Box 1) (5). Evaluation indicators included: basic information of hospitals, major maternal and child health outcomes, and implementing coverage rates of the core interventions. The questionnaires were issued by NHC through each provincial health authority to the hospitals. Provincial health authorities were responsible for providing training and guiding all counties and township level midwifery hospitals to fill out the questionnaire. All the collected data were the data by the end of 2016. No personal information was collected from individual patients and medical staff.

Data were entered into EpiData database using double-entry method. After the data were checked for quality and cleaned up, SPSS 22.0 (IBM, New York, USA) software was used for data analysis. Descriptive statistical analysis was used to compare the frequency and percentage of indicators among provinces.

There were 21 counties, 417 townships, and 5,352 villages in the project area. State-poverty counties accounted for 85.7% of all counties. There were 59 county-level and 211 township-level midwifery hospitals. A total of 233 midwifery hospitals completed the questionnaire, accounting for 86% of the targeted hospitals. In 2016, the population of 15 to 49 year-old women and 0 to 5 year-old children was 2.44 million and 0.52 million, respectively. The number of pregnant women was 95,430 and the number of live births was 95,764 (Table 1).

Regarding implementation of maternal health interventions, the gestational hypertension management rate (98.3%), maternal syphilis treatment rate (97.9%), and folic acid intake rate (88.8%) in the project area were high. The average cesarean section rate was 30.4%, of which 84.6% had medical indications. Approximately 60.1% of hospitals could implement antibiotics for management of preterm rupture of membranes, but only 77.3% of women with membrane preterm ruptures received this treatment. The average incidence of obstetric hemorrhage was 1.5%, and 70.9% of women received obstetric hemorrhage prevention interventions.

Regarding implementation of childbirth interventions,

Box 1. The 14-core newborn health care interventions recommended by EENC guideline.

Maternal health interventions	Childbirth interventions	Neonatal disease interventions
1. Maternal syphilis detection and treatment	7. Delayed umbilical cord clamping and proper care	11. Neonatal resuscitation
2. Gestational hypertension management	8. Immediate skin-to-skin contact of mother and newborn for at least 90 minutes after birth	12. Neonatal intramuscular injection of vitamin K_1
3. Pregnant women take folic acid orally	9. Exclusive breastfeeding	13. Neonatal eye care
4. Antibiotics for management of preterm rupture of membranes	10. Kangaroo mother care for premature newborns	14. Common neonatal diseases diagnosis and treatment
5. Strict control of indications for cesarean section		
6. Prevention of obstetric hemorrhage		

TABLE 1. Basic information and key maternal and child health indicators of the 21 counties in 4 provinces in 2016.

Indicator	Guizhou	Ningxia	Qinghai	Sichuan	Total
Number of project counties	5	4	7	5	21
Number of project townships	108	47	101	161	417
Number of villages	1,705	506	1,220	1,921	5,352
Proportion of state-poverty county (%)	100	100	57.1	100	85.7
Number of county-level hospitals	13	6	16	24	59
Number of township-level hospitals	66	24	33	88	211
Total population (ten thousand)	267.8	100.8	167.6	375. 0	911.2
Number of women aged 15−49 years old (ten thousand)	82.0	21.1	44.3	96.9	244.3
Number of children aged 0−5 years old (ten thousand)	16.5	8.4	11.4	16.0	52.3
Number of pregnant women	23,885	15,340	23,979	32,226	95,430
Number of live births	24,813	15,406	23,256	32,289	95,764

the proportion of immediate skin-to-skin contact of mother and newborn for at least 90 minutes after birth was 41.8%. Only 17.5% of newborns received delayed umbilical cord clamping, 24.7% of hospitals could implement kangaroo mother care (KMC) for premature newborns, 31.8% of preterm babies received any types of KMC, and 77.7% of newborns completed the first breastfeeding within 1 hour after birth. The exclusive breastfeeding rate at discharge was 83.8%.

Regarding implementation of neonatal disease interventions, the neonatal asphyxia rate was 3.2% in project area. The rate in Guizhou (6.1%) was higher than the other provinces, and the incidence of neonatal sepsis and neonatal pneumonia was 0.1% and 2.9%, respectively. The proportions of hospitals that carried out neonatal sepsis and pneumonia management were 33.5% and 47.8%, respectively. The rate of transferring newborns to neonatal intensive care unit (NICU) was 9.8%, with the rate in Guizhou (21.0%) higher than the other provinces. About 50.9% of hospitals carried out neonatal eye care intervention, and 74.2% of hospitals could implement intramuscular injection of vitamin K_1 to prevent intracranial hemorrhage, but only 69.8% newborns received this intervention (Table 2).

Discussion

The EENC guidelines aim to improve the quality of maternal and child health care services in health facilities. Because of the higher risk of neonatal death during childbirth and within a few days after birth, the EENC guideline emphasizes interventions during this time period (*5–7*). The WHO has set an ambitious target that at least 80% of midwifery hospitals in each Member States should have fully implemented EENC by 2020 (*3*). The current study found that, in the project area of the "Safe Neonatal Project", there are gaps between the current implementation and the WHO recommendations.

Although the coverage of major maternal health care services was high, some interventions still need improvement. For example, the use of antibiotics in mothers with premature rupture of membranes is an effective intervention to prevent neonatal infectious diseases. About 60.1% of the hospitals carried out this intervention, but around 40% of patients with medical indications did not receive this treatment. The average cesarean section rate in project areas was close to the national cesarean section rate (34.1%) and rural cesarean section rate (30.3%) (*1*).

In terms of interventions during childbirth, the implementation rates of immediate skin-to-skin contact (41.8%), delayed umbilical cord clamping (17.5%), and kangaroo mother care for preterm newborn (24.7%) were below WHO targets (80%). A previous study conducted in the same area found that medical staff had a misunderstanding on the concept of "skin-to-skin contact between mother and baby" (*8*). According to the EENC guideline, skin-to-skin contact should be the contact of bare breast and belly, rather than face-to-face contact (*9*). The results also indicated that, although more than 60% of hospitals reported they could implement delayed umbilical cord clamping, only 17.5% of newborns received this treatment. Further research is needed to explore barriers that hinder the implementation of this intervention.

In terms of neonatal disease interventions, less than 50% of hospitals could carry out neonatal sepsis and pneumonia diagnosis and treatment services. This was also below the WHO target (80%). In addition, there were gaps among provinces in the NICU transferring rate. NICU transfer rate is related to the diagnosis and treatment capacity, but on the other hand, it is also influenced by the mastery of medical indications (*8*). Unnecessary NICU transfer and excessive medical interventions may not only increase the economic burden of patients, but may also negatively affect the health of newborns (*10*).

This study has some limitations. First, data was self-reported by hospitals. Due to the differences in understanding of study significance, data collection capacity, and workload among hospitals, reporting bias may exist. Second, self-reported data might overestimate the actual implementation of these interventions. A previous study conducted in the same areas collected data using face-to-face interviews with women after delivery (*8*), and the results indicated the proportion of immediate skin-to-skin contact of mother and newborn after birth was 36.1%, which was lower than finding of this study (41.8%). Third, most of the project counties are state-poverty counties. The health care resources and capacities cannot represent the level of the province. The results may not be extrapolated to the whole province or the country. Nevertheless, this is the first study to investigate the current situation of EENC implementation in base-level hospitals in China. The results may provide directions for further research and for developing targeted interventions.

TABLE 2. Comparison of coverage of 14 EENC core interventions of the 21 counties in 4 provinces in 2016 (%).

Core intervention	Indicator	Guizhou	Ningxia	Qinghai	Sichuan	Total
1. Maternal syphilis detection and treatment	Treatment rate of pregnant women with syphilis	83/83 (100)	11/12 (91.7)	132/137 (96.4)	49/49 (100)	275/281 (97.9)
2. Gestational hypertension management	Management rate of pregnant women with hypertension	235/235 (100)	355/355 (100)	268/268 (100)	54/70 (77.1)	912/928 (98.3)
3. Pregnant women take folic acid	Folic acid intake rate	22,295/24,199 (92.1)	14,143/14,740 (95.9)	15,993/21,598 (74.0)	27,706/29,682 (93.3)	80,137/90,219 (88.8)
4. Strict control of indications for cesarean section	Caesarean section rate	8,123/24,153 (33.6)	2,321/14,712 (15.8)	2,695/21,303 (12.7)	14,058/29,395 (47.8)	27,197/89,563 (30.4)
	Cesarean section with medical indications	6,498/8,123 (80)	2,265/2,321 (97.6)	2,578/2,695 (95.7)	11,673/14,058 (83)	23,014/27,197 (84.6)
5. Antibiotics for management of preterm rupture of membranes	Proportion of hospitals implemented	38/60 (63.3)	12/19 (63.2)	14/44 (31.8)	76/110 (69.1)	140/233 (60.1)
	Proportion of mothers treated	932/1,083 (86.1)	1,571/1,712 (91.8)	1,329/1,636 (81.2)	1,062/1,904 (55.8)	4,894/6,335 (77.3)
6. Prevention of obstetric hemorrhage	Incidence of obstetric hemorrhage	581/24,199 (2.4))	258/14,740 (1.8)	247/21,598 (1.1)	258/29,682 (0.9)	1,344/90,219 (1.5)
	Obstetric hemorrhage mortality (100 thousand)	0/24,199 (0)	1/14,740 (6.8)	0/21,598 (0)	0/29,682 (0)	1/90,219 (1.1)
7. Neonatal resuscitation	Incidence of birth asphyxia	1,474/24,153 (6.1)	293/14,712 (2)	846/21,303 (4)	241/29,395 (0.8)	2,854/89,563 (3.2)
	NICU transfer rate	5,067/24,153 (21)	1,377/14,712 (9.4)	1,055/21,303 (5)	1,284/29,395 (4.4)	8,783/89,563 (9.8)
8. Immediate skin-to-skin contact of mother and newborn for at least 90 minutes after birth	Proportion of hospitals implemented	12/60 (20)	1/19 (5.3)	2/44 (4.5)	5/98 (5.1)	20/221 (9)
	Proportion of babies skin to skin contact for at least 90 minutes	5,636/24,153 (23.3)	7,927/14,712 (53.9)	7,648/21,303 (35.9)	16,251/29,395 (55.3)	37,462/89,563 (41.8)
9. Exclusive breastfeeding	First breastfeeding within 1 hour after birth	17,475/24,153 (72.4)	9,419/14,712 (64)	17,522/214,303 (82.3)	25,147/29,395 (85.5)	69,563/89,563 (77.7)
	Exclusive breastfeeding at discharge	18,907/24,153 (78.3)	12,474/14,712 (84.8)	17,998/21,303 (84.5)	25,657/29,395 (87.3)	75,036/89,563 (83.8)
10. Delayed umbilical cord clamping and proper care	Delayed umbilical cord clamping rate	1,992/24,153 (8.2)	2,101/14,712 (14.3)	3,734/21,303 (17.5)	7,861/29,395 (26.7)	15,688/89,563 (17.5)
	Neonatal umbilical infection rate	7/24,153 (0)	22/14,712 (0.1)	54/21,303 (0.3)	1/29,395 (0)	84/89,563 (0.1)
11. Neonatal eye care	Proportion of hospitals implemented	43/60 (71.7)	6/19 (31.6)	15/44 (34.1)	54/109 (49.5)	118/232 (50.9)
	Incidence of neonatal eye infection	27/24,153 (0.1)	16/14,712 (0.1)	273/21,303 (1.3)	127/29,395 (0.4)	443/89,563 (0.5)
12. Neonatal intramuscular injection of vitamin K_1	Proportion of hospitals implemented	49/60 (81.7)	14/19 (73.7)	21/44 (47.7)	89/110 (80.9)	173/233 (74.2)
	Vitamin K_1 injection rate	19,143/24,153 (79.3)	12,484/14,712 (84.9)	11,538/21,303 (54.2)	19,321/29,395 (65.7)	62,486/89,563 (69.8)
13. Kangaroo mother care for premature newborns	Proportion of hospitals implemented	21/60 (35)	6/19 (31.6)	6/44 (13.6)	24/108 (22.2)	57/231 (24.7)
	Proportion of babies received	36/520 (6.9)	331/626 (52.9)	39/487 (8)	291/556 (52.3)	697/2,189 (31.8)
14. Common neonatal diseases diagnosis and treatment	Proportion of hospitals implemented neonatal sepsis management	29/59 (49.2)	6/19 (31.6)	6/43 (14)	36/109 (33)	77/230 (33.5)
	Proportion of hospitals implemented neonatal pneumonia management	39/60 (65)	9/19 (47.4)	16/44 (36.4)	47/109 (43.1)	111/232 (47.8)
	Incidence of neonatal sepsis	31/24,153 (0.1)	58/14,712 (0.4)	17/21,303 (0.1)	1/29,395 (0)	107/89,563 (0.1)
	Incidence of neonatal pneumonia	691/24,153 (2.9)	503/14,712 (3.4)	708/21,303 (3.3)	659/29,395 (2.2)	2,561/89,563 (2.9)

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[#] Corresponding author: Tao Xu, xutao6622@chinawch.org.cn.

[1] National Center for Women and Children's Health, Chinese Center for Disease Control and Prevention, Beijing, China; [2] UNICEF China, Beijing, China.

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Preplanned Studies

Co-Administration of Multiple Childhood Vaccines — Guangdong Province, 2019

Hai Li[1,2]; Yanqiu Tan[1,3]; Haiying Zeng[1,3]; Fengmei Zeng[1,4]; Xing Xu[1,5]; Yu Liao[1,6]; Qi Zhu[6]; Meng Zhang[1,6]; Xuguang Chen[1,6]; Min Kang[1,6]; Fujie Xu[7]; Huizhen Zheng[1,6,#]

Summary

What is already known about this topic?

The Co-Administration of Multiple Vaccines were implemented in many countries and have been shown to significantly reduce many times of visiting the vaccination clinic.

What is added by this report?

It is the first time to calculate the cost of visiting vaccination clinic from transportation and work-absence for children's families in Guangdong.

What are the implications for public health practice?

We demonstrated the importance of Co-Administration of Multiple Vaccines that reduce the vaccination cost of children's families. The policy should be promoted as soon as possible.

In Guangdong Province, children under 2 years old are commonly given 10 types of National Immunization Program (NIP)-recommended vaccines (BCG, HepB, IPV, bOPV, DTaP, MPV-A, MR, JE-L, HepA-L, MMR) given in 17 doses and 6 non-NIP vaccines (Rotavirus, PCV13, Hib, EV71, Influenza, and Chicken Pox) given in 16 doses (*1–2*). Then Guangdong issued the vaccination abnormal response compensation insurance and Co-Administration of Multiple Vaccines policy (*3–4*). Previously, to administer these 33 vaccine doses, 25 visits to the vaccination clinic were required, but the policy has theoretically reduced the number of required visits to 14 (*1*,*5*). This study used children under 2 years old registered in the National Immunization Program Information Management System (NIPIMS) as the sampling population, and survey participants were selected by stratified random sampling. Relevant data were collected through interviews conducted in-person or by telephone, and costs due to transportation and work absences to receive these vaccinations were estimated for the children's families. A total of 591 children's parents were interviewed, and the average costs were estimated at 103.42 RMB per clinic visit. This policy could save about 1137.62 RMB for each child during their first 2 years of life. To provide scope, 1.8 million infants in Guangdong received the first dose of Hepatitis B vaccine in 2018; based on the number of children, this policy could therefore save up to 2.0 billion RMB for families in Guangdong Province for this single vaccination event. The Co-Administration of Multiple Vaccines Policy can significantly reduce vaccination costs for children's families and can greatly improve the social cost-effectiveness of childhood vaccinations. Our findings suggest that Co-Administration of Multiple Vaccines should be implemented as soon as possible.

This study estimated the cost incurred by the families with children under 2 years old in Guangdong Province during the process of inoculation. Children were randomly selected from NIPIMS, and duplicate cases and cases without phone numbers were excluded. In Guangzhou and Shenzhen, relevant phone numbers could not be collected so children's families were interviewed in-person. The cost of transportation included the fee of taking public traffic (subway, bus, or taxi) or by calculating unit distance or unit time (driving cars, motorcycles, or battery cars) (*6–8*). Work absences were measured as the time required for all the accompanying personnel to complete the whole inoculation process. The data was inputted by double-entry using Epidata3.1 and then organized into a database with Excel 2016, and descriptive statistical analysis was performed with SPSS 21.0.

A total of 1,720 calls were made, 635 persons answered the phone (response-rate 36.92%), and 430 persons were effectively interviewed (effective-response-rate 67.72%). An additional 219 persons were interviewed in-person (response-rate 100%), and 161 persons were effectively interviewed (effective-response-rate 73.52%). Ultimately, 591 children's families were included in the final sample (Table 1).

The median total cost was 103.42 RMB per clinic visit, the median transportation cost was 5.20 RMB per clinic visit, and the median work-absence cost was 93.42 RMB per clinic visit. The region with the highest total cost per clinic visit was the Pearl River

Delta, the median total cost was 148.56 RMB per clinic visit (Table 2).

Before the Co-Administration of Multiple Vaccines Policy, vaccines in different category could not be co-administered. As a result, children under 2 years in Guangdong Province required 25 visits to the vaccination clinic to complete the 33 required doses of 16 types of vaccines. After implementing the Co-Administration of Multiple Vaccines Policy, the number of required clinic visits has potential to be reduced from 25 visits to 14 visits. But there were some vaccines (DTaP-IPV/Hib, DTaP/Hib, PCV13, Bivalent HPV and Tetravalent HPV) that could not be recommended to be co-administered under Chinese vaccine instructions. (Figure 1)

Discussion

Previous research on vaccines focuses more on the cost of production, storage, and transportation as well as the valuation of vaccine effectiveness. However, fewer studies evaluate the cost to families associated with visiting the clinic in terms of transportation and absences from work that exclude the cost of vaccines.

In the past, NIP vaccines and non-NIP vaccines generally could not be co-administered because of the different funding sources for compensation insurance for routine immunization. In 2018, Guangdong Province issued adverse events compensation insurance for routine immunization. The insurance cost is jointly shared by the government and by the vaccine enterprises. The basic insurance costs of NIP vaccines are paid using the special fund for the development of health and family planning. The basic insurance costs of non-NIP vaccines are paid by vaccine enterprises. Insurance companies will pay for all abnormal reactions following vaccination (*3*).

The amount in savings (2.2 billion RMB) for families in Guangdong Province as a result of the Co-Administration of Multiple Vaccines Policy was a theoretical maximum savings as it was not based upon the actual uptake of non-NIP vaccines. The actual savings will depend on how many families use non-NIP vaccines that are co-Administered with NIP vaccines. We found that savings in the Pearl River Delta (1.9 billion RMB) far exceeded other regions (0.3 billion RMB). This may be due to the larger number of people accompany the children, the longer work-absences, and the higher level of per-capita wages in the Pearl River Delta.

This study is subject to at least four limitations. First, the telephone interviews might be subject to recall bias, and in-person interviews may be subject to selection bias. Second, using both telephone interviews and in-person interviews might affect the consistency of the data (*9–10*). Third, there is no comparison between urban and rural areas, which may include

TABLE 1. The aspects of vaccination clinic visits in Guangdong Province.

Region	Number of interviews (%)	Accompanied persons			Clinic distance * (km)	Work absence time * (Hour)	Transportation time † (Hour)	Total time per clinic visit * (Hour)
		1	2	>2				
Pearl River Delta	351(59.39)	117	215	19	2.00(1.00, 4.00)	2.00(1.00, 3.00)	0.44(0.41, 0.47)	1.65(1.57, 1.74)
East Guangdong	80(13.54)	18	59	3	3.30(2.00, 8.50)	1.00(1.00, 2.00)	0.44(0.38, 0.49)	1.33(1.18, 1.49)
West Guangdong	85(14.38)	27	54	4	4.25(2.00, 5.15)	2.00(1.50, 3.00)	0.50(0.43, 0.57)	1.50(1.33, 1.66)
North Guangdong	75(12.69)	38	37	0	3.00(1.28, 6.00)	1.50(1.50, 2.00)	0.38(0.33, 0.43)	1.24(1.07, 1.41)
Guangdong	591(100)	200	365	26	2.00(1.00, 5.00)	2.00(1.00, 3.00)	0.44(0.41, 0.46)	1.54(1.47, 1.60)

* The data presented a non-normal distribution and was represented by median and quartile (P_{25}, P_{75}).
† The data was normally distributed and expressed as a mean and 95% Confidence Interval.

TABLE 2. The costs of vaccination clinic visits in Guangdong Province.

Region	Hourly wage per capita (RMB)	Transportation cost per clinic visit * (RMB)	Work absence cost per clinic visit * (RMB)	Total cost per clinic visit * (RMB)
Pearl River Delta	62.28	4.00(0.00, 16.00)	124.56(41.30, 186.84)	148.56(124.56, 253.12)
East Guangdong	17.92	10.00(4.00, 20.00)	35.85(26.88, 53.76)	52.30(35.84, 73.76)
West Guangdong	21.96	2.80(0.40, 11.00)	43.92(21.96, 76.86)	52.92(37.11, 88.64)
North Guangdong	16.52	4.00(0.00, 10.00)	24.78(16.52, 33.04)	33.04(20.52, 46.52)
Guangdong	39.59	5.20(0.00, 16.00)	93.42(41.30, 186.84)	103.42(50.78, 186.84)

* The data presented a non-normal distribution and was represented by median and quartile (P_{25}, P_{75}).

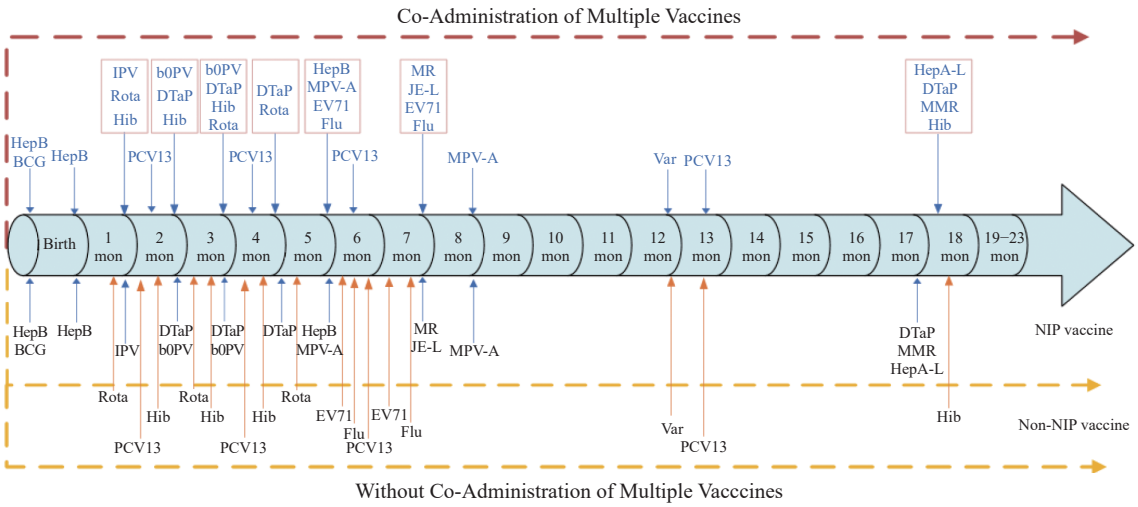

FIGURE 1. Comparison of inoculation schedule before and after the Co-Administration of Multiple Vaccines Policy.

Note: PCV13 cannot be administered with other vaccines because of the Chinese vaccine instruction.

Abbreviation: BCG: Bacillus Calmette – Guerin Vaccine; Hep-B: Hepatitis B Vaccine; IPV: Inactivated Poliovirus Vaccine; b-OPV: Bivalent Oral Poliomyelitis Vaccine; DTaP: Diphtheria Tetanus Pertussis Vaccine; MPV-A: Meningococcal Poly-saccharide Vaccine, A; MR: Mumps and Rubella Vaccine; JE-L: Japanese Encephalitis Vaccine, Live; HepA-L: Hepatitis A Vaccine, Live; MMR: Measles, Mumps and Rubella Vaccine; PCV13: Pneumococcal Polysaccharide Conjugate Vaccine, 13-valent; Hib: Haemophilus influenzae type B Vaccine; EV71: Enterovirus 71 Inactivated Vaccine.

relatively large disparities in results. Fourth, this study did not account for differences in the willingness of people in different regions to consume non-NIP vaccines.

Future research could evaluate the precision of vaccine co-administration, whether the NIP vaccines could be administered on schedule, and if this policy could increase coverage for non-NIP vaccines. To reduce the number of vaccination clinic visits required for children, more research should be done on co-administration of vaccines and on combining vaccinations.

[#] Corresponding author: Huizhe Zheng, zhz@cdcp.org.cn.

[1] Field Epidemiology Training Project of Guangdong Province, Guangzhou, Guangdong, China; [2] Guangzhou Liwan CDC, Liwan, Guangzhou, China; [3] Qingyuan Yingde CDC, Qingyuan, Guangdong, China; [4] Shaoguan Renhua CDC, Shaoguan, Guangdong, China; [5] Heyuan Zijin CDC, Heyuan, Guangdong, China; [6] Guangdong Center for Disease Control and Prevention, Guangzhou, Guangdong, China; [7] The first affiliated hospital of Zhejiang University, Hangzhou, Zhejiang, China.

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Notifiable Infectious Diseases Reports

Reported Cases and Deaths of National Notifiable Infectious Diseases — China, November, 2019

Diseases	Cases	Deaths
Plague	4	0
Cholera	1	0
SARS-CoV	0	0
Acquired immune deficiency syndrome	7,366	2,245
Hepatitis	127,706	53
Hepatitis A	1,230	0
Hepatitis B	102,174	45
Hepatitis C	21,182	5
Hepatitis D	28	0
Hepatitis E	2,062	2
Other hepatitis	1,030	1
Poliomyelitis	0	0
Human infection with H5N1 virus	0	0
Measles	250	0
Epidemic hemorrhagic fever	1,445	13
Rabies	23	22
Japanese encephalitis	7	1
Dengue	1,767	1
Anthrax	22	0
Dysentery	4,680	0
Tuberculosis	73,000	177
Typhoid fever and paratyphoid fever	642	0
Meningococcal meningitis	11	0
Pertussis	1,653	0
Diphtheria	0	0
Neonatal tetanus	11	0
Scarlet fever	10,215	0
Brucellosis	2,892	0
Gonorrhea	10,448	1
Syphilis	50,439	7
Leptospirosis	7	0
Schistosomiasis	12	0
Malaria	258	2
Human infection with H7N9 virus	0	0
Influenza	156,205	5
Mumps	27,704	0
Rubella	952	0

Continued

Diseases	Cases	Deaths
Acute hemorrhagic conjunctivitis	3,206	0
Leprosy	37	0
Typhus	146	0
Kala azar	8	0
Echinococcosis	469	1
Filariasis	0	0
Infectious diarrhea*	89,252	3
Hand, foot and mouth disease	100,161	0
Total	**670,999**	**2,531**

* Infectious diarrhea excludes cholera, dysentery, typhoid fever and paratyphoid fever.

The number of cases and cause-specific deaths refer to data recorded in National Notifiable Disease Reporting System in China, which includes both clinically-diagnosed cases and laboratory-confirmed cases. Only reported cases of the 31 provincial-level administrative divisions in Mainland China are included in the table, whereas data of Hong Kong Special Administrative Region, Macau Special Administrative Region, and Taiwan are not included. Monthly statistics are calculated without annual verification, which were usually conducted in February of the next year for de-duplication and verification of reported cases in annual statistics. Therefore, 12-month cases could not be added together directly to calculate the cumulative cases because the individual information might be verified via National Notifiable Disease Reporting System according to information verification or field investigations by local CDCs.

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