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Preplanned Studies

HIV-Positive Men Are More Likely to Be Hyper Linked Within College Student Social Network — Northeast China, 2017–2018

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Summary

What is already known about this topic?

Men who have sex with men (MSM) bear a disproportionate burden of new human immunodeficiency virus (HIV) infections and young MSM demonstrate parallel internet-driven HIV incident infection and dynamic social network.

What is added by this report?

The HIV positive prevalence and incidence among college MSM were 3.8% and 2.9 per 100 person-years, respectively, while these rates were 13.9% and 10.5 per 100 person-years, respectively, among their social contacts. The overall HIV positive prevalence was 7.2% in Northeast China. HIV-positive MSM have comparatively more social contacts than HIV-seronegative MSM.

What are the implications for public health practice?

Hyper-linkages found in app-based social networks play an important role in HIV transmission via risky sexual behavior and suggest options for online intervention to promote HIV prevention.

The incidence of human immunodeficiency virus (HIV) cases in young male students who had sex with men (MSM) has reported an average annual 10% increase in HIV diagnoses from 5,841 in 2010 to 13,717 in 2019 in China (*1*). The rise and popularity of geo-social networking apps used by young MSM (YMSM) have a parallel increased risk for sexually transmitted infections (STIs), due to an increase in the number of partners and a reduction in sexual health behaviors (*2*). However, lowering community viral load through treatment as prevention (TasP) (*3*) has become a critical HIV response strategy, by reducing sexual transmission among persons living with HIV (PLHIV) (*4*). In this paper, we sought to describe and examine the association and magnitude of social contacts within the social network of an app that employs serosorting to identify the uneven social linkage among college MSM in Northeast China. In this study, we recruited 759 college MSM and 382 of their social contacts from the Yiyou app from April 2017 to June 2018. A total of 98 participants (8.6%) were confirmed HIV positive during baseline and follow-up serology tests, of whom 34 were college MSM. For college MSM, HIV positive prevalence at baseline and incidence at follow-ups were 3.8% (29/759) and 2.9 per 100 person-years (PY) (5/170.50 PY). Network graphing visualization showed that HIV-positive MSM had comparatively more social contacts (social dynamic) than the seronegative MSM. Therefore, identifying certain individuals as hyper-linkages within college MSM social network can inform tailored HIV prevention strategies such as sending reminders for information about antiretroviral therapy (ART) and promoting safer sexual behaviors.

We conducted a prospective longitudinal study and recruited participants among Yiyou app (developed by Heilongjiang Kangtong Community [HKC]) users. HKC manages 21 offline voluntary counseling and testing (VCT) sites using the Yiyou app umbrella in 16 cities within Northeast China to facilitate serosorting and other offline services, by appointment. The Yiyou app users must register with a cell phone number that is later used to share testing information with a mutual agreement upon inquiry, i.e., partner informed serosorting purposes (Figure 1A). That is the main reason for the app's popularity. We recruited participants via three methods, including online advertisements on the Yiyou app homepage, person-to-person sharing by HKC visitors, and public service announcements in offline VCT clinics of HKC. The participants' recruitment and follow-up procedures were detailed in Figure 1B. A self-administered structured questionnaire was conducted via the Yiyou app on sociodemographic information, perceived risk of HIV infection, sexual behaviors, recreational drug use in the past 6 months, and HIV self-testing experience. Upon completion of the online survey, participants were asked to undertake dual rapid HIV

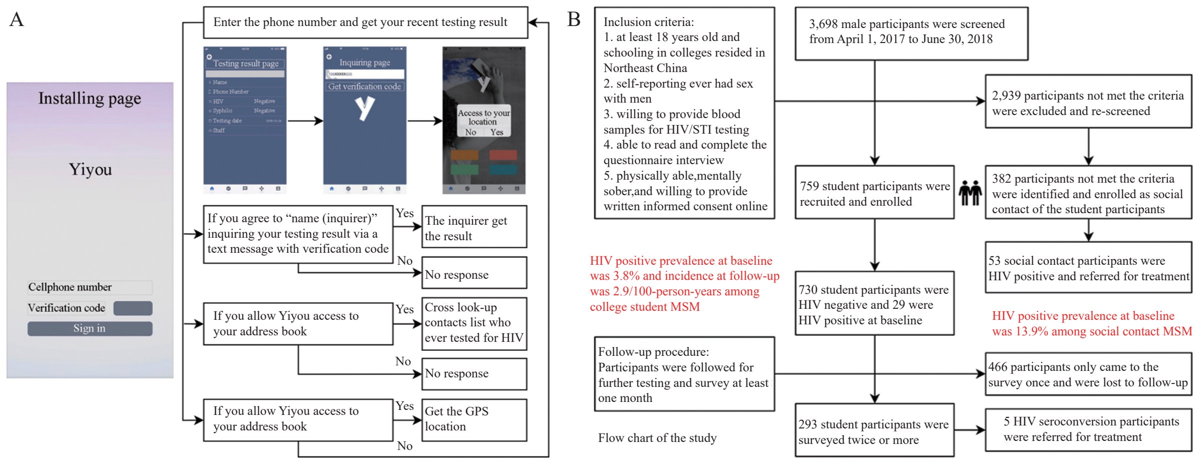

FIGURE 1. Illustration and flowchart of the study. (A) The illustration of Yiyou App installation and use process; (B) The flowchart of participants' recruitment and follow-up procedure of the study.
Abbreviation: HIV=human immunodeficiency virus; STI=sexually transmitted infection.

and syphilis tests and a parallel rapid HIV test by trained workers in offline VCT sites and confirmed HIV testing at a provincial CDC. Descriptive analyses were performed to identify the distribution of sociodemographic and behavioral characteristics and a Mann–Whitney *U* test was used to identify the difference in number of social contacts between the two HIV statuses.

As per informed consent, we enhanced the Yiyou app information with a social parameter, using latitude and longitude from GPS data of all universities in Northeast China to verify the students' identity by their geolocation sign-in, in addition to self-reported student identity. After a predesigned de-identification procedure, contact lists were linked to registered users of the Yiyou app and the social contacts were filtered by logical inference from the label information of phone contacts. Furthermore, we calculated the number of social contacts for each participant and determined the linkage for each participant as a snapshot of the whole social network at the end of the study, midnight of June 30, 2018. We used network analytic techniques to provide a "snapshot" to characterize what the network looks like as a static social structure. Nodes represent users and links represent interactions between users; the size of the node is proportional to the number of social contacts. The algorithm finds each node by minimizing the dispersion of the whole system. Microsoft Excel (Microsoft®, Albuquerque, New Mexico, USA) and Statistical Analysis System (Version 9.4, SAS Institute Inc., Cary, North Carolina, USA) were used to manage the dataset and conduct analyses and Gephi® software for Windows (V.0.9.2) was used to visualize the social network.

Of 3,698 persons approached, 1,141 (30.9%) became study participants aged 24 years old [interquartile range (IQR)=21–33]; 759 (66.5%) were college students and 382 (33.5%) non-student contacts. A total of 98 participants (8.6%) were confirmed HIV positive during baseline and follow-ups, of whom 34 were college MSM. For college MSM and their social contacts, HIV prevalence at baseline and incidence in follow-ups were 3.8% (29/759) and 2.9 per 100 PY (5/170.50 PY), 13.9% (53/382), and 10.5 per 100 PY (11/105.06 PY), respectively.

Among college MSM, 97% were Han ethnic, 96% were not married to a woman, 44.3% were migrants without local residency permits (*hukou*), 61.7% lived in Northeast China for >2 years, and 75.6% self-identified as homosexual. Regarding risk perception and sexual behavior, 29.8% perceived their risk of HIV infection as moderate or high. In the past 6 months, 49.5% reported anal sex, 47.6% used condoms consistently, 25.8% had >1 regular partner, and 18.3% used recreational drugs (Table 1). The median number of social contacts of college students was zero compared to two of their social contacts. The number of social contacts showed a significant difference (Z=6.1, P<0.001) between 98 HIV positive MSM (median: 1, IQR: 1–2) and 1,043 HIV negative MSM (median: 0, IQR: 0–1).

Figure 2 allows us to identify highly connected individuals (i.e., hyper-linkages) with different HIV statuses among college students and their social contacts. It showed that HIV-positive MSM had comparatively more social contacts than their seronegative counterparts. However, some of the HIV

TABLE 1. Demographic and behavioral characteristics of college students and their social contacts among MSM in Northeast China, 2017-2018 (*N*=1,141).

Factors	College students, n=759	Social contacts, n=382	Total, N=1,141
	n **(%)**	***n*** **(%)**	***n*** **(%)**
Age (years)*			
Median	22	33	24
IQR	20–26	26–47	21–33
Ethnic			
Han	736 (97.0)	370 (96.9)	1,106 (96.9)
Minority	22 (2.9)	8 (2.1)	30 (2.6)
Marital status			
Married	25 (3.3)	47 (12.3)	72 (6.3)
Unmarried	729 (96.0)	334 (87.4)	1,063 (93.2)
Residence			
Local	422 (55.6)	254 (66.5)	676 (59.2)
Other cities/PLADs	336 (44.3)	128 (33.5)	464 (40.7)
Time spent locally			
<12 months	126 (16.6)	42 (11.0)	168 (14.7)
12–24	164 (21.6)	56 (14.7)	220 (19.3)
>24 months	468 (61.7)	284 (74.3)	752 (65.9)
Sexual orientation			
Homosexual	574 (75.6)	271 (70.9)	845 (74.1)
Heterosexual	17 (2.2)	8 (2.1)	25 (2.2)
Bisexual	115 (15.2)	81 (21.2)	196 (17.2)
Uncertain	52 (6.9)	22 (5.8)	74 (6.5)
Perceived risk of HIV infection			
No-low	533 (70.2)	223 (58.4)	756 (66.3)
Moderate	171 (22.5)	118 (30.9)	289 (25.3)
High-very high	55 (7.3)	41 (10.7)	96 (8.4)
Having anal sex in the past 6 months			
Yes	376 (49.5)	266 (69.6)	642 (56.3)
No	330 (43.5)	116 (30.4)	446 (39.1)
Condom use with male partners in the past 6 months†			
Never	23 (6.1)	16 (6.0)	39 (6.1)
Sometimes	174 (46.3)	91 (34.2)	265 (41.3)
Every time	179 (47.6)	158 (59.4)	337 (52.5)
Number of regular partners in the past 6 months†			
0	48 (12.8)	42 (15.8)	90 (14.0)
1	231 (61.4)	148 (55.6)	379 (59.0)
2	74 (19.7)	53 (19.9)	127 (19.8)
≥3	23 (6.1)	23 (8.6)	46 (7.2)
Any recreational drug use in the past 6 months			
Yes	139 (18.3)	103 (27.0)	242 (21.2)
No	619 (81.6)	279 (73.0)	898 (78.7)

TABLE 1. (Continued)

Factors	College students, n=759 *n* (%)	Social contacts, n=382 *n* (%)	Total, N=1,141 *n* (%)
Ever had HIV self-test			
Yes	282 (37.2)	124 (32.5)	406 (35.6)
No	424 (55.9)	257 (67.3)	681 (59.7)
Syphilis status			
Negative	698 (92.0)	329 (86.1)	1,027 (90.0)
Positive	60 (7.9)	51 (13.4)	111 (9.7)
Not sure	1 (0.1)	2 (0.5)	3 (0.3)
Number of social contacts*			
Median	0	2	0
IQR	0–0	1–3	0–1
HIV status			
Negative	725 (95.5)	318 (83.2)	1,043 (91.4)
Positive	34 (4.5)	64 (16.8)	98 (8.6)
HIV positive rate			
Baseline (%)	29 (3.8)	53 (13.9)	82 (7.2)
Follow-up (per 100 PY)	5 (2.9)	11 (10.5)	16 (5.8)

Abbreviation: PLADs=provincial-level administrative divisions; MSM=men who have sex with men; IQR=interquartile range; HIV=human immunodeficiency virus; PY=person-years.

* Age and number of social contacts are skewed distributions; hence, we present median and interquartile range.

† Total number is of men who had anal sex in the past 6 months. PY stands for person-years. When numbers do not add to the expected sample size, it means that some men did not answer a given question.

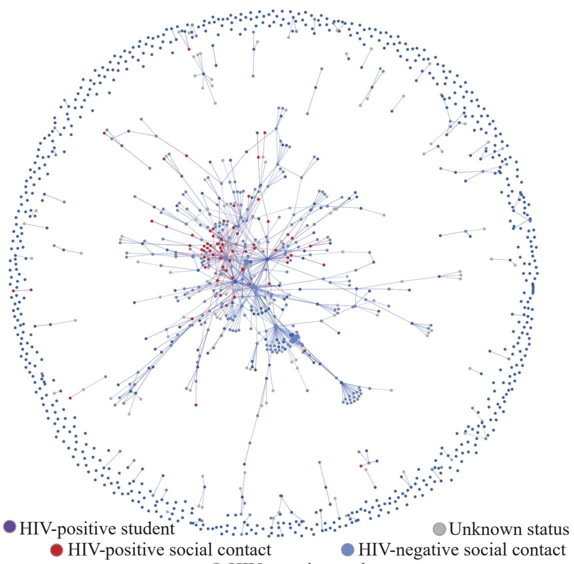

FIGURE 2. Network graph of the young men who have sex with men in Northeast China, 2017–2018, categorized by HIV sero-status and social identity (college students and social contacts, N=1,141).
Note: Nodes represent users and links represent interactions between users; the size of the node is proportional to the number of social contacts.
Abbreviation: HIV=human immunodeficiency virus.

positive students showed no social contact or declined to share social contact with us. Therefore, they are dispersed outside.

DISCUSSION

We used HIV testing services data from the offline VCT sites and innovative app-derived social network data to describe and identify the HIV-positive men as hyper-linkages among college MSM who used the Yiyou serosorting app in Northeast China. HIV-positive men had comparatively more social contacts than HIV-negative people, presenting disproportionately more hyper-linkages within the MSM social networks.

In recent years, MSM bear a disproportionate burden of new HIV infections in China, and YMSM aged 15–24 are the most vulnerable population. In our study, the HIV prevalence and incidence were estimated as 3.8% and 2.9 per 100 PY, respectively, among college MSM aged 22 years old. A 7-city cross-sectional survey reported that YMSM had a higher HIV incident infection (up to 5.4% per annum) compared to MSM who were older (*5*). The drastic increment of annual reported cases among YMSM, including many university students, has garnered attention from the Chinese government and society (*1*).

It is noteworthy that HIV-positive MSM had comparatively more social contacts than the seronegative MSM. Not surprisingly, YMSM typically get to know each other through mobile dating apps, and they would leave mobile phone numbers to social contact only if they choose to meet or intend to have further communication (*6*). YMSM may be more easily influenced by a social contact, particularly one who exhibits trust by disclosing his sexual orientation. To safeguard their privacy, some college MSM may have more social contacts outside of the school than with student peers (*7*). Most YMSM prefer to use online dating apps when seeking potential sexual partners and calculating risk of HIV transmission (*8*). Moreover, homophobia or related stigmatization may be a barrier to accessing HIV prevention knowledge, an obstacle overcome by LGTBQ-friendly social media (*9*). We noticed that some HIV positive college men had no social contacts during the study period. It is possible some students caught HIV earlier than the research app launched. Therefore, dating apps and other social media apps can be used as an important prevention platform, especially if artificial intelligence algorithms can enable more individual tailoring for intervention.

The major strengths of this study include the following: the participation rate (>30%), which is high compared to many other internet-based surveys with a representative sample of MSM users of social apps in the real world; and the innovative app-derived social networking data, which enabled us to explore social network utilization. Limitations of this study include the following: the social networks were limited in the Yiyou app users and these findings cannot be generalized to other LGTBQ-friendly dating apps; the cross-sectional social contact information does not permit ascertainment of the direction of the findings or confidence in causal pathways; and the social contact information is unavoidably biased towards a minimum estimate in terms of the number, density, or breadth of their sexual network, due to the complexity of technology and human interaction.

In the following stages of our ongoing studies, we will focus on the key population at high HIV transmission risk and send reminders for information about ART and promote safer sexual behaviors to tap into the potential of LGTBQ-friendly apps for HIV prevention.

Conflicts of interest: No conflicts of interest.

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Preplanned Studies

The Incidence, Mortality, and DALYs Trends Associated with Esophageal Cancer — China, 1990–2019

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Summary

What is already known about this topic?

Esophageal cancer (EC) is one of the most common malignant tumors in China. The new cases and deaths in China account for more than half of the world, and the disease burden of esophageal cancer is serious.

What is added by this report?

From 1990 to 2019, the disease burden of EC in China showed a decrease overall; it first increased between 1990 and 2004, but then decreased between 2004 and 2019. The burden of EC in men was much higher than that in women. Age was an important factor affecting the burden of EC, with disease burden rising rapidly after 40 years old.

What are the implications for public health practices?

The screening, early diagnosis, and treatment for EC should continue to be strengthened in China. Middle-aged and elderly men are high-risk groups of EC and should be a key population for EC prevention and control.

Esophageal cancer (EC) is one of the common malignant tumors that cause death and disability among Chinese people. According to the latest analysis of malignant tumors in China, EC is the sixth most common cancer and the fourth leading cause of death from cancer in China (*1*). The burden of EC in China is serious: in 2019, there were 278,121 new cases and 257,316 deaths by EC in China, accounting for more than half of the number of cases and deaths in the world (*2*). The standardized incidence rate (SIR) and standardized mortality rate (SMR) of EC in China were 13.90/100,000 and 13.15/100,000, respectively, which were far higher than the global levels of 6.51/100,000 and 6.11/100,000, respectively (*2*). The prognosis of EC is poor, and the five-year survival rate was only 30.3% (*3*). The data in this report were obtained from the latest estimates of the Global Burden of Disease Study 2019 (GBD 2019) (*2*), which were used to analyze the burden of EC in China from 1990–2019. The results of this study showed that the burden of EC in men was much higher than that in women from 1990–2019. Age was an important factor affecting the burden of EC, with the disease burden rising rapidly after 40 years old. The screening, early diagnosis, and treatment for high-risk groups of EC should continue to be strengthened in China.

The data in this report were extracted from the GBD 2019 (*2*). Related indicators of incidence, mortality, and disability-adjusted life years (DALYs) in 1990, 2004, and 2019 were used to evaluate the trend of the burden of EC in China. DALYs refer to all healthy life years lost from illness to death. DALYs include the years of life lost (YLLs) caused by premature death and the years lived with disability (YLDs) caused by disability due to disease. The incidence, mortality, and DALYs of EC in China from 1990 to 2019 were described by gender. The burden of EC of different age groups in 2019 was analyzed in the 5-year-old group distance. This study aimed to update and present the incidence and deaths of EC and provide the basis for the prevention and control of EC.

From 1990 to 2019, the number of cases of EC increased from 173,687 to 278,121, an increase of 60.13%; the crude incidence rate increased from 14.67/100,000 to 19.55/100,000, an increase of 33.27%. In 2019, the SIR of EC was 13.90/100,000, a 33.71% decrease compared to the SIR of 1990 (Table 1). Similarly, from 1990 to 2019, the number of deaths caused by EC increased from 176,602 to 257,316, an increase of 45.70%; the crude mortality rate increased from 14.92/100,000 to 18.09/100,000, an increase of 21.25%. In 2019, the SMR of EC was 13.15/100,000, a decrease of 40.44% compared to the SMR of 1990 (Table 1). The overall DALYs of EC in China from 1990 to 2019 increased from 4,494,070 to 5,759,997 person years, an increase of 28.17%; the crude DALYs rate increased from 379.67/100,000 to 404.96/100,000, an increase of 6.66%. In 2019, the standardized DALYs rate of EC was 277.50/100,000,

TABLE 1. Overall incidence, deaths, and burden indicators of esophageal cancer for the years 1990, 2004, and 2019 in China.

Gender	Year	Incidence			Deaths			DALYs			YLLs			YLDs		
		N	P	P*	N	P	P*	N	P	P*	N	P	P*	N	P	P*
		Cases	1/100,000	1/100,000	Cases	1/100,000	1/100,000	Cases	1/100,000	1/100,000	Cases	1/100,000	1/100,000	Cases	1/100,000	1/100,000
Men	1990	115,475	18.92	28.70	117,085	19.19	30.53	3,127,519	512.55	707.12	3,097,716	507.67	699.98	29,803	4.88	7.14
	2004	199,091	29.15	33.08	199,078	29.15	34.49	5,129,816	751.13	782.60	5,078,004	743.54	774.28	51,811	7.59	8.33
	2019	207,924	28.69	21.94	197,716	27.28	21.69	4,622,298	637.72	458.55	4,566,573	630.03	452.83	55,725	7.69	5.72
	2019 *vs.* 1990 (%)	80.06	51.64	−23.55	68.87	42.16	−28.96	47.79	24.42	−35.15	47.42	24.10	−35.31	86.98	57.58	−19.89
	2004 *vs.* 1990 (%)	72.41	54.07	15.26	70.03	51.90	12.97	64.02	46.55	10.67	63.93	46.46	10.61	73.84	55.33	16.67
	2019 *vs.* 2004 (%)	4.44	−1.58	−33.68	−0.68	−6.42	−37.11	−9.89	−15.10	−41.41	−10.07	−15.27	−41.52	7.55	1.32	−31.33
Women	1990	58,212	10.15	13.94	59,517	10.38	14.69	1,366,551	238.28	311.63	1,351,838	235.72	308.19	14,713	2.57	3.45
	2004	90,571	14.00	14.73	86,299	13.34	14.44	1,888,217	291.83	296.22	1,864,158	288.11	292.40	24,059	3.72	3.83
	2019	70,197	10.06	6.83	59,600	8.54	5.92	1,137,699	163.10	108.46	1,117,181	160.16	106.48	20,518	2.94	1.97
	2019 *vs.* 1990 (%)	20.59	−0.89	−51.00	0.14	−17.73	−59.70	−16.75	−31.55	−65.20	−17.36	−32.05	−65.45	39.45	14.40	−42.90
	2004 *vs.* 1990 (%)	55.59	37.93	5.67	45.00	28.52	−1.70	38.17	22.47	−4.94	37.90	22.23	−5.12	63.52	44.75	11.01
	2019 *vs.* 2004 (%)	−22.50	−28.14	−53.63	−30.94	−35.98	−59.00	−39.75	−44.11	−63.39	−40.07	−44.41	−63.58	−14.72	−20.97	−48.56
Total	1990	173,687	14.67	20.97	176,602	14.92	22.08	4,494,070	379.67	506.98	4,449,555	375.91	501.75	44,516	3.76	5.23
	2004	289,663	21.78	23.54	285,377	21.46	23.91	7,018,033	527.68	537.02	6,942,162	521.98	531.01	75,871	5.70	6.01
	2019	278,121	19.55	13.90	257,316	18.09	13.15	5,759,997	404.96	277.50	5,683,755	399.60	273.75	76,243	5.36	3.75
	2019 *vs.* 1990 (%)	60.13	33.27	−33.71	45.70	21.25	−40.44	28.17	6.66	−45.26	27.74	6.30	−45.44	71.27	42.55	−28.30
	2004 *vs.* 1990 (%)	66.77	48.47	12.26	61.59	43.83	8.29	56.16	38.98	5.92	56.02	38.86	5.83	70.44	51.60	14.91
	2019 *vs.* 2004 (%)	−3.98	−10.24	−40.95	−9.83	−15.70	−45.00	−17.93	−23.26	−48.33	−18.13	−23.45	−48.45	0.49	−5.96	−37.60

Abbreviation: DALYs=disability adjusted of life years, YLLs=years of life lost, YLDs=years lived with disability; N=number of cases for incidence and deaths / number of person years for DALYs, YLLs, and YLDs; P=crude rate, expressed as 1/100,000; P*=standardized rate, expressed as 1/100,000.

which was 45.26% lower than the DALYs rate in 1990 (Table 1). DALYs of EC were mainly caused by early death of YLLs, and the proportion of YLLs in DALYs was about 99% (Table 1).

From 1990 to 2019, the crude incidence rate, crude mortality rate, and crude DALYs rate of EC in China showed an overall increasing trend. The rates first increased, reaching a peak in 2004 but then decreased in the years following (Figure 1). The SIR, SMR, and standardized DALYs rate also showed an increase at first followed by a decline, but the decline was faster, and the overall trend was declining compared to the crude rate (Figure 1). From 1990 to 2019, the incidence, mortality, and DALYs rate of EC in men were much higher than those in women. The SIR of EC in men was about 2–3 times that of women (Figure 1). From 1990 to 2019, the crude incidence rate, crude mortality rate, and crude DALYs rate of EC in men increased by 51.64%, 42.16%, and 24.42%, respectively, and those in women decreased by 0.89%, 17.73%, and 31.55%, respectively. From 1990 to 2019, the SIR, SMR, and standardized DALYs rate of EC in men decreased by 23.55%, 28.96%, and 35.15%, respectively, and those in women decreased by 51.00%, 59.70%, and 65.20%, respectively. All these indicators of the burden of EC decreased significantly in women than in men (Figure 1 & Table 1).

The age distributions of EC incidence rate, mortality rate, and DALYs rate were similar. The incidence rate, mortality rate, and DALYs rate among people under 20 years old were all 0. Those indicators in people under 40 years old were at a relatively low level but rose after the age of 40. The incidence rate and mortality rate of EC increased monotonously with the increase of age groups and reached the highest in the age group over 85 years old. The highest DALYs rate was found in 75–79 year-old population. Among these, the incidence, mortality, and DALYs rate of all age groups in men were much higher than those in women (Figure 2).

DISCUSSION

The results of this study showed that the crude incidence rate, crude mortality rate, and crude DALYs rate of EC in China increased overall from 1990 to 2019, which indicated that the burden of EC in China was still heavy. Different from the increasing trend of crude rate, the SIR, SMR, and standardized DALYs rate showed an overall decreasing trend, which is consistent with the previous research results reported in China (*4*). This phenomenon is related to the change in population structure caused by aging.

The burden of EC first increased and then decreased. The "Outline of China Cancer Prevention and Control Program (2004–2010)" issued by the Ministry of Health is a programmatic document on cancer prevention and treatment (*5*), which has played an important role in promoting cancer prevention and treatment in China. In 2005, China carried out cancer screening and early diagnosis and treatment (including esophageal, stomach, liver, nasopharyngeal, female breast, and cervical cancers) in rural high-risk areas in the form of central fiscal transfer payments (*3*,*6*). Screening has found a considerable number of precancerous lesions and esophageal cancer patients, urged them to seek medical treatment as early as possible and inhibited the progression of the disease to advanced esophageal cancer, and also reduced the death of EC. Thereby the incidence and mortality rate of EC decreased. This may be an important reason for the decrease in the burden of EC after 2004. It shows that screening and early diagnosis of esophageal EC have achieved certain preventive effects (*7*). YLLs account for about 99% of DALYs, indicating that the life loss caused by early death of esophageal cancer is still at a high level. China should continue to strengthen early screening for EC.

From 1990 to 2019, the incidence, mortality, and DALYs rate of EC in men were much higher than those in women, and the crude incidence rate, crude death rate, and crude DALYs rate of men increased, while those of women decreased. This may be closely related to the drinking and smoking habits of the male population (*8*), so the male population should be the key intervention group. Women's burden of EC decreased more than men's, which may be related to women's high fruit intake (*9*), low drinking and smoking rates and other habits (*8*). The estrogen in women can also affect the disease as it has been shown to have a preventive and therapeutic effect (*10*).

The results of the analysis of EC burden among different age groups in China in 2019 showed that the incidence, mortality, and DALYs rate of EC in people under 40 years old were at a relatively low level, but rose rapidly after the age of 40. Age was an important factor influencing the burden of EC, and it increased with age. In all age groups, the burden of EC in men was significantly higher than that in women. It is suggested that middle-aged and elderly men are high-risk populations for EC and should be regarded as a

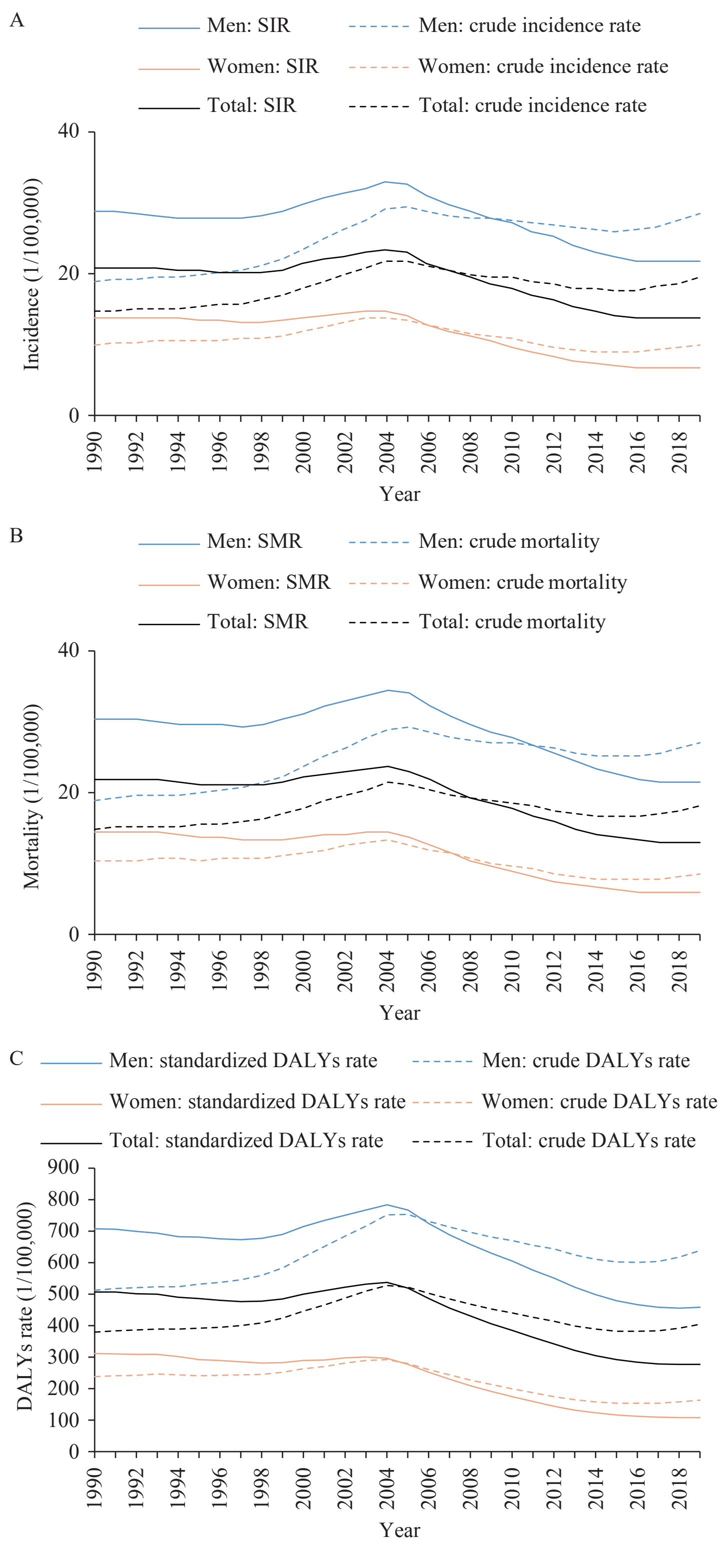

FIGURE 1. The incidence, mortality, and DALYs rate of esophageal cancer from 1990 to 2019 in China. (A) The incidence of esophageal cancer from 1990 to 2019 in China; (B) The mortality of esophageal cancer from 1990 to 2019 in China; (C) The DALYs rate of esophageal cancer from 1990 to 2019 in China.
Abbreviation: SIR=standardized incidence rate; SMR=standardized mortality rate; DALYs=disability adjusted of life years.

key population for EC prevention and control and regular screening measures should be taken.

After analysis, we observed the EC data collected from GBD 2019 were close to reports on EC incidence

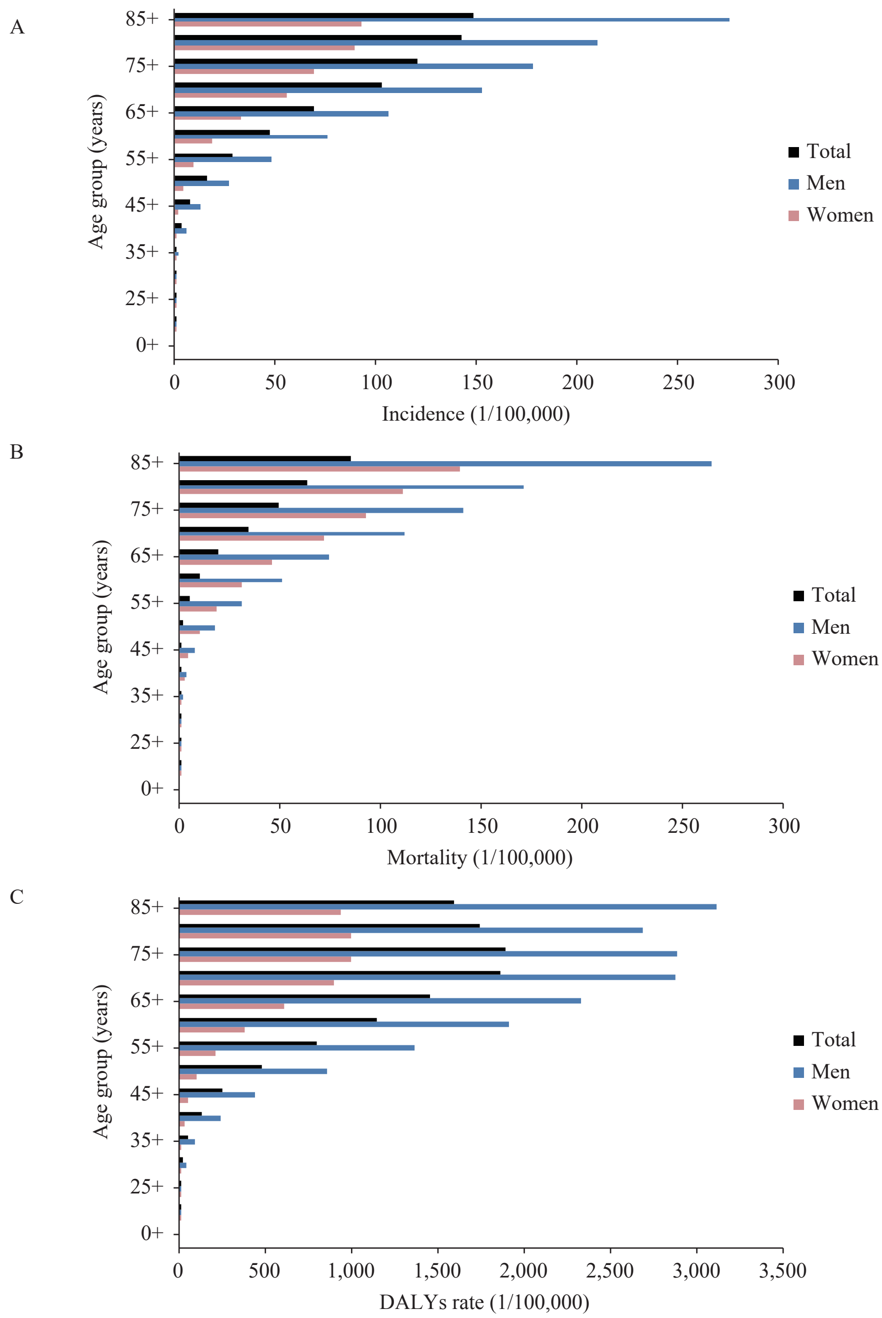

FIGURE 2. The incidence, mortality, and DALYs rate of esophageal cancer among different age groups in 2019. (A) The incidence of esophageal cancer among different age groups in 2019; (B) The mortality of esophageal cancer among different age groups in 2019; (C) The DALYs rate of esophageal cancer among different age groups in 2019.
Abbreviation: DALYs=disability adjusted of life years.

and mortality data in Chinese cancer registration areas as the ratio of incidence was between 0.88 and 1.24 and the ratio of mortality was between 1.12 and 1.52 (*11–12*). The two different sources provided comparable data.

This study still has certain limitations. First, EC includes two main histological subtypes: adenocarcinoma (AC) and squamous cell carcinoma (SCC) (*13*), which were not classified in the analysis. Second, this study did not differentiate between urban and rural areas and different regions in detail.

In summary, the SIR and SMR of EC in China from 1990 to 2019 showed decreases, but the burden of EC in China was still severe due to the large aging population. EC is a great hazard to the health of the population, especially in men over 40 years of age. It is necessary to increase the detection rate and early diagnosis and treatment for high-risk groups of EC, which is the basis for greatly reducing the incidence and mortality.

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Preplanned Studies

Regional Patterns of Disability and Their Relationship with Socioeconomic Conditions — China, 2006

Huiyun Fan[1]; Yanan Luo[2,#]

Summary

What is already known about this topic?

Understanding the regional distributions of disability is helpful for policymaking in precise disability prevention and control, especially in China. However, only a few studies have focused on the regional distributions of disability and their relationships with socioeconomic conditions, and almost all of them have ignored the variances of disability within provinces in China.

What is added by this report?

This research found that with the increase in the regional income level, the prevalence of disability showed a decreasing trend. The aging process of disability in high-income regions is more serious than that in other income level regions, and with the improvement of income level, the prevalence of disability in males declines rapidly.

What are the implications for public health practice?

The study analyzed the county-level distribution patterns of disability and their relationship with socioeconomic factors to provide a basis for implementing regional policies on disability prevention and control.

Disability is a part of the living condition of human beings, and almost everyone will experience temporary or permanent impairment at some stage of life (*1*). Although China has made remarkable achievements in disability prevention and control, the scale of disability is still increasing due to accelerated population aging and continuously increasing risks from chronic diseases (*2*). Implementing timely and effective control is important to postpone the rapid increase in disability, and locating the regional distributions of disability would be helpful for precise disability prevention. However, only a few studies have focused on the regional distributions of disability and their relationships with socioeconomic conditions in China, and almost all of them have ignored the variances of disability within provinces in China (*3*–*4*). Our study analyzed the county-level distribution patterns of disability and their relationship with socioeconomic factors to provide a basis for implementing regional policies on disability prevention and control.

This study used the Second National Sample Survey on Disability (SNSSD) in China, covering 31 provincial-level administrative divisions (PLADs), 734 counties or districts, 2,980 towns or streets and 5,964 communities or villages in China, involving 2,526,145 participants. More details about the survey can be found elsewhere (*5*). Disability was identified by trained field interviewers with a structured five-item screening questionnaire developed according to the 'Guidelines and Principles for the Development of Disability Statistics' (*6*), and individuals who answered a positive response to the questionnaire were labeled as likely to meet the criteria for disability. Experienced specialists diagnosed the types of disability, which included visual disability, hearing disability, speech disability, physical disability, intellectual disability and mental disability. A county-level disability database was established after comorbidity rounds of quality verification based on county-level pooled data from the Second National Sample Survey on Disability in China. Stata (15.1, Stata Corp, College Station, TX, USA) was used for data analysis.

The average annual per capita income for participants was 4,261.44 CNY (standard deviation was 2,769.67 CNY), and the average prevalence of disability at the county level was 6.29%. With the increase in the per capita annual income at the county level, the prevalence of disability rate at the county level gradually decreased (Supplementary Figure S1, available in http://weekly.chinacdc.cn/).

The prevalence of disability among older adults aged 65 or above was the highest, and the lowest prevalence was in individuals aged 14 years and below regardless of the incomes of the areas (Figure 1A). Although high-income counties had the lowest prevalence of

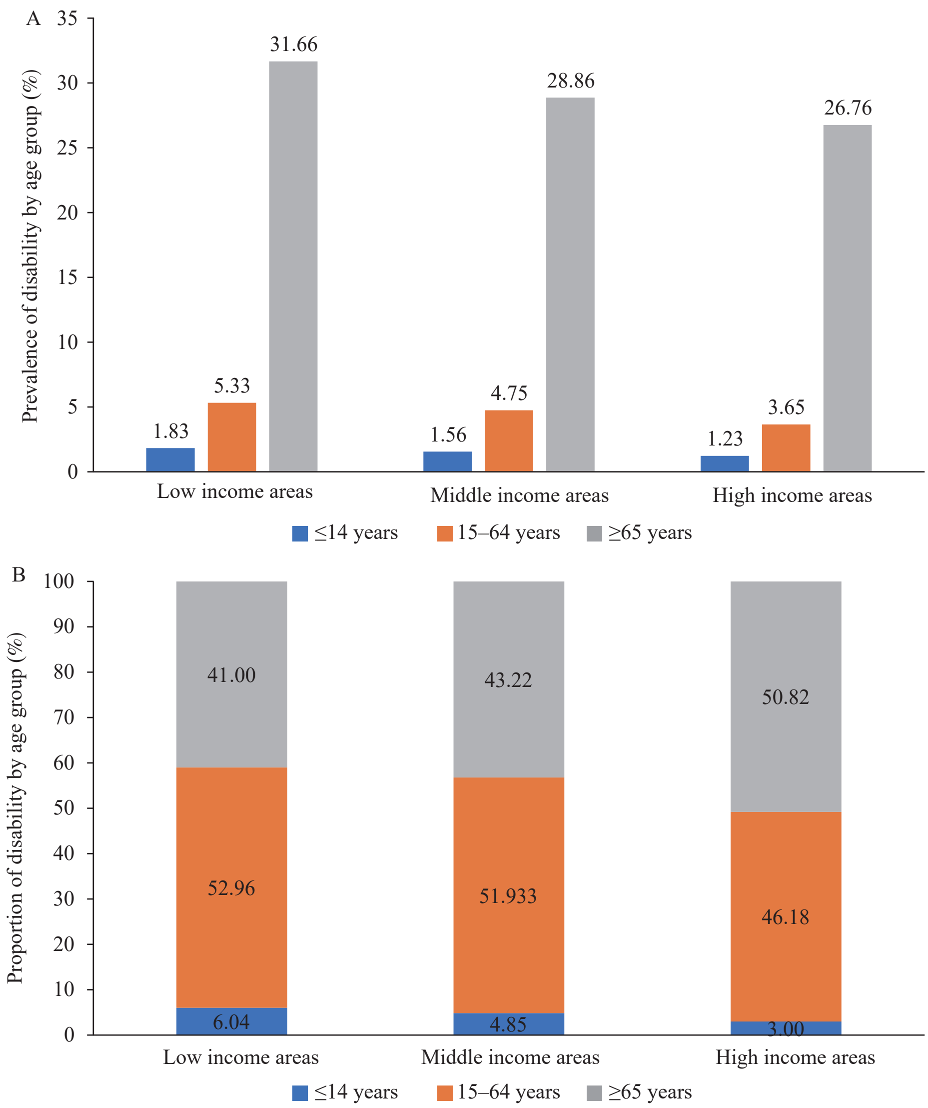

FIGURE 1. The prevalence and proportion of disability across counties with various incomes by age group. (A) Prevalence of disability; (B) Proportion of disability.

disability for older adults aged 65 years and above, the proportion of older adults with disability was the highest in the high-income counties (50.82%). The highest proportions of disability under 14 years of age (6.04%) and under 15–64 years of age (52.96%) were in low-income regions, and the lowest were in high-income regions (Figure 1B).

The prevalence of disability for both males and females in low-income areas (males: 7.03%, females: 6.72%) was higher than that in middle-income (males: 6.55%, females: 6.32%) and high-income areas (males: 5.96%, females: 5.81%). Moreover, in counties with a higher average income per capita, the prevalence of disability in males decreased faster than that in females (Figure 2A). Furthermore, the higher the income level of county areas, the smaller the difference in the proportion of disability between males and females (Figure 2B).

The prevalence of physical disability in county was the highest (2.35%), and the prevalence of speech disability in county was the lowest (0.53%). Compared with people in low-income regions, middle- and high-income regions have a lower prevalence of physical disability (low-income regions: 2.64%; middle-income regions: 2.23%; and high-income regions: 2.16%), but the prevalence of hearing, visual, and comorbid disabilities was higher (low-income regions: 2.04%, 1.08%, 0.97%; middle-income regions: 2.13%, 1.33%, 1.02; and high-income regions: 2.15%, 1.44%, 1.10% for hearing, visual, and comorbid disabilities, respectively) (Figure 3A). The proportion of visual, hearing and comorbid disabilities in high-income

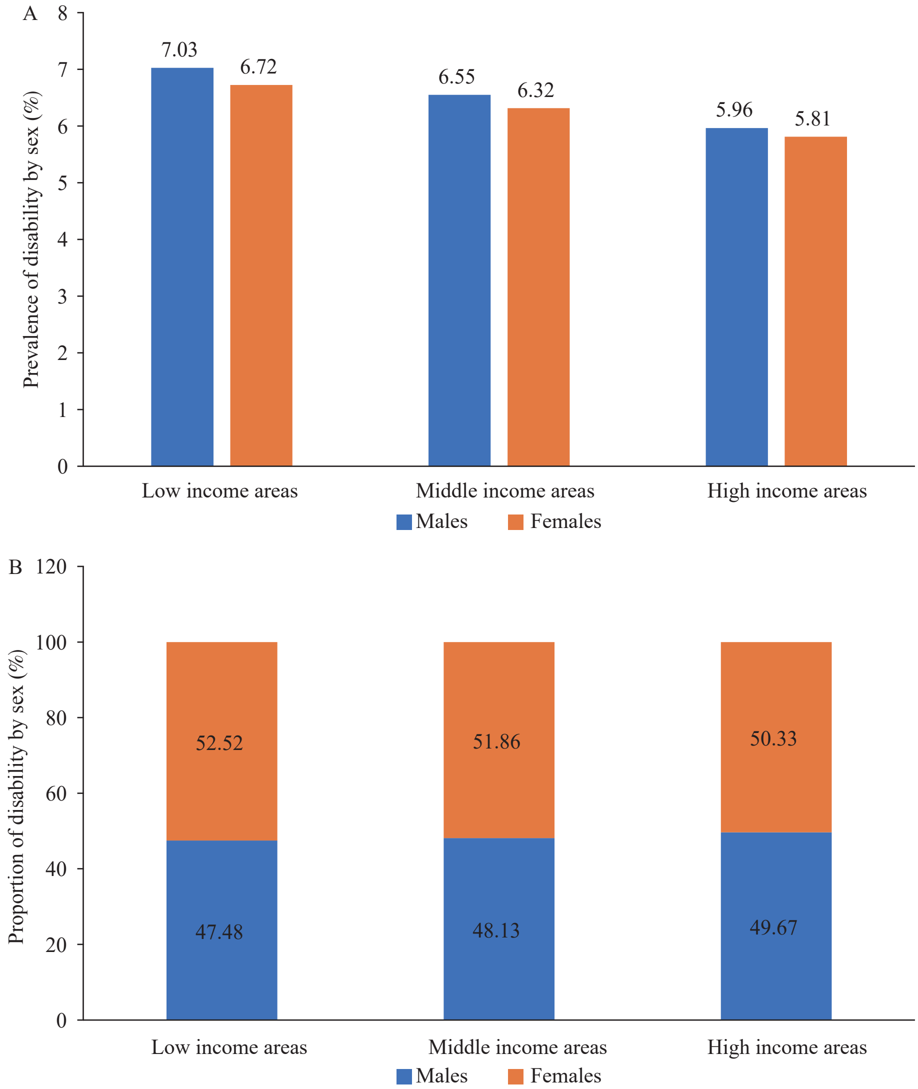

FIGURE 2. The prevalence and proportion of disability across counties with various incomes by sex. (A) Prevalence of disability; (B) Proportion of disability.

regions was higher than that in other regions, while the proportion of physical, mental, and intellectual disabilities in high-income regions was lower than that in other regions (Figure 3B).

Among the 0–4 years age group (N=479,581), the proportion of intellectual, hearing and visual disabilities was lower in high-income regions than in low-income and middle-income regions, (low-income: 37.91%, 15.43%, 17.32%; middle-income: 36.52%, 15.21%, 17.42%; and high-income: 32.85%, 15.10%, 16.85% for intellectual, physical and visual disabilities, respectively), while the proportion of comorbid, physical, speech, and mental disabilities was higher in high income regions. Among people aged 15–64 years (N=1,795,812), the proportion of intellectual and hearing disabilities was lower in high-income regions than in low-income and middle-income regions, while the proportion of comorbid disabilities, physical, mental, and visual disabilities was higher in low-income and middle-income regions. For people over 65 years of age (N=250,752), the proportion of hearing was similar in the 3 regions. The proportion of visual disability and comorbid disability was highest in high-income regions, and the proportion of mental disability, intellectual disability and speech disability was highest in low-income regions (Supplementary Figure S2, available in http://weekly.chinacdc.cn/).

DISCUSSION

This study took the county level as the analytical unit and found that with the rise of the regional

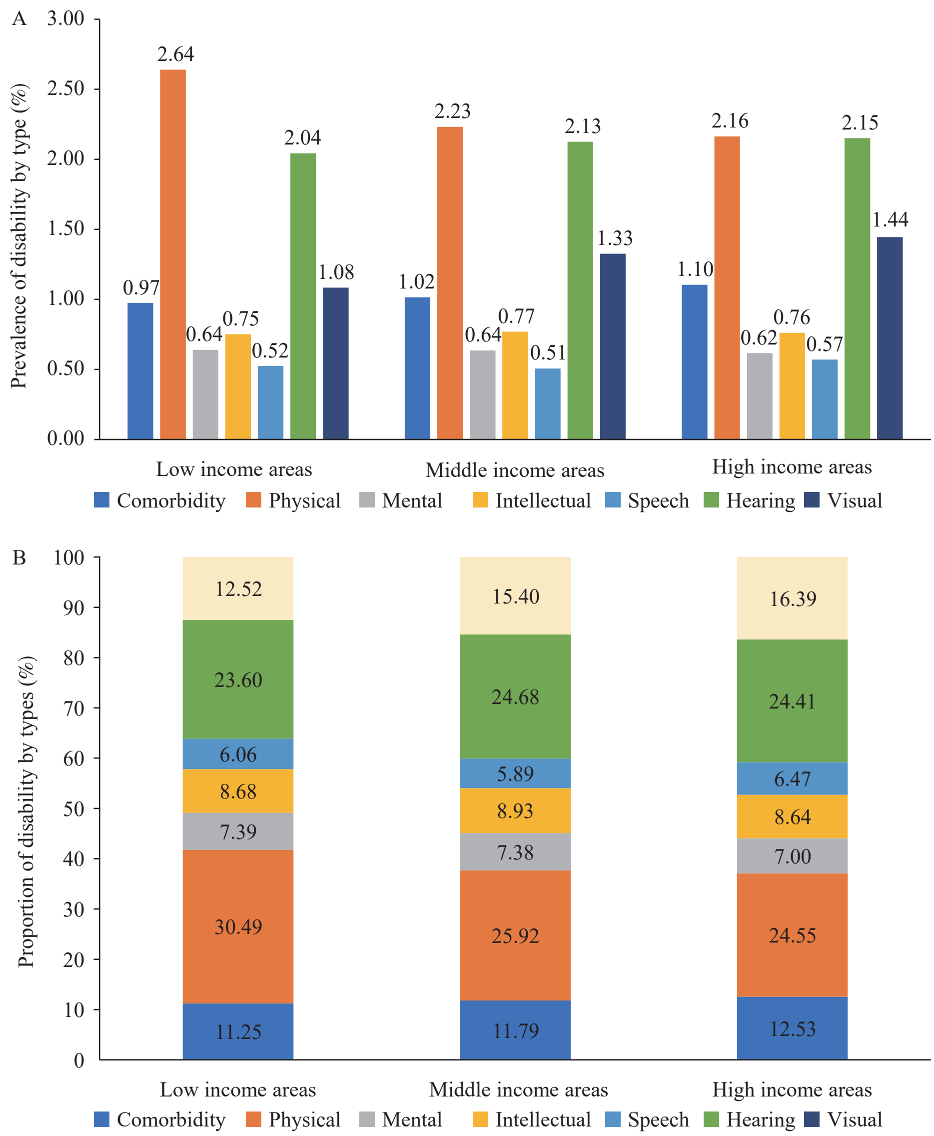

FIGURE 3. The prevalence and proportion of disability across counties with various incomes by type. (A) Prevalence of disability; (B) Proportion of disability.

income level, the prevalence of disability showed a decreasing trend. The increase in income for areas may help to improve people's health. People in areas with higher income levels have more opportunities to access better self-care and social services and a higher quality of life (*7*), so the prevalence of disability in the areas with high income is kept at a low level.

This study found that although the prevalence of disability among older adults in high-income regions is lower than that in other income regions, the aging process of disability in high-income regions is more serious than that in other income regions. This may be due to the longer life expectancy of people with disability in high-income regions. High-income areas have better service facilities, wealth, employment opportunities, social support, and other resources, which can promote the improvement of individual health levels. In the sex heterogeneity analysis, we found that with the improvement of social and economic levels, the prevalence of disability in males declines rapidly. One of the possible reasons for this sex difference may be the different compositions of types of disability in males and females. Compared with females, males may be at higher risk of physical disability, leading to the rapid decline in the prevalence of disability after the improvement of the regional economic level. Moreover, we found that a higher proportion of the types of aging-related disability (e.g., comorbid disability, hearing disability or visual disability) tended to be in high-income areas.

However, a higher proportion of the types of socioeconomic factors related to disability (e.g., physical disability) tended to be in low-income areas.

This study was subject to some limitations. First, few studies were available for comparison with our findings because it is the first to explore the regional distribution of disabilities at county-level. Second, findings from this study only can present a historical phenomenon because we used the survey data in 2006, which is the latest national sample survey about disability in China so far. Third, this study was an ecological studies at the county level, and, therefore, it has the implicit limitations of this design, and in the future, further study at the individual level should be undertaken. We used the Second National Sample Survey on Disability in China to detect the regional distributions of disability and its distributions across different counties with various socioeconomic conditions. We concluded that with the rise of the regional income level, the prevalence of disability showed a decreasing trend. The aging process of disability in high-income regions is more serious than that in other income regions, and with the improvement of income level, the prevalence of disability in males declines rapidly.

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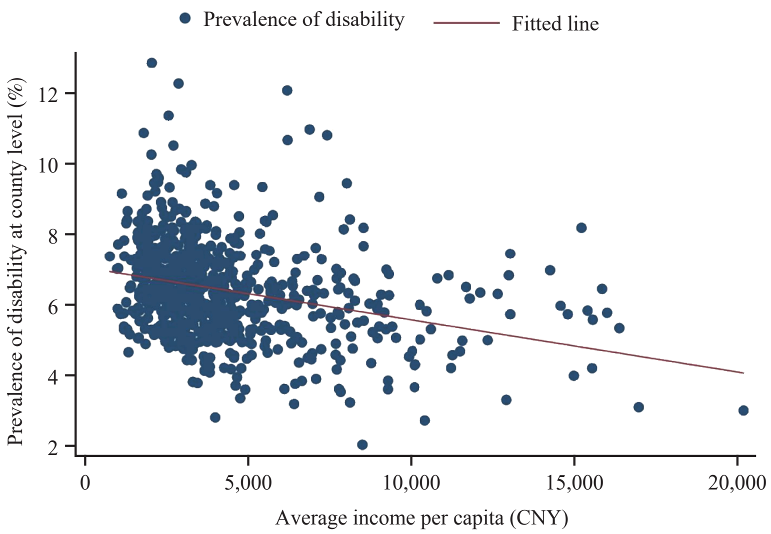
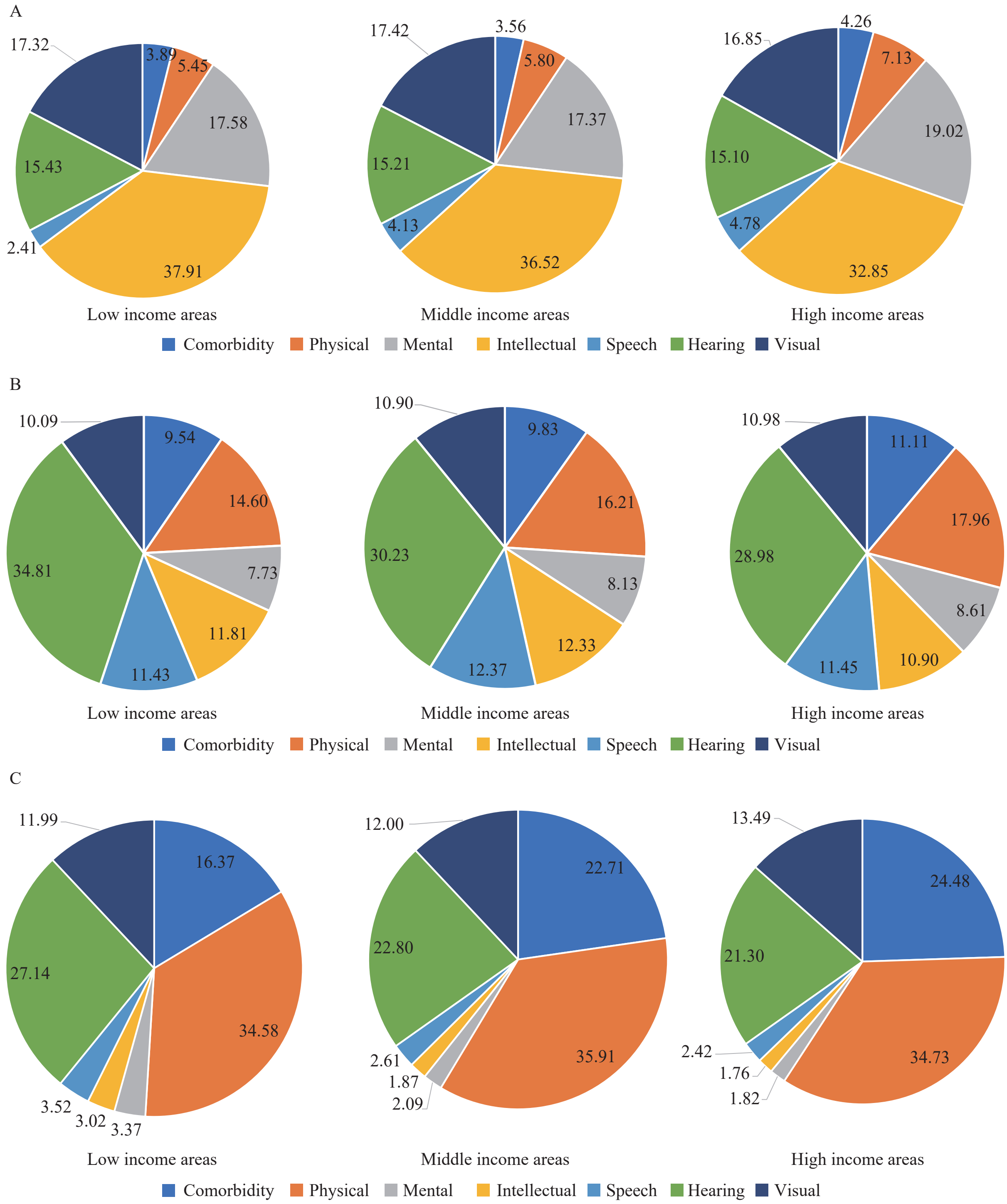


SUPPLEMENTARY FIGURE S1. Scatter plot of the relationship between income and the prevalence of disability at the county level.



SUPPLEMENTARY FIGURE S2. The proportion of disability across counties with various incomes by age group and type. (A) 0–14 years old; (B) 15–64 years old; (C) ≥65 years old.

Vital Surveillances

The Impact of Pregnancy Termination before 28 Weeks of Gestation on the Overall Prevalence of Birth Defects — Shaanxi Province, China, 2014–2020

Min Li[1]; Le Zhang[2,3,#]; Lu Gan[1,#]; Zhiwen Li[2,3]

ABSTRACT

Introduction: The prevalence of birth defects (BDs) at ≥28 gestational weeks in China has declined significantly in recent years. However, a few studies have implied that the prevalence is underestimated due to pregnancies with severe BDs often being terminated before 28 weeks of gestation. This study sought to contribute to this data conflict by determining the total prevalence of BDs throughout the entirety of pregnancies, depicting the epidemiological distribution of BDs in Shaanxi Province, and examining the impact of pregnancy termination before 28 weeks of gestation on overall BD prevalence.

Methods: Based on data extracted from the provincial Birth Defects Surveillance Network in Shaanxi Province, from 2014 to 2020, the trends of 18 frequent, major BDs at any gestational age were analysed.

Results: The total prevalence of BDs throughout pregnancy in Shaanxi Province increased significantly from 2014 to 2020, partly due to the inclusion of slight congenital heart diseases. It was also shown that the prevalence of all major types of BD had been previously underestimated, particularly severe external BDs, anywhere from 10% to 100% due to the previous sole measurement of terminations after 28 gestational weeks. Neural tube defects, however, remained one of the top five BDs with the highest total prevalence.

Conclusions: The exclusion of pregnancy terminations <28 weeks of gestation resulted in a severe underestimation of the total birth prevalence of BDs, particularly severe external defects. To estimate the true population-level prevalence of BD better, the current BD surveillance system should include pregnancy terminations before 28 weeks of gestation.

INTRODUCTION

Birth defects (BDs) are defined as structural or functional anomalies that occur before or at birth. BDs affect 6% of babies worldwide, resulting in 410,000 deaths annually (*1*). The prevalence of BDs in China is approximately 5.6% (*2*), which results in the deaths of 35,700 children younger than 5 years annually (*3*). However, the actual prevalence may be much higher because statistics rarely consider pregnancies terminated due to severe BDs before 28 weeks of gestation. Studies have reported that the regional prevalence of neural tube defects (NTDs) at ≥28 weeks of gestation is 66.0%–73.0% lower than that throughout pregnancy (*4*–*5*), but few have reported the total prevalence of overall BDs throughout pregnancy in China. Based on data extracted from the Birth Defects Surveillance Network, this study determined the total prevalence of BDs throughout pregnancy, depicted the epidemiological distribution of BDs in Shaanxi Province, and examined the impact of pregnancy termination before 28 weeks of gestation on the overall prevalence.

METHODS

This study examined trends in BD prevalence using data from the hospital-based BD surveillance system, which includes 22 member hospitals in 10 districts in Shaanxi Province, from 2014 to 2020. The surveillance system collected information on livebirths or stillbirths of 28 or more complete gestational weeks, and pregnancy terminations at any gestational age occurring in member hospitals. Perinatal infants born at 28 weeks gestation to 7 days after birth, including live and stillborn infants, were subject to hospital monitoring of BDs. In addition, all terminated BDs were recorded, regardless of gestational age. All births and terminated pregnancies following a prenatal diagnosis of BD were included and coded by health professionals according to the Tenth Revision of the International Classification of Diseases (ICD-10).

This study used that data to analyze 18 frequent, major BDs in Shaanxi Province: NTDs (Q00, Q01, and Q05), hydrocephalus (Q03), anotia/microtia (Q16.0 and Q17.2), other deformities of the outer ear (Q17), Congenital Heart Defects (CHDs) (Q20–Q26), cleft palate (CP; Q35), cleft lip with or without cleft palate (CL/P; Q36–Q37), esophageal atresia/stenosis (Q39), anorectal atresia/stenosis (Q42), hypospadias (Q54), club foot (Q66.0), polydactyly (Q69), syndactyly (Q70), limb reduction defects (LRD; Q71–Q73), congenital diaphragmatic hernia (Q79.2), omphalocele (Q79.2), gastroschisis (Q79.3), and Down syndrome (Q90).

According to the guidelines for the Chinese Birth Defects Monitoring Network, the perinatal prevalence rate was defined as the number of BD cases per 10,000 live and still perinatal births born in the range of 28 weeks gestation to 7 days after birth. The total prevalence rate (including BDs≥28 gestational weeks and BDs terminated at any gestational week) was also calculated. Any under-estimation of BDs was accounted for through the formula: under-estimated proportion equals to unreported cases divided by all cases then multiplied by 100%. This study calculated prevalence rates by calendar year, infant sex (female/male), and maternal residence area (urban/rural). Pearson chi-square tests were used to examine differences in prevalence between various groups, and linear chi-square tests were used to determine time-based trends. Two-tailed $P≤0.05$ was considered statistically significant. All statistical analyses were performed using SPSS (version 24.0. IBM Corp., Armonk, NY, USA). The study was approved by the Institutional Review Board of Northwest Women's and Children's Hospital, Shaanxi Province, China.

RESULTS

From 2014 to 2020, the system recorded 536,212 births and 12,790 cases of BDs. The prevalence of BDs at ≥28 gestational weeks and the total prevalence in Shaanxi Province have been increasing annually since 2016 (≥28 weeks: χ^2_{trend} =58.224, $P<0.01$; total: χ^2_{trend} =243.787, $P<0.01$), with a total prevalence of 318.6 per 10,000 in 2020. The prevalence would be underestimated by 40% at most, if counting only BDs at ≥28 gestational weeks (Figure 1). The annual increase in the total prevalence since 2016 includes both sexes and urban and rural areas in Shaanxi Province. The total prevalence in males was approximately 15% higher than in females each year (χ^2=63.456, $P<0.001$). It was higher in urban areas than in rural areas each year except in 2014 (χ^2=77.415, $P<0.001$), with a proportion of 47.2% in 2020 (Figure 2).

From 2014 to 2020, the prevalence of all major types of BD was underestimated by 10% to 100%–particularly severe external BDs such as NTDs, total cleft lip, Down syndrome, congenital hydrocephalus, and limb shortening (Table 1). In recent years, the rates of such severe defects after 28 weeks of gestation have declined steadily: not even reaching the top 10 in 2020. However, these still rank high when taking into account those terminated before

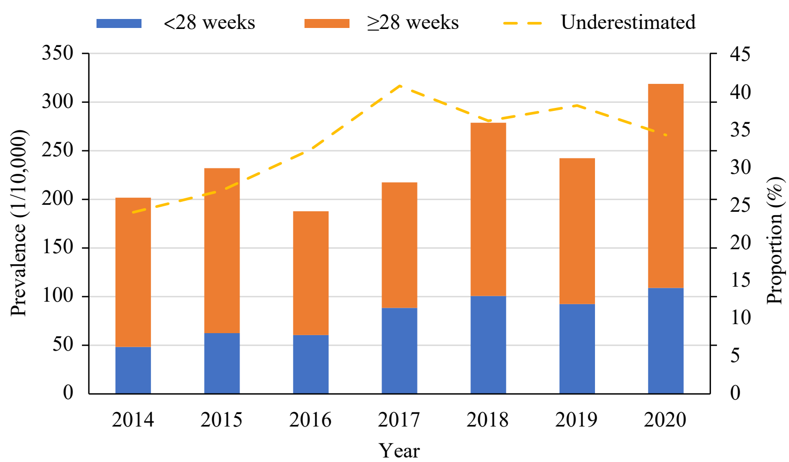


FIGURE 1. The overall prevalence and underestimated proportion of birth defects in Shaanxi Province, 2014−2020.
Note: Perinatal prevalence (cases of 28 or more gestational weeks), the prevalence before 28 gestational weeks and under-estimated proportion of birth defects were calculated. Total prevalence (all cases regardless of gestational age) was shown as perinatal prevalence plus the prevalence before 28 gestational weeks.

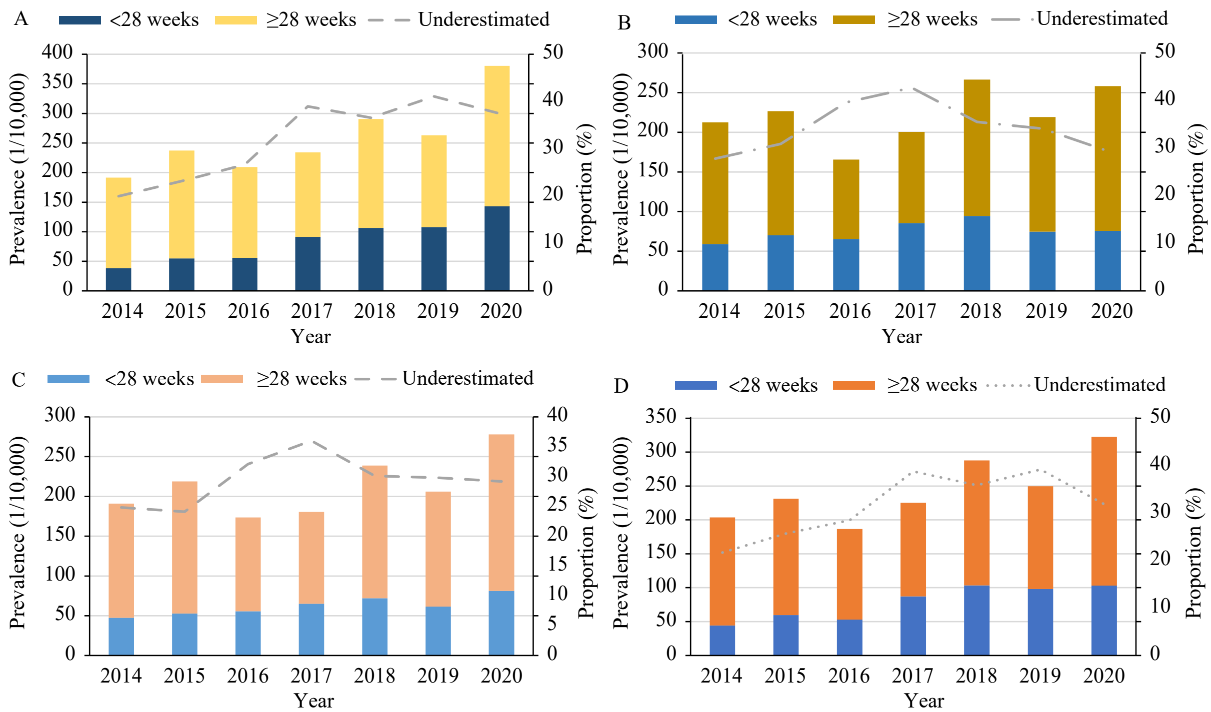


FIGURE 2. The prevalence and underestimated proportion of BDs in (A) urban areas*, (B) rural areas†, and among (C) males§, and (D) females¶ in Shaanxi Province, 2014−2020.

Note: Perinatal prevalence (cases of 28 or more gestational weeks), the prevalence before 28 gestational weeks and underestimated proportion of birth defects were calculated. Total prevalence (all cases regardless of gestational age) was shown as perinatal prevalence plus the prevalence before 28 gestational weeks.

Abbreviation: BD=birth defect.

* The perinatal prevalence of BDs: χ^2_{trend}=38.043, P<0.01; the total prevalence of BDs: χ^2_{trend}=249.138, P<0.01.

† The perinatal prevalence of BDs: χ^2_{trend}=21.110, P<0.01; the total prevalence of BDs: χ^2_{trend}=34.686, P<0.01.

§ The perinatal prevalence of BDs: χ^2_{trend}=31.520, P<0.01; the total prevalence of BDs: χ^2_{trend}=143.089, P<0.01.

¶ The perinatal prevalence of BDs: χ^2_{trend}=26.059, P<0.01; the total prevalence of BDs: χ^2_{trend}=56.366, P=0.01.

28 weeks of gestation. The top five BDs with the highest total prevalence in 2020 were CHD (155.0 per 10,000), cleft lip with or without palate (20.0 per 10,000), polydactyly (19.7 per 10,000), Down syndrome (12.2 per 10,000), and NTDs (11.6 per 10,000) in 2020. The overall prevalence of CHD increased significantly in 2020, and was about 50% higher than that in 2019 (Table 2).

DISCUSSION

BDs are increasing worldwide due to an increase in known risk factors, such as maternal diabetes and obesity, as well as emerging threats, such as the Zika epidemic (*6*). The total prevalence of BDs in Shaanxi Province from 2014 to 2020 trended upward, similar to the global trend. In recent years, with improvements in prenatal screening, diagnostic technology, and ultrasound technology, external BDs are more likely to be detected than ever before. In addition, the detection rate of congenital heart diseases, especially micro-malformation, has greatly increased, which is one reason for the increase in the incidence of BDs. In most years, the prevalence has been higher in males and in urban areas. These results are consistent with studies in other areas of China, such as Shanxi Province and Ningxia Hui Autonomous Region (*7*–*8*). Compared to many developed countries (*9*), the prevalence of BDs in Shaanxi Province is lower, mainly because BD monitoring usually begins from 20–22 weeks in Western countries as opposed to after 28 weeks in China. Many domestic studies have reported the prevalence of BDs after 28 weeks of gestation, while few have reported the total prevalence including those before 28 weeks. Excluding BDs before 28 weeks likely significantly underestimates the prevalence of BDs in China. The World Health Organization (WHO) proposes that countries may determine the feasibility of earlier gestation monitoring according to the capacity to ascertain cases prior to 28 weeks'

TABLE 1. Underestimated status of the main BDs in Shaanxi Province, 2014–2020.

Item	2014			2015			2016			2017			2018			2019			2020		
	≥28 weeks	Total	Under-estimated (%)	≥28 weeks	Total	Under-estimated (%)	≥28 weeks	Total	Under-estimated (%)	≥28 weeks	Total	Under-estimated (%)	≥28 weeks	Total	Under-estimated (%)	≥28 weeks	Total	Under-estimated (%)	≥28 weeks	Total	Under-estimated (%)
NTDs	5.4	16.0	66.2	3.4	12.0	71.6	2.5	12.8	80.4	2.2	12.6	82.5	1.0	11.8	91.5	0.9	6.8	86.8	1.7	11.6	85.4
Hydrocephalus	7.5	13.3	43.6	4.8	10.4	54.0	4.8	8.0	39.8	4.2	8.3	49.3	3.4	6.6	48.3	2.5	4.6	45.1	3.3	6.7	50.4
Cleft palate	1.0	1.3	21.5	2.2	2.6	14.3	2.5	3.0	15.6	2.2	2.6	14.1	2.7	3.0	11.1	2.3	2.3	−1.0	3.0	3.8	21.6
Cleft lip with or without palate	6.7	14.3	53.1	6.2	16.4	62.3	5.4	16.1	66.4	4.9	21.5	77.2	5.4	22.7	76.2	3.4	17.8	80.9	3.3	20.0	83.5
Anotia/microtia	2.0	2.0	−0.9	1	1.5	35.1	0.7	0.7	−2.4	1.6	1.7	6.3	1.0	1.3	21.0	1.5	1.7	12.2	1.1	1.4	22.3
Other deformities of the outer ear	2.4	2.4	0.3	4.5	4.6	2.6	4.1	4.1	0.1	2.6	2.6	−1.5	2.5	2.7	5.9	3.5	3.8	6.9	5.4	5.5	2.3
Esophagus atresia/stenosis	1.8	2.3	20.5	1.2	1.5	22.1	2.1	2.3	7.9	0.7	1.1	36.2	0.6	0.9	32.3	1.0	1.3	20.2	1.8	2.0	9.2
Anorectal atresia/stenosis	2.0	2.4	16.9	1.9	2.2	14.6	2.3	2.5	8.3	2.0	2.2	8.9	3.2	3.2	−1.1	1.8	2.4	24.7	2.1	2.7	22.0
Hypospadias	2.6	2.7	3.3	3.8	3.8	−0.9	4.0	4.1	2.5	6.2	6.2	0.3	5.8	6.1	4.5	4.2	4.6	7.8	5.2	5.2	0.8
Club foot	2.7	4.2	36.4	3.1	6.5	52.3	1.8	4.8	62.4	1.6	4.0	60.2	1.8	4.3	58.2	3.0	5.4	43.9	2.0	4.4	54.5
Polydactyly	13.6	13.9	2.0	15.4	15.6	1.2	14.4	14.9	3.6	13.5	14.3	5.4	16.5	17.2	4.4	13.6	15.0	9.9	18.8	19.7	4.3
Syndactyly	4.1	4.1	0.1	2.9	3.3	10.8	4.3	4.6	5.7	5.5	5.6	1.9	6.0	6.5	7.8	6.4	7.3	12.5	7.1	7.4	3.9
Limb reduction defects	2.0	3.4	41.1	2.6	4.1	36.7	1.6	3.6	56.1	1.2	5.1	76.6	1.0	4.3	76.8	1.0	3.8	73.4	1.7	4.7	63.6
Congenital diaphragmatic hernia	1.7	3.0	42.8	1.4	3.3	57.0	1.0	1.9	48.4	0.6	1.5	59.0	0.9	2.4	62.6	1.5	3.3	54.6	0.9	2.5	64.7
Omphalocele	0.1	0.4	76.5	0	1.2	100.0	0.6	1.5	59.5	1.0	2.7	62.7	0.6	3.3	80.9	1.0	3.6	72.6	0.3	4.5	93.4
Gastroschisis	0.9	2.1	57.6	0	3.1	100.0	0.1	1.3	92.0	0.4	2.0	79.5	0.3	1.0	75.3	0.0	0.7	100.0	0.3	2.1	85.9
Down syndrome	1.7	3.5	52.0	1.7	5.3	68.0	1.4	6.7	79.2	1.3	12.6	89.6	1.7	12.8	86.7	1.7	11.6	85.4	0.9	12.2	92.6
CHDs	82.3	92.7	11.3	97.2	112.8	13.8	54.8	68.7	20.3	64.8	82.4	21.4	108.5	137.2	20.9	79.6	104.8	24.0	128.1	155.0	17.3

Note: Perinatal prevalence (the number of cases of 28 or more gestational weeks per 10,000 births), total prevalence (the number of cases regardless of gestational age per 10,000 births) and underestimated proportion (cases before 28 gestational weeks accounting for all cases) of birth defects were calculated.

Abbreviation: BD=birth defect; NTDs=neural tube defects; CHDs=congenital heart defects.

TABLE 2. The ranking for top 10 most common BDs in Shaanxi Province, 2014–2020.

Rank	Perinatal prevalence (1/10,000)							Total prevalence (1/10,000)						
	2014	2015	2016	2017	2018	2019	2020	2014	2015	2016	2017	2018	2019	2020
1	CHDs (82.3)	CHDs (97.2)	CHDs (54.8)	CHDs (64.8)	CHDs (108.5)	CHDs (79.6)	CHDs (128.1)	CHDs (92.8)	CHDs (112.8)	CHDs (68.7)	CHDs (82.5)	CHDs (137.2)	CHDs (104.8)	CHDs (155.0)
2	Polydactyly (13.6)	Polydactyly (15.4)	Polydactyly (14.4)	Polydactyly (13.5)	Polydactyly (16.5)	Polydactyly (13.6)	Polydactyly (18.8)	NTDs (16.0)	Cleft lip with or without palate (16.4)	Cleft lip with or without palate (16.1)	Cleft lip with or without palate (21.5)	Cleft lip with or without palate (22.6)	Cleft lip with or without palate (17.7)	Cleft lip with or without palate (20.0)
3	Hydrocephalus (7.5)	Cleft lip with or without palate (6.2)	Cleft lip with or without palate (5.4)	Hypospadias (6.2)	Syndactyly (6.0)	Syndactyly (6.4)	Syndactyly (7.1)	Cleft lip with or without palate (14.3)	Polydactyly (15.6)	Polydactyly (14.9)	Polydactyly (14.3)	Polydactyly (17.3)	Polydactyly (15.1)	Polydactyly (19.7)
4	Cleft lip with or without palate (6.7)	Hydrocephalus (4.8)	Hydrocephalus (4.8)	Syndactyly (5.5)	Hypospadias (5.8)	Hypospadias (4.2)	Other deformities of the outer ear (5.4)	Polydactyly (13.9)	NTDs (12.0)	NTDs (12.8)	NTDs (12.6)	Down syndrome (12.8)	Down syndrome (11.6)	Down syndrome (12.2)
5	NTDs (5.4)	Other deformities of the outer ear (4.5)	Syndactyly (4.3)	Cleft lip with or without palate (4.9)	Cleft lip with or without palate (5.4)	Other deformities of the outer ear (3.5)	Hypospadias (5.2)	Hydrocephalus (13.3)	Hydrocephalus (10.4)	Hydrocephalus (8.0)	Down syndrome (12.6)	NTDs (11.8)	Syndactyly (7.3)	NTDs (11.6)
6	Syndactyly (4.1)	Hypospadias (3.8)	Other deformities of the outer ear (4.1)	Hydrocephalus (4.2)	Hydrocephalus (3.4)	Cleft lip with or without palate (3.4)	Cleft lip with or without palate (3.3)	Club foot (4.2)	Club foot (6.5)	Down syndrome (6.7)	Hydrocephalus (8.3)	Hydrocephalus (6.6)	NTDs (6.8)	Syndactyly (7.4)
7	Club foot (2.7)	NTDs (3.4)	Hypospadias (4.0)	Other deformities of the outer ear (2.6)	Anorectal atresia stenosis (3.2)	Club foot (3.0)	Cleft palate (3.0)	Syndactyly (4.1)	Down syndrome (5.3)	Club foot (4.8)	Hypospadias (6.2)	Syndactyly (6.5)	Club foot (5.4)	Hydrocephalus (6.7)
8	Hypospadias (2.6)	Club foot (3.1)	NTDs (2.5)	NTDs (2.2)	Cleft palate (2.7)	Hydrocephalus (2.5)	Anorectal atresia/ stenosis (2.1)	Down syndrome (3.5)	Other deformities of the outer ear (4.6)	Syndactyly (4.6)	Syndactyly (5.6)	Hypospadias (6.1)	Hydrocephalus (4.6)	Other deformities of the outer ear (5.5)
9	Other deformities of the outer ear (2.4)	Syndactyly (2.9)	Anorectal atresia/ stenosis (2.3)	Anorectal atresia/ stenosis (2.0)	Other deformities of the outer ear (2.5)	Cleft palate (2.3)	Club foot (2.0)	limb reduction defects (3.4)	limb reduction defects (4.1)	Other deformities of the outer ear (4.1)	limb reduction defects (5.1)	Club foot (4.3)	Hypospadias (4.6)	Hypospadias (5.2)
10	Anorectal atresia/ stenosis (2.0)	Limb reduction defects (2.6)	Esophagus atresia/ stenosis (2.1)	Club foot (1.6)	Club foot (1.8)	Anorectal atresia/ stenosis (1.8)	Esophagus atresia/ stenosis (1.8)	Congenital diaphragmatic hernia (3.0)	Hypospadias (3.8)	Hypospadias (4.1)	Club foot (4.0)	limb reduction defects (4.3)	Other deformities of the outer ear (3.8)	Limb reduction defects (4.7)

Note: Perinatal prevalence (cases of 28 or more gestational weeks), total prevalence (all cases regardless of gestational age) and underestimated proportion (cases before 28 gestational weeks accounting for all cases) of birth defects were calculated.

Abbreviation: BD=birth defect; NTDs=neural tube defects; CHDs=congenital heart defects.

gestation (*10*). With the development of capacity of ascertaining BDs, such as due to aforementioned technological advances, the beginning week of BD surveillance ought to be earlier than 28 gestation weeks in China. The inclusion of BDs before 28 weeks of gestation in order to obtain the true incidence of BDs could provide a basis for assessing the true effect of primary prevention measures and encourage health authorities at all levels to pay attention to the better implementation of primary prevention measures in the future.

The incidence of several severe BDs that are monitored in Shaanxi Province, such as NTDs, limb shortening, omphalocele, gastroschisis, and Down syndrome, has been underestimated by 40%–90%. A few domestic studies have reported an underestimation of NTDs and cleft lip and palate in local areas. For example, in one study, the incidence of NTDs was underestimated by 62.2% and that of cleft lip was underestimated by 12.6% in Shanxi Province (*5*). A study in the Tongzhou District of Beijing showed that, if BD surveillance began at 13 weeks of gestation, the number of reported NTDs cases would increase by about 2.7 times (*4*). In this study, the incidence of NTDs monitored in Shaanxi Province was underestimated by 80.1%, while the incidence of cleft lip and palate was underestimated by 78.5%. The underestimation of other major defects has not been reported in China. To the best of authorial knowledge, this study is the first to describe the underestimation of all major BDs systematically.

The top 10 most frequent BDs in Shaanxi Province are the same as those in China overall when those before 28 weeks of gestation are not included (*11*). However, their ranking changed significantly when considering both those before and after 28 weeks of gestation. The top five BDs are similar, particularly NTDs and cleft palate. In addition to preventing NTDs, periconceptional supplementation with folic acid appears to prevent CHD and oral clefts (*12*). Good adherence to folic acid supplementation may reduce the prevalence of NTDs to 6/10,000 or lower, according to a bayesian model (*13*). However, a large-scale cross-sectional study showed that less than 10% of pregnant women in northwest China take folic acid effectively for more than 3 months (*14*). Based on the higher prevalence of NTDs, cleft palate, and CHD, interventions for effective folic acid administration should continue to be strengthened in Shaanxi Province.

CHD is the most prevalent BD and its rate increased dramatically from 2014 to 2020, both after 28 weeks of gestation and overall. The causes of CHD are complicated and their etiology is not clear. Some studies have shown that advanced maternal age (AMA) increases risk for aneuploidy, which is associated with an overall increased risk for major anomalies including CHD (*15*). The dramatic increase in the proportion of women with AMA may be an important reason for the rapidly increasing prevalence of CHD, with the enactment of a universal two-child policy. In addition, the incidence of CHD increased significantly in Shaanxi Province in 2020, which was attributed to changes in the diagnostic standards and the inclusion of micro-lesions in CHD. Note that the increasing number of women with AMA following a three-child policy might continue to contribute to the increasing prevalence of CHD.

This study had at least two limitations. First, as the underestimated proportion of BDs was calculated from provincial data, the results are not generalizable to the entire country. Second, because some congenital metabolic diseases and functional abnormalities may not be identified in infancy, the prevalence of BDs might still be underestimated. Nevertheless, considering the large sample size, the results depict the epidemiological characteristics of most structural malformations in Shaanxi Province.

Conflicts of interest: No conflicts of interest.

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Notifiable Infectious Diseases Reports

Reported Cases and Deaths of National Notifiable Infectious Diseases — China, July 2022

Diseases	Cases	Deaths
Plague	1	0
Cholera	10	0
SARS-CoV	0	0
Acquired immune deficiency syndrome*	4,667	1,562
Hepatitis	138,449	43
Hepatitis A	1,069	0
Hepatitis B	112,648	23
Hepatitis C	21,867	18
Hepatitis D	16	0
Hepatitis E	2,225	1
Other hepatitis	624	1
Poliomyelitis	0	0
Human infection with H5N1 virus	0	0
Measles	92	0
Epidemic hemorrhagic fever	404	3
Rabies	17	12
Japanese encephalitis	13	1
Dengue	3	0
Anthrax	64	0
Dysentery	5,055	0
Tuberculosis	71,422	367
Typhoid fever and paratyphoid fever	741	0
Meningococcal meningitis	5	0
Pertussis	4,234	0
Diphtheria	1	0
Neonatal tetanus	2	0
Scarlet fever	1,758	0
Brucellosis	9,683	0
Gonorrhea	9,263	1
Syphilis	51,391	6
Leptospirosis	24	0
Schistosomiasis	6	0
Malaria	79	1
Human infection with H7N9 virus	0	0
COVID-19†	3,919	0
Influenza	648,465	4
Mumps	9,391	0

Continued

Diseases	Cases	Deaths
Rubella	106	0
Acute hemorrhagic conjunctivitis	2,629	0
Leprosy	35	0
Typhus	179	0
Kala azar	29	0
Echinococcosis	316	0
Filariasis	0	0
Infectious diarrhea[§]	103,468	1
Hand, foot and mouth disease	108,973	2
Total	1,174,894	2,003

* The number of deaths of acquired immune deficiency syndrome (AIDS) is the number of all-cause deaths reported in the month by cumulative reported AIDS patients.

[†] The data were from the website of the National Health Commission of the People's Republic of China.

[§] 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 the mainland of China are included in the table, whereas data of Hong Kong Special Administrative Region, Macau Special Administrative Region, and Taiwan, China 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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