The Morbidity Analysis of 17 Notifiable Bacterial Infectious Diseases in China, 2004-2019

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Abstract

Background

To better understand the epidemic dynamic of notifiable BIDs in China, and to provide scientific evidence for the prevention and control measures.

Methods

we gathered data from the NIDRIS in China from 2004 to 2019. The methods of descriptive epidemiology were applied to analyze the data of BIDs. The Joinpoint Regression analysis was utilized to examine trends in the incidence rates of BIDs.

Results

During 2004–2019, the average annual incidence rate reported for notifiable BIDs was 134.00 of 100 000. The overall average annual percent changes (AAPC) for RTDs and DCFTDs was -1.98% and -11.66%, respectively. Both of BSTDs and ZVDs showed increasing trends with AAPCs of 4.74% and 4.46%, respectively. Pertussis and scarlet fever showed the fastest increase of the incidence rate in the age group of 0~5 years with AAPC of 15.17% and 12.05%. RTDs had the highest incidence rate in Northwest China. South and East China represented a higher morbidity in BSTDs. The proportion of laboratory confirmation of BIDs have increased from 43.80–64.04%.

Conclusions

RTDs and DCFTDs showed an overall downward trend in China for a dozen years, while BSTDs and ZVDs indicated significantly upward trends.

Background

With substantial economic and social developments, improvements of the healthcare system and prevention consciousness, the morbidity and mortality of infectious diseases have decreased, but the emerging and re-emerging infectious diseases are still a threat to human health and social stability.

The National Notifiable Infectious Disease Reporting Information System (NIDRIS) was launched in the 1950s as an authorized infectious disease monitoring system in China. After the outbreak of SARS in 2003, the Chinese government originated internet-based NIDRIS nationwide on January 1, 2004 [1, 2]. The NIDRIS currently monitors 40 notifiable infectious diseases, which are classified into three categories according to different pathogens: bacteria, viruses, and parasitic [3]. Bacterial infectious diseases (BIDs) include 17 species (plague, cholera, tuberculosis, etc.) (Table S1).

Although most bacterial infectious diseases are basically under control, such as respiratory transmitted diseases (RTDs), blood-borne/sexually transmitted diseases (BSTDs) remain a significant public health problem.

Epidemiological patterns of BIDs change over time. Investigating the incidence trend of BIDs is continuously concerned. The purpose of the current study was to describe the epidemic patterns of BIDs during 2004–2019, to clarify surveillance needs and provide scientific evidence for the prevention and control measures.

Methods

Data source

The data of infectious diseases and population were collected from the NIDRIS (which does not include Hong Kong, Macao, and Taiwan).

Statistical rules

We collected data from the NIDRIS in China from 2004 to 2019. Among the notifiable infectious diseases, according to different pathogens, split into three categories: bacteria (17 diseases), viruses (16 diseases), and parasitic (6 diseases). According to different routes of transmission, they are classified into four categories: RTDs, direct contact/fecal-oral transmitted diseases (DCFTDs), BSTDs, and zoonotic and vector-borne diseases (ZVDs), and the classification does not include neonatal tetanus (Table S1). We analyzed epidemic trends by 5 age groups (0–5, 6–14, 15–24, 25–64, ≥ 65 years). According to the geographical locations of provinces, the mainland of China is divided into 7 regions including Northeast, North, Northwest, Central, East, South, and Southwest China (Figure S1). The proportion of laboratory confirmation refers to the percentage of laboratory-confirmed cases of infectious diseases in the total number of reported cases.

Statistical analysis

We performed a descriptive analysis of BIDs in the mainland of China from 2004 to 2019 (Table S1). The temporal trends of incidence rate in notifiable BIDs were characterized by Joinpoint regression approach, and Joinpoint Regression Analysis program (version 4.8.0.1) was used ([https:// surveillance.cancer.gov/joinpoint/](https://surveillance.cancer.gov/joinpoint/)). Statistical significance was set at $P < 0.05$. We also calculated the percentage of laboratory-confirmed cases.

Results

Between 2004–2019, a total of 28 779 thousand cases of BIDs were reported in the mainland of China, and the average annual incidence rate was 134.00 per 100,000 persons, that generally indicated a 1.87% declining trend from 146.18 per 100,000 in 2004 to 118.94 per 100,000 (Figure 1A). Among them, the RTDs and DCFTDs showed overall declining trends, while the two categories including BSTDs and ZVDs were the reverse, indicating overall upward trends (Figure 1B). RTDs had the highest proportion among the reported BID cases during study period, accounting for 57.02% of overall number of reported BID cases with 16 410 639 reported cases and average annual incidence rate of 76.41 per 100,000. As followed, a total of 7 583 871 BSTD cases (35.31 per 100,000), 4 165 931 DCFTD cases (19.39 per 100,000), and 618 559 ZVD cases (2.88 per 100,000) were reported (Figure 1A&2A). The morbidity of RTDs and DCFTDs showed a significant decrease by -1.98% (95%CI: -3.08 to -0.87) and -11.66% (95%CI: -12.03 to -11.29) per year, respectively, while incidence rates of BSTDs and ZVDs represented a significant increase by 4.74% (95%CI: 3.74 to 5.74) and 4.46% (95%CI: 1.59 to 7.42) per year, respectively (Figure 1B, Table S2).

The average annual incidence rate of four BIDs including scarlet fever, pertussis, syphilis and brucellosis indicated a significant increase from 2004 to 2019, with the AAPCs of 9.06%, 14.49%, 11.52%, 5.84%, respectively (Figure 1C, 1E, 1F). Pertussis had the greatest increase of the incidence, which have increased by 59.33% per year during 2013–2019. Only one inflection point was identified for the brucellosis in 2014 by the joinpoint method, indicating a remarkable increase during 2004–2014 with an APC of 13.20% (95%CI: 9.21 to 17.34), and then a decrease after 2014 with an APC of -7.47% (95%CI: -14.12 to -0.31). The average annual incidence rate of cholera, meningococcal meningitis, leptospirosis showed the fastest decrease with the AAPCs of -26.32% (95%CI: -30.77 to -21.57), -20.67% (95%CI: -26.21 to -14.72) and -12.55% (95%CI: -14.27 to -10.79) respectively (Figure 1C, 1D, 1F). Although gonorrhea had an AAPC of -3.80% (95%CI: -5.73 to -1.83), however, a significant increase was found by 4.06% per year after 2011 (Figure 1E). The number of plague and diphtheria cases is small, with the cumulative reported cases of 68 cases and 3 cases. Neonatal tetanus is not included in the classification by transmission routes.

Tuberculosis and syphilis were the top 2 BIDs with high average annual incidence rate of 72.60 and 25.74 per 100 000, respectively (Figure 2A), which also had the highest morbidity both in males and females. Males had higher morbidity than females for the tuberculosis, and syphilis were inverse (Figure 2B). Compared by age, bacillary dysentery and scarlet fever had highest incidence rate than others in age groups of 0–5 and 6–14 years, while tuberculosis and syphilis had predominantly higher morbidity than others in age groups of 15–24, 25–64, and ≥65 years (Figure 2C). In addition, The North and Northwest of China had higher incidence rates of tuberculosis and bacillary dysentery, while other regions had higher morbidity of tuberculosis and syphilis (Figure 2D). Compared by occupation, Children and students accounted for higher proportion in patients of scarlet fever, pertussis, meningococcal meningitis and bacillary dysentery, while other BIDs were mainly reported among farmers and persons involving animal husbandry (Figure 2E).

The overall average annual incidence rate of RTDs was shown a significantly upward trend in the age group of 0–5 years, with the AAPC of 8.10%, among them, pertussis and scarlet fever had the higher AAPCs of 15.17% and 12.05%, respectively. In the age group of 6–14 years, syphilis, scarlet fever, and brucellosis presented significant increase with AAPCs of 12.05% (95%CI: 5.83 to 18.63), 9.86% (95%CI: 7.06 to 12.75), 4.67% (95%CI: 0.28 to 9.26), respectively. Although pertussis had an overall stable trend during 2004–2019, a rapid increase by 89.93% (95%CI: 59.14 to 126.67) after 2016 was shown. Pertussis was also shown to have a quick increase by 17.10% (95%CI: 5.40 to 30.10) in the age group of 25–64 years. In the age group of ≥65 years, syphilis was indicated to have the greatest rise with the APPC of 17.85% (95%CI: 13.65 to 22.20) (Table 1, Table S3).

Table 1

Temporal trend of age-specific morbidity of bacterial infectious diseases by Joinpoint regression analysis, China, 2004–2019 (AAPC, 95%CI)

Bacterial infectious diseases	Age groups				
	0-5	6-14	15-24	25-64	≥65
Respiratory transmitted diseases[#]					
Tuberculosis ^a	8.10* (2.31~14.22)	4.95* (2.92~7.01)	-3.41 (-4.15~-2.67)	-3.86* (-4.31~-3.39)	-3.94* (-7.26~-0.51)
Scarlet fever	12.05* (8.80~15.40)	9.86* (7.06~12.75)	1.28 (-10.03~14.01)	0.91 (-0.70~2.55)	-2.44 (-5.00~0.18)
Pertussis	15.17* (9.22~21.44)	8.64 (-6.01~25.57)	3.07 (-7.39~14.70)	17.10* (5.40~30.10)	-
Meningococcal Meningitis	-18.08* (-24.48~-11.13)	-17.76* (-24.87~-9.97)	-22.45* (-25.94~-18.79)	-24.59* (-27.57~-21.48)	-16.45* (-24.03~-8.11)
Leprosy	-	-0.90 (-5.58~4.00)	-0.87 (-3.68~2.01)	-1.03 (-3.36~1.36)	-0.74 (-6.43~5.29)
Direct contact/fecal-oral transmitted diseases					
Bacillary dysentery	-12.00* (-13.46~-10.52)	-12.39* (-14.92~-9.78)	-15.12* (-15.97~-14.27)	-11.50* (-12.05~-10.96)	-10.62* (-11.26~-9.97)
Typhoid & paratyphoid fever	-2.97* (-5.39~-0.48)	-9.78* (-12.21~-7.27)	-14.79* (-17.29~-12.21)	-11.67* (-13.53~-9.77)	-5.22* (-8.49~-1.85)
Cholera	-	-	-	-26.19* (-30.93~-21.13)	-
Blood-borne/sexually transmitted diseases					
Syphilis	-1.68 (-4.15~0.85)	12.05* (5.83~18.63)	9.03* (7.55~10.53)	10.13* (7.94~12.36)	17.85* (13.65~22.20)
Gonorrhea	-11.23* (-12.76~-9.66)	-3.03 (-6.12~-0.15)	-0.08 (-2.50~2.39)	-5.75* (-8.55~-2.86)	-3.20 (-6.72~0.45)
Zoonotic and vector borne diseases					
	0.45 (-2.71~3.71)	-3.34 (-10.98~4.97)	-3.34 (-6.71~0.15)	4.63* (1.65~7.69)	9.58* (6.23~13.04)

1. ^a indicates that rifampicin resistance cases of tuberculosis in 2017-2019 were removed from AAPC and APC calculations; 2. Neonatal tetanus is not included in the classification by transmission routes; 3. AAPC, average annual percentage change; APC, annual percentage change; 5. * indicate where AAPC or APC differed significantly (p<0.05) from zero.

Bacterial infectious diseases	Age groups				
	0-5	6-14	15-24	25-64	≥65
Brucellosis	8.56* (4.01~13.32)	4.67* (0.28~9.26)	-1.40 (-5.22~2.57)	5.50 * (2.28~8.82)	11.06* (7.40~14.84)
Typhus	-9.90* (-12.80~-6.90)	-10.67* (-12.00~-9.31)	-14.95* (-18.41~-11.33)	-8.13* (-9.49~-6.75)	-1.30* (-2.33~-0.27)
Leptospirosis	-	-22.82* (-25.37~-20.18)	-18.79* (-24.23~-12.96)	-12.26* (-14.44~-10.03)	-
Anthrax	-17.45* (-20.62~-14.16)	-7.28 (-15.01~1.14)	-4.84* (-8.85~0.65)	-4.29 (-10.26~2.07)	-3.10 (-6.21~0.11)
1. ^a indicates that rifampicin resistance cases of tuberculosis in 2017-2019 were removed from AAPC and APC calculations; 2. Neonatal tetanus is not included in the classification by transmission routes; 3. AAPC, average annual percentage change; APC, annual percentage change; 5. * indicate where AAPC or APC differed significantly (p<0.05) from zero.					

The incidence rates of RTDs were the highest in some of counties, Northwest and Southwest China, while BSTDs were represented to have a higher morbidity in coastal regions and inland border areas of North and Northwest China (Figure 3A, 3C). DCFTDs had higher morbidity in western China, and showed a significant seasonality, mainly occurred in summer and autumn seasons (Figure 3B, Figure S2). Northern China was the areas with higher morbidity of ZVDs (Figure 3D). DCFTDs indicated a rapid decline in all seven regions, especially the region of East China with the AAPC of -14.19% (95%CI: -16.41 to -11.90). RTDs also showed a downward trend, but more slowly than DCFTDs and only in the regions of Northeast, North, Central and East China. BSTDs and ZVDs had the greatest increase by 9.21% (95%CI: 7.16~11.31) and 14.68% (95%CI: 7.40 to 22.45) in the region of Central China. Brucellosis, pertussis, and scarlet fever had the fastest increase in South China than other regions, with the AAPCs of 33.58% (95%CI: 24.41 to 43.43), 26.27% (95%CI: 9.79 to 45.22), and 20.57% (95%CI: 15.32 to 26.06), respectively. Southwest China indicated the greatest increase of Meningococcal Meningitis with the AAPC of -22.90% (95%CI: -29.65~-15.67), while gonorrhea and typhus had the largest decrease by -7.80% (95%CI: -9.87~-5.69) and -22.55% (95%CI: -26.35~-18.55) in Northeast China (Figure 3, Table S4).

The percentage of laboratory confirmation of BIDs significantly increased from 43.80% in 2004 to 64.04% in 2019 with the average laboratory confirmation proportion was 52.22%. The percentage of RTDs (39.38%) and DCFTDs (22.66) were lower than average, while BSTDs and ZVDs showed a higher rates of laboratory diagnosis, 93.47 and 87.20%, respectively. The ratio of syphilis, cholera, and brucellosis is higher than 90%, and anthrax, scarlet fever was less than 20% (Table S5).

Discussion

In this study, we analyzed epidemiological patterns and dynamics of four categories of BIDs in China by time, region, and population during recent a dozen years, which are helpful for clarifying surveillance needs and provide scientific evidence for the prevention and control measures of BIDs. Over the past decades, China's health sector had made strenuous efforts to improve people's health, significantly raising the overall strength of public health and the capacity of basic medical services and medical security, substantially enhancing the physical and

health literacy of the entire population, the incidence rate of BIDS in China decreased overall from 2004 to 2019. It was mainly related to the reduction in RTDs and DCFTDs.

Although the overall incidence rate of BIDS showed a declining trend, the problem remained considerable. Our data showed that tuberculosis was still at a high epidemic level, the northern regions such as Xinjiang had a high incidence rate of tuberculosis, which might be related to the low level of economic development and the lack of health education [4]. We also found that the morbidity of tuberculosis increased with age, indicating that the elderly were at high risk. To eliminate the epidemic of TB, strengthening multi-sector cooperation, developing new TB vaccines, producing new diagnostic and therapeutic drugs, expanding medical insurance coverage, standardizing medical care, and optimizing prevention and treatment strategies are needed [5]. The morbidity of scarlet fever showed the fastest increase in the age groups of 0–5 and 6–14 years. The relevant study showed that the average annual incidence of scarlet fever was highest among children aged six years [6]. This age group is at the stage of establishing protective immune function and may lack herd immunity to prevent *A streptococcus* infection [7]. Pertussis first showed a downward pattern, and then upward, especially in recent years when the incidence rate of this disease has increased rapidly in all age groups except for those over 65 years old. The first reason might be waning immunity. Natural infection and vaccination could not obtain lifelong immunity, people could be infected many times in their lifetime. At the same time, compared with WPV, the APV solved the reactogenicity problem, but didn't provide optimal boosting and long-term protection [8]. Second, the genetic of *B. pertussis* changed, the newly emerging *B. pertussis* lineages (PtxP3 lineage) might be related to the resurgence of pertussis [9], and the allele ptxP3 had been 46.7% of the circulating isolates in Shenzhen, southern China [10]. Third, enhanced surveillance and thematic studies had also been strongly associated with increased morbidity. In recent years, medical institutions in many areas had significantly improved their ability to culture pertussis bacteria and to detect pertussis by PCR, which had improved the level of disease surveillance.

Blood-borne/sexually transmitted diseases incidence rate increased, with syphilis playing a predominant role. During 2004–2006 and 2006–2010, APCs were 35.58% and 19.94%, respectively, but growth rate slowed about 3.38% during 2010–2019. The morbidity of blood-borne/sexually transmitted diseases, especially syphilis, had increased in all seven major regions of China, with higher average annual incidence rate in coastal regions and inland border areas of North and Northwest China. As the pioneers of economic reform in coastal areas, the rapid development of commercial industries might have led to a higher morbidity. Over time, the mobility of sex workers in coastal provinces, mostly migrants from inland provinces, might have helped bridge the spread of syphilis, which was one of the reasons for the increase in other regions [11]. Syphilis showed the largest increase of the age-specific incidence rate in the age group of ≥ 65 years (AAPC, 17.85%). The rising trend of other age groups (except for 0-5 years) were also very severe. The increasing morbidity in syphilis may be a result of the expansion of syphilis screening. Joint screening through HIV and syphilis, voluntary counselling and testing clinics were important reason, preoperative screening for syphilis also plays a key role. In addition, western lifestyles and cultures, such as talk about sex and openness, and tolerance for pre-marriage and homosexuality are already flooded with Chinese mass media [12]. Therefore, the Chinese are more tolerant of a variety of sexual behaviors such as homosexuality and premarital sex. It indicated that we should pay special attention to the sexually transmitted diseases in the age groups of them, which should be regarded as the key groups. In 2010, China promulgated the national syphilis prevention and control program (2010–2020) [13], which might have acted as the key driver of the decrease of syphilis morbidity. The large disease burden of syphilis in China demands more epidemiological investigation, increased screening, expanded partner services, more effective behavioral interventions, and multisectoral commitment [14]. The overall trend of zoonotic and vector-borne

diseases was upward, mainly due to the epidemic of brucellosis. During 2004–2014, the morbidity of brucellosis increased by about 13.20% per year. In the early stages, the reported cases were mostly in the northern pastureland provinces that were dominated by animal husbandry, which had led to more opportunities to contact infected livestock, coupled with increasing attention to brucellosis and the adoption of measures such as strengthened surveillance. However, in recent years, with the transfer of animals from different regions, the epidemic had gradually been imported into the southern region [15, 16]. After 2014, the incidence rate decreased by about 7.47% per year, China had promulgated the National Medium and Long-term Animal Disease Prevention and Control Plan (2012–2020), the National Disease Control Plan (2016–2020), which might be the main reason for the decline in the incidence of brucellosis. The northern region still had a higher morbidity than other regions. To reduce the prevalence of brucellosis, it is recommended to continue to enhance vaccination work for animals such as cattle and sheep, reduce occupational exposure, and conduct health education on exposed populations [2].

Etiological diagnosis is an essential basis for clinical management of infectious diseases and also a key for monitoring and early warning of infectious diseases [17]. The laboratory diagnostic capacity of infectious diseases in primary medical institutions is seriously insufficient in China, which might be due to the financial constraints of central medical institutions or the overall low level of personal technology. Therefore, the construction of the infectious disease monitoring laboratory network should be further strengthened [18, 19].

Our study had several limitations. The infectious diseases data were from the NIDRIS, that might not be representative of real-world incidence data, and the cases of BIDs might be fewer. Second, we didn't calculate the temporal trends for all bacterial infectious diseases, for example, age-specific trends of leprosy, cholera, because of the small number of cases enough not to meet the calculation conditions of joinpoint regression.

In conclusion, our results indicated that the morbidity of BIDs showed a downward trend, especially RTDs and DCFTDs, but tuberculosis still had a higher morbidity. The overall trends of BSTDs and ZVDs were upward, as we adopted various control measures against these diseases, the growth rate of incidence rate had slowed or decreased in recent years. We should pay more attention to BIDs, strengthen active monitoring and the construction of the laboratory networks, adopted timely control measures to reduce the incidence of infectious disease.

Abbreviations

AAPC: Overall average annual percent changes; NIDRIS: The National Notifiable Infectious Disease Reporting Information System; BIDs: Bacterial infectious diseases; RTDs: Respiratory transmitted diseases, BSTDs: Blood-borne/sexually transmitted diseases; DCFTDs: Direct contact/fecal-oral transmitted diseases; ZVDs: Zoonotic and vector-borne diseases.

Declarations

Ethics approval Ethics approval and consent to participate

Standards of animal care was not required.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

No potential conflict of interest was reported by the author(s).

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Contributions

Yuliang Zhu, Liping Wang, Liqun Fang and Zhongjie Li conceived and designed the study. Yuliang Zhu and Lusha Shi performed the main data collection and analyses under supervision of Liping Wang, Liqun Fang and Zhongjie Li. Shuaibing Dong, Cuihong Zhang, Shenghong Lin and Xiang Ren helped with the analyses. Yuliang Zhu wrote the draft of the manuscript. All authors have contributed to, seen, and approved the final, submitted version of the manuscript.

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Figures

Figure 1

Temporal trend of incidence of the notifiable BIDs by different transmission routes in China, 2004–2019. (A) Number of cases of the notifiable BIDs by different transmission routes, Bacterial infectious diseases were 28,779,000, AAPC (95%CI), $-1.87^* (-2.56 \sim -1.17)$; (B) Annual average incidence rate and average annual percentage change (AAPC) of the notifiable bacterial infectious diseases by different transmission routes, Respiratory transmitted diseases (RTDs): AAPC (95%CI), $-1.98^* (-3.08 \sim -0.87)$; Direct contact/fecal-oral transmitted diseases (DCFTDs), $-11.66^* (-12.03 \sim -11.29)$; Blood-borne/sexually transmitted diseases (BSTDs), $4.74^* (3.74 \sim 5.74)$; Zoonotic and vector-borne diseases (ZVDs), $4.46^* (1.59 \sim 7.42)$. (C) Annual average incidence rate and AAPC of RTDs, Tuberculosis, $-2.93^* (-4.79 \sim -1.03)$; Scarlet fever, $9.06^* (6.47 \sim 11.71)$; Pertussis, 14.49^*

(9.12~20.12); Meningococcal Meningitis, -20.67* (-26.21~-14.72); Leprosy, -0.79 (-3.29~1.77); (D) Annual average incidence rate and AAPC of DCFTDs, Bacillary dysentery, -11.74* (-12.18~-11.29); Typhoid & paratyphoid fever, -10.45* (-12.23~-8.63); Cholera, -26.32* (-30.77~-21.57). (E) Annual average incidence rate and AAPC of Blood-borne/sexually transmitted diseases (BSTDs), Syphilis, 11.52* (8.82~14.29); Gonorrhea, -3.80* (-5.73~-1.83). (F) Annual average incidence rate and AAPC of zoonotic and vector-borne diseases (ZVDs), Brucellosis, 5.84* (2.64~9.14); Typhus, -8.95* (-10.05~-7.83), Leptospirosis, -12.55* (-14.27~-10.79), Anthrax, -4.86 (-9.67~0.20). Dots indicate the observed incidence rates and lines indicate the slope of the AAPC.

Figure 2

Demographic characteristics of bacterial infectious diseases. (A) Annual average incidence rate of bacterial infectious diseases; (B) Annual average incidence rate of bacterial infectious diseases by sex groups; (C) Annual average incidence rate of bacterial infectious diseases by age groups; (D) Annual average incidence rate of bacterial infectious diseases by seven regions; (E) Annual average incidence rate of bacterial infectious diseases by occupation.

Figure 3

Spatial distribution and temporal trend of morbidity for BIDs by disease and region. (A) Respiratory transmitted diseases (RTDs); (B) Direct contact/fecal-oral transmitted diseases (DCFTDs); (C) Blood-borne/sexually transmitted diseases (BSTDs); (D) zoonotic and vector-borne diseases (ZVDs). The spatial distribution of each category of bacterial infectious diseases was shown by map, and the AAPCs of combined and single disease for each category of bacterial infectious diseases were shown in chart by each region.

Supplementary Files

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