

# BMJ Open Sharp instrument injuries among hospital healthcare workers in mainland China: a cross-sectional study

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## ABSTRACT

**Objectives** To determine the prevalence of sharp instrument injuries in hospital-based healthcare workers (HCWs) in mainland China and the contributing factors.

**Design** Cross-sectional study.

**Setting** The data were derived from public hospitals.

**Participants** A total of 360 hospitals were recruited in the study, including 289 general hospitals and 71 specialised hospitals. Among them, 194 are tertiary-level hospitals and 166 are secondary level. The study population finally consisted of 223 149 hospital HCWs.

**Primary outcome measures** A questionnaire was designed based on the aim of the study. Profession of HCWs, workplace, circumstance and medical apparatus and instrument were covered in the survey. HCWs completed a self-administered questionnaire regarding details of sharp instrument injuries within the previous month. Prevalence estimates for the injuries were calculated for the overall HCWs and for subgroups according to profession, workplace, circumstance or instrument.

**Results** Within the included HCWs, the prevalence of sharp instrument injuries was 0.08 per person-month. Only 4.6% of the HCWs reported to their hospitals after injury. The highest number of injuries occurred in nursing staff (10.3%). Injuries took place most frequently on general wards (44.5%). The circumstances that involved most frequent injuries include surgical needle insertion, removing an arteriovenous needle from a patient and recapping the needle. Single-use syringe caused more injuries incidents than other instruments.

**Conclusions** These results indicate that sharp instrument injuries have become a major occupational problem of HCWs in mainland China. Attention needs to be paid to the issue and strategies for preventing such injuries are needed.

## Strengths and limitations of this study

- Our study assessed the prevalence of sharp instrument injuries in a representative sample of healthcare workers in mainland China.
- The study is the first nationally representative investigation of sharp instrument injuries among healthcare workers in developing countries.
- The primary limitation of this study is that the accuracy of the estimates of sharp instrument injuries was limited by the accuracy of recall of the participants.

routes are injuries due to contact with sharp instruments contaminated by blood or body fluids.<sup>9 10</sup> Sharp instrument injuries, which are mostly preventable, jeopardise the safety of HCWs and represent a major occupational challenge. It is an important labour issue for HCWs in the world.

Sharp instrument injuries provide routes for transmission of pathogens such as hepatitis B virus (HBV), hepatitis C virus (HCV) and HIV, which result in bloodborne diseases.<sup>11 12</sup> The incidence of exposure to bloodborne pathogens among HCWs has been studied in developed countries,<sup>2</sup> but the concern remains largely ignored in developing countries. China is the world's largest developing country with the largest population and correspondingly a large body of medical staff who are facing occupational exposure on a daily basis. However, there are few reports of studies investigating sharp instrument injuries among HCWs in mainland China. Many of these studies<sup>13–17</sup> were conducted on small sample sizes, involving a limited number of medical staff and/or covering a non-representative number of hospitals. This has limited the generalisability of the findings from these studies. To our knowledge, there is by far no large-scale study regarding sharp instrument injuries among HCWs in mainland China. The true prevalence of such injuries may have



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## INTRODUCTION

Occupational exposure among healthcare workers (HCWs) has been gaining increasing attention in recent decades.<sup>1–8</sup> HCWs are at risk of serious consequences from exposure to certain medical instruments. For example, most infections among medical staff can be attributed to occupational exposure, and the most commonly reported

remained unknown. To address this gap in knowledge, a national prevalence survey covering a large number of hospitals in a wide range of areas was done in 2011.

## METHODS

### Study design and participants

This survey was a cross-sectional observational study. Since mainland China has various geographical regions and the prevalence rates of the injuries in different regions may be affected by local socioeconomic, traditional and rural or urban factors, a multistage stratified sampling method was employed to select a set of nationally representative samples of HCWs. First, one province was selected from each of the five large geographical regions in mainland China, namely northeast, northwest, southeast, southwest and south. The selected province was typical of a certain region in that no specialised policy or practice existed for public hospital administration. In addition, a municipality and an autonomous region were chosen to represent these two types of regions in mainland China. As a result, Shaanxi province, Sichuan province, Liaoning province, Zhejiang province, Guangdong province, Shanghai municipality and Guangxi Zhuang Autonomous Region were selected out of the 31 provinces, municipalities and autonomous regions in mainland China. These places were not sampled randomly but were chosen to span a range of medical care practices and socioeconomic conditions of the corresponding large regions, aiming to retain a nationwide geographic and social balance.

In the next stage, hospitals in each of the seven regions were selected using a stratified sampling based on their types and levels. In mainland China, hospitals are mainly classified as general and specialised in type and as tertiary and secondary in level. There are also a small number of community-level clinics, but they were not included in the survey due to the tiny portion they had accounted for in the whole medical care system in mainland China. In each province or autonomous region, we enrolled academic hospitals in the capital city and a local hospital from a smaller city or rural county. Hopefully, this sampling would generate reliable representation of the sharp instrument injuries among HCWs in Chinese medical system.

### Survey design

We could rely on only self-reported data but not on objective observations. To minimise the recall bias, injuries to be reported were limited to those that had occurred within a month before the participants were surveyed. We focused on percutaneous injuries caused by at least one of the sharp medical devices in their work environment, including needle, lancet, scalpel, broken glass (excluding broken ampoule), and so on. All participants had the ability to answer a written questionnaire. It included two sections: the first section asked about the participant's name, department, occupation, knowledge training on occupational exposure and history of sharp instrument

injuries in the past month, and the second section asked about the number of injuries having occurred within the past month, the involved devices, the procedures, the exact places of the reported incidents, information about exposure to blood and body fluids of patients, and so on. Multiple choice questions, with just one correct answer, were used to collect the information.

### Procedures

The survey was conducted in three steps. First, written notifications were sent to the participating hospitals. The hospital-caused infection management officers then were recruited and trained for 1 week to serve as data collectors. The training was focused on survey management and interview techniques. Second, questionnaires were distributed in all hospital departments and collected within a 1-week period. All people in the departments, except those holding solely administrative positions, completed the first section of the questionnaire. Finally, people who had reported sharp instrument injuries were interviewed face to face and the second section of the questionnaire was filled out during the interviews. Data collection was completed in a month. The institutional review board of the Second Affiliated Hospital of Xi'an Jiaotong University provided review and ethics approval of the survey (no 2011112). All respondents were read a statement that explained the purpose of the survey. Written informed consent was obtained from each participant before data collection, and questionnaires were voluntarily completed and returned.

Sharp instrument injury has been defined as an injury caused by a sharp device which penetrates the skin. The instrument can be contaminated when it contacts with blood or body fluids of a patient. Exposure of intact skin or mucous membrane to bloodborne pathogens was not included in this study, so the participants were not to report the incidents of blood or body fluid splashing on intact skin. The knowledge or training on occupational exposure was hinted by the participants' report of attending postgraduate courses on occupational exposure to bloodborne pathogens and prevention of the infections. All participants were informed clearly that the exposure incidents they would report should have had occurred within the past month. Supervisors were responsible to review the questionnaires to ensure completion and accuracy.

### Statistical analysis

The Mandarin version of EPINet (Exposure Prevention Information Network) was used for data entry and management. Analysis of the data was performed by the SPSS V17.0 software and using the descriptive statistic method. A two-sided *p* value of 0.05 or less was regarded as of statistical significance. Categorical variables were expressed as percentages.

Professions of the participants were categorised as doctor, nurse, laboratory technician, sanitation worker (cleaners and medical waste collectors), student (interns

**Table 1** Characteristics of survey hospitals

	Total	Tertiary hospital		Secondary hospital	
		n	%	n	%
<b>Hospitals</b>					
Total	360	194	53.9	166	46.1
General hospital	289	146	40.6	143	39.7
Specialised hospital	71	48	13.3	23	6.4
<b>Questionnaires</b>					
Total	223 149	161 519	72.4	61 630	27.6
General hospital	193 546	136 475	61.2	57 071	25.6
Specialised hospital	29 603	25 044	11.2	4 559	2.0

and practical nurses) and other work (nursing assistants, laboratory attendants, mortuary attendants, ward orderlies, ambulance driver and other paramedical staff). The overall prevalence rate and the stratum-specific rates for various professions were calculated. The injuries were stratified according to workplace, circumstance and device. Workplace variables included blood drawing room and injection room for outpatients, outpatient clinic, emergency department, stomatology department, intensive care unit, haemodialysis unit, general ward, clinical laboratory, operating room and sterile processing centre, as well as room for temporarily disposing medical waste and others. The proportions of injury in terms of workplace were calculated in each of the six profession categories, and intergroup comparisons were performed using  $X^2$  test.

## RESULTS

Altogether 360 hospitals were included in this study, among which 289 were general hospitals and 71 were specialised. Among them, 194 are tertiary-level hospitals and 166 are secondary level. A total number of 223 149 full-time HCWs were included in the survey. The response rate was 100.0%. Among these participants, 193 546 (86.8%) were from general hospitals, and 29 603 (13.2%) were from specialised hospitals (table 1).

In terms of profession categorisation, the survey population was composed of 63 379 doctors (28.4%), 106 056 nurses (47.5%), 10 463 laboratory technicians (4.7%), 16 415 sanitation workers (7.4%), 15 131 students (6.8%) and 11 705 other workers (table 2). At the time of interview, approximately 88% of all participants across different professions had attended certain training programs about sharp injury prevention, except that around 25.9% of the students had not taken such training because they were at early stages of their education process and had not yet taken relevant courses. Incidence of sharp instrument

**Table 2** Sharp instrument injuries incidents in profession

	Doctors		Nurses		Laboratory technicians		Sanitation workers		Students		Other workers		Total
	n	%	n	%	n	%	n	%	n	%	n	%	
No of questionnaires	63 379		106 056		10 463		16 415		15 131		11 705		223 149
No of knowledge training on occupational exposure	53 196		98 464		9056		14 358		11 214		9646		195 934
Attending training rate	83.9% (53 196/63 379)		92.8% (98 464/106 056)		86.6% (9056/10 463)		87.5% (14 358/16 415)		74.1% (11 214/15 131)		82.4% (9646/11 705)		87.8% (195 934/223 149)
No of people in sharp injuries	3505		8547		341		642		1142		264		14 441
Incidents of sharp injuries	4408		10 867		433		873		1451		312		18 344
Incidence rate	7.0% (4408/63 379)		10.3% (10 867/106 056)		4.1% (433/10 463)		5.3% (873/16 415)		9.6% (1451/15 131)		2.7% (312/11 705)		8.2% (18 344/223 149)
Reported incidents	175		470		13		51		124		11		844
Reporting rate (%)	4.0% (175/4408)		4.3% (470/10 867)		3.0% (13/)		5.8% (51/873)		8.5% (124/1451)		3.5% (11/312)		4.6% (844/18 344)

injuries was significantly different across professions ( $\chi^2=6384$ ,  $p=0.000$ ), with nurses showing the highest prevalence (92.8%).

A total of 18344 sharp instrument injuries were reported out of the 223 149 participants. This translated into 8221 cases per 100 000 HCWs for 1 month, or 0.08 per person-month. In other words, the incidence of sharp instrument injuries was 8.2%. Some participants reported multiple injuries. Both the number of injuries and the number of injured individuals were documented. Table 2 displays the numbers of injuries as well as injured people in various profession categories. There were significant differences between professions ( $\chi^2=1642$ ,  $p=0.000$ ). Nurses were identified to be the most vulnerable population to sharp object injuries. Incidents reported by this population accounted for 59.2% of all the injuries documented in the survey. The incidence of injuries in nurses was 10.3%, exceeding the 7.0% incidence in doctors. Students reported the largest proportion of injuries (8.5%), followed by sanitation workers (5.8%). Students had a higher reported incidence ( $\chi^2=63.733$ ,  $p=0.000$ ) compared with other professions. Noticeably, among 14 441 HCWs that had history of injury, less than 5% (4.6%) claimed reporting of the incident.

Table 3 shows the distribution of HCWs in terms of profession and instruments contaminated with bloodborne pathogens. Of the 18 344 reported injuries, 14 208 (77.5%) were caused by instruments used for patients with known infectious status. The rest 22.5% occurred during the disposal of sharp objects after using, which means that the sources of the injuries were unknown. The incidence of contact with bloodborne diseases was 6.7%. Of these 1226 cases, 670 (54.6%) involved a patient infected with HBV as source, 71 (5.8%) involved a patient infected with HCV, 137 (11.2%) had a patient infected with syphilis and 19 (1.5%) had a patient infected with HIV. The remaining 329 (26.8%) injuries involved patients with none of these four diseases at the time of exposure. The rate of injuries involving HBV, HCV, HIV and syphilis differed between doctors and nurses ( $\chi^2=85.686$ ,  $p=0.000$ ).

Regarding workplaces where sharp instrument injuries occurred, general wards (44.5%) were the most common places of occurrence, followed by operating rooms (22.2%) (table 4). Nearly two-thirds (65.3%) of the injuries in doctors had occurred in operating rooms, and more than half (58.3%) of those in nurses had occurred in medical wards.

Of all the incidents, 12.1% occurred during surgical needle insertion, 11.2% during removing an arteriovenous needle, 10.7% during recapping of used needles, 9.0% during handling of medical waste, 8.7% during preparing solution and 8.4% during discarding used needles into a container (table 4 and online supplementary table 1). The device that caused the highest proportion of injuries was single-use syringe needle (35.2%), followed by scalp wire needle (23.3%) and surgical suture

**Table 3** Infectious status of the patient with bloodborne disease

	Incidents of sharp injuries	Identification of source	Identification of sharp instrument with blood	Contaminated instrument with bloodborne disease					Others
				Total number	HBV	HCV	Syphilis	HIV	
Doctors	4408	3644 (82.7%, 3644/4408)	2353 (53.4%, 2353/4408)	432 (9.8%, 432/4408)	260 (5.9%, 260/4408)	22 (0.5%, 22/4408)	50 (1.1%, 50/4408)	4 (0.1%, 4/4408)	96 (2.2%, 96/4408)
Nurses	10867	8529 (78.5%, 8529/10867)	4783 (44.0%, 4783/10867)	669 (6.2%, 669/10867)	348 (3.2%, 348/10867)	43 (0.4%, 43/10867)	74 (0.7%, 74/10867)	11 (0.1%, 11/10867)	193 (1.8%, 193/10867)
Laboratory technicians	433	309 (71.4%, 309/433)	178 (41.1%, 178/433)	15 (3.5%, 15/433)	9 (2.1%, 9/433)	0	1 (0.2%, 1/433)	0	5 (1.2%, 5/433)
Sanitation workers	873	428 (49.0%, 428/873)	294 (33.7%, 294/873)	23 (2.6%, 23/873)	8 (0.9%, 8/873)	3 (0.3%, 3/873)	4 (0.5%, 4/873)	0	8 (0.9%, 8/873)
Students	1451	1118 (77.1%, 1118/1451)	585 (40.3%, 585/1451)	77 (5.3%, 77/1451)	37 (2.5%, 37/1451)	3 (0.2%, 3/1451)	8 (0.6%, 8/1451)	2 (0.1%, 2/1451)	27 (1.9%, 27/1451)
Other workers	312	180 (57.7%, 180/312)	95 (30.4%, 95/312)	10 (3.2%, 10/312)	8 (2.6%, 8/312)	0	0	2 (0.6%, 2/312)	0
Total	18344	14208 (77.5%, 14208/18344)	8288 (45.2%, 8288/18344)	1226 (6.7%, 1226/18344)	670 (3.7%, 670/18344)	71 (0.4%, 71/18344)	137 (0.7%, 137/18344)	19 (0.1%, 19/18344)	329 (1.8%, 329/18344)

HBV, hepatitis B virus; HCV, hepatitis C virus.

**Table 4** Characteristics of sharp injuries

Workplace	Doctors (%)	Nurses (%)	Laboratory technicians (%)	Sanitation workers (%)	Students (%)	Other (%)	Total, % (n)
Room for drawing of outpatient blood samples	0.1	0.7	13.4	40.5	2.4	0.6	1.0 (179)
Stomatology department	6.3	1.6	19.4	1.9	2.4	6.4	3.3 (606)
Injection room for outpatient	0.2	7.7	0.0	5.8	5.1	0.6	5.3 (978)
Outpatient clinic	4.0	1.9	3.0	5.3	2.0	6.1	2.7 (493)
Emergency department	3.2	3.0	0.7	4.1	4.5	2.6	3.1(577)
Intensive care unit	1.8	6.6	0.0	4.4	2.2	1.3	4.8 (875)
Units for haemodialysis	0.1	0.8	0.0	0.8	0.3	0.3	0.6 (106)
General ward	13.4	58.3	2.1	31.3	61.8	16.7	44.5 (8157)
Clinical laboratory	0.4	0.2	35.1	3.8	0.2	7.1	1.4 (253)
Operating room	65.3	8.7	0.9	4.9	11.9	10.9	22.2 (4076)
Sterile processing centre	0.2	2.2	0.0	5.8	0.4	13.8	1.9(346)
Room for temporarily depositing medical waste	0.2	1.7	0.5	22.9	1.2	2.9	2.3(427)
Other	4.7	6.5	24.9	8.5	5.6	30.8	6.9 (1271)
<b>Circumstance of sharp injuries</b>							
Recapping	9.4	11.4	8.1	2.2	16.3	4.2	10.7 (1962)
Hollow bore	6.9	30.3	27.0	2.9	31.1	9.0	23.0 (4215)
Preparing and discarding	20.8	44.3	13.4	85.5	36.5	31.7	39.1 (7166)
scalpel and sharps	48.4	6.0	5.1	0.6	8.1	5.8	16.1 (2945)
Others	14.5	8.0	46.4	8.9	7.9	49.4	11.2 (2056)
<b>Sharp device</b>							
Hollow bore	34.8	81.4	38.8	69.2	81.8	40.4	68.0 (12 466)
scalpel and sharps	54.7	13.0	38.6	21.5	13.5	26.0	24.3 (4458)
Others	10.5	5.5	22.6	9.3	4.7	33.7	7.7 (1420)

needle (14.0%) (table 4 and online supplementary table 2).

## DISCUSSION

Among the Chinese HCWs involved in this survey, the incidence of sharp instrument injuries is 8.2%, while the rate of reported incidents is 0.1%. The rate of reporting an incident is extremely low. Professional activity is identified to be a predisposing factor for sharp instrument injuries. Nurses appear to be the most vulnerable population, followed by students who face a higher risk of the injuries than all other professions except nurses. This survey, covering different geographical regions, types and levels of hospitals, professions, workplaces and contexts of incidents and instruments, has uncovered the current situation and added insight into the epidemiology of sharp instrument injuries in mainland China. Furthermore, the data from China, the world's largest developing country, provide valuable information for depicting these occupational hazards encountered by HCWs worldwide.

One characteristic of this study is the representativeness of the samples included. The survey involved altogether 223 149 HCWs, forming a comparatively large sample size. The participants were drawn from places representative of different geographical regions and from a diversity of hospitals that are typical in Chinese healthcare system. It has been indicated in some previous studies that the prevalence of sharp instrument injuries differs substantially between geographical regions in mainland China.<sup>13–17</sup> However, the regional data documented in most of these studies cannot be compared directly owing to differences in methods of sampling and criteria for defining sharp instrument injury. Compared with these studies, the present study is based on a large, comprehensive and representative sample, and the findings therefore more accurately reflect the current status of sharp instrument injuries in mainland China.

Some participants in our survey reported multiple incidents of injury, which is consistent with those reported elsewhere.<sup>2</sup> Nurses were the occupational group with the highest incidence of injuries, as reported similarly in other studies.<sup>18–20</sup> It is not uncommon that nurses get injured repeatedly within a short period of time. This may be attributed to the nature of their jobs. They contact with sharp devices directly and frequently in their daily duties. The fact that the lowest prevalence was found in laboratory technicians helps prove this. The technicians have less touch with sharp instruments in their work than other profession groups do. In this study, students presented a high incidence of injuries (only lower than nurses) and a low rate of learning or training on occupational exposure. This is in conformity with the findings in previous studies that students face high risk of sharp instrument injuries owing to their lack of training and experience.<sup>6 13 21 22</sup> Therefore, training programs on prevention of such injuries among students seem necessary and beneficial.<sup>23</sup>

Transmission of bloodborne diseases has long been recognised as a potential threat to the health of HCWs. HCWs have a high probability of exposure to bloodborne pathogens due to sticks or cuts from sharp instruments contaminated with the blood of infected patients.<sup>24</sup> HBV, HCV and HIV are some of the most serious bloodborne infections transmitted by sharp instrument injuries. In mainland China, the seroprevalence of HBV infection ranges from 6% to 8% of the population,<sup>25–28</sup> HCV has a prevalence of 3%<sup>26</sup> and the prevalence of HIV is rapidly rising.<sup>29</sup> Syphilis is also prevalent in mainland China.<sup>30</sup> All these four infections were included in this survey. The rates of injuries involving HBV, HCV and HIV documented in our survey are lower than those in Shiao's report,<sup>5</sup> but this might be due to the low incidences of these diseases in mainland China. Still, our results have confirmed the threat of these infections to HCWs and remind us of the necessity of dealing with the transmission of these diseases through sharp instrument injuries. Supposedly, improving knowledge about occupational exposure and practice should contribute to reducing the spread of bloodborne diseases among HCWs. However, most HCWs in mainland China attended lecture-based training sessions usually without or with very limited demonstration and/or practice. This type of training is not sufficient for medical staff to gain sound knowledge of occupational exposure, and this does not offer them opportunities for hands-on practice. An implication of this situation is that implementation of infection control strategies and procedures needs attention particularly in developing countries.

Reporting and documenting incidents is one of the basic steps to preventing infectious diseases.<sup>19</sup> Lack of reporting of exposure increases the likelihood of infection. In developed countries, 58% of such injuries are reported.<sup>31</sup> The reporting rate in Taiwan, China, is 21.2%.<sup>4</sup> However, only less than 5% of the HCWs in our study reported their injuries; more than 95% of the incidents were unknown or ignored since they were not reported. Further research is needed to explore the reasons why HCWs do not report exposures and what can be done to improve the situation. Our study suggests a need of establishing a national surveillance system for occupational exposure to sharp instrument injuries in mainland China.

Based on our survey, the incidence of sharp instrument injuries varied across workplaces. The general ward was identified to be the most common place of occurrence, followed by operating room, injection room for outpatient and intensive care units. Similar with that reported in other studies,<sup>32–34</sup> most of the reported injuries in this survey had taken place in the general ward, and the main reason should be the higher number of invasive interventions. Most incidents occurred during surgical needle insertion, recapping of used needles or removing an arteriovenous needle from a patient. The circumstances involving sharp instrument injuries differed markedly. In our study, approximately 50% of the reported accidents had occurred while working with or dealing with needles.

The devices that most commonly caused injuries were single-use syringes, scalp wire needles and suture needles. These findings conform to the results of some studies that a large portion of sharp instrument injuries is caused by disposable syringes with needles.<sup>35 36</sup>

From the perspective of public health, investigation of the presence of sharp instrument injuries in HCWs is important to the prevention of such injuries. As there are about six million physicians and nurses in mainland China, sharp instrument injuries pose a serious occupational problem. Many developed countries follow universal precautions including using protective gloves, masks and eyewear. In mainland China, issues such as potential occupational burden due to such injuries must be considered, and actions need to be taken to prevent injuries in the process of patient care and treatment.

In mainland China, staff in public hospitals usually do not refuse to respond to healthcare studies proposed by the government. This survey was organised by the Ministry of Health, and the response rate was 100%. To ensure privacy, names of the participants were kept confidential. There were no penalties or rewards for participation.

This study had some limitations. First, the data were collected retrospectively through participants recalling their experience in the past. The participants' memory might not be accurate, which in turn could influence the accuracy of the research results. It is likely that some participants might forget to report their injuries and this under-reporting would cause the documented number of incidents lower than the actual number. Second, even though we tried hard to select samples from various regions, selection bias could not be completely avoided and the included participants might not satisfactorily represent the body of HCWs in mainland China. Third, only hospitals were included in this study, which may not be able to represent the overall healthcare settings in mainland China. Smaller, lower-level, special and private clinics were left out. Fourth, traditional cultural differences in HCWs may be responsible for some discrepancies. Chinese nurses also perform tasks such as cleaning reusable medical equipment, which are generally done by ancillary personnel in the USA.

## CONCLUSIONS

The high prevalence of sharp instrument injuries in HCWs in mainland China indicates that such injuries should not be neglected as they represent a significant cause of bloodborne infections in the workplace. Attention should be paid to unreported injury incidents. This finding is very worrisome and indicates the need for further action, such as improving the education/training programme, promoting universal precautions, increasing awareness of the seriousness, and so on.

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**Contributors** S-LH searched the literature, analysed the data, interpreted the results and drafted the report. QL and S-HF searched the literature, analysed the data and interpreted the results. Z-YZ, T-YH, B-YC and J-AQ analysed the data and interpreted the results. YS and X-DG conceived the study, designed the study, supervised the study, interpreted the results and revised the report. N-NW analysed the data, interpreted the results and revised the report. S-LH, QL and S-HF contributed equally.

**Competing interests** None declared.

**Patient consent** Obtained.

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