BMJ Open Doctor's presenteeism and its relationship with anxiety and depression: a cross-sectional survey study in China

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ABSTRACT

Objectives The impact of presenteeism on doctors' health, quality of patient care and overall performance of health institutions has been reported. The study aimed to investigate the prevalence of presenteeism among doctors, the association between presenteeism and anxiety/depression, and aspects that can help alleviate presenteeism.

Design A cross-sectional anonymous survey study was conducted between 2017 and 2018.

Setting 30 hospitals in Hangzhou city, Zhejiang Province, China including 10 category 1 hospitals (20–99 beds), 10 category 2 hospitals (100–499 beds) and 10 category 3 hospitals (> 500 beds) which had the highest population coverage.

Participants At least 3 doctors from each department in the studied hospitals participated. Each participant received a gift worth around US\$5 at completion of the survey.

Primary and secondary outcome measures The prevalence of presenteeism and its relationship with anxiety or depression were evaluated as the primary outcomes. Secondary outcomes included the prevalence of abnormal cases of anxiety and depression.

Results The survey was completed by 1153/1309 hospital doctors (response rate 88.1%). Presenteeism was reported by 66.4% of participants. Using the Hospital Anxiety and Depression Scale, 68.8% and 72.3% of participants had abnormal cases of anxiety and depression, respectively. Logistic regression analysis showed that participants with abnormal cases of anxiety, borderline cases of depression or abnormal cases of depression were more likely to practice presenteeism (all $p < 0.05$). Other significant work-related contributing factors included: time working at the current hospital, management duty, monthly salary and ease of replacement (all $p < 0.05$).

Conclusion Presenteeism was prevalent among doctors in China and the association of presenteeism with abnormal cases of anxiety or depression was significant. Considering the modifiable work-related contributing factors, appropriate measures at the healthcare institutions to support doctors' mental health, help them develop and reinforce management skills, and ensure appropriate manpower are important to alleviate presenteeism behaviour.

Strengths and limitations of this study

- This study surveyed a representative sample of doctors from three categories of hospitals in China about their practice of presenteeism and its correlation with their mental health status.
- This study setting was one of the most populous capital cities in an economically advanced province. It covered different levels of hospitals to give findings representable of the overall hospital doctor workforce in areas with similar socioeconomic backgrounds in China. The findings may also have implications to other advanced cities/countries.
- Presenteeism and the states of anxiety and depression were measured using self-assessment with a recall period of 12 months which might result in inaccuracy in self-reporting due to memory loss.
- The influence of hospital category and other practice settings, which may influence doctors' presenteeism behaviour due to the different intensity of service and severity of illness of patients, was not evaluated in this study warranting further investigation.
- Causal relationships between presenteeism and mental health conditions cannot be inferred from the data presented due to the cross-sectional nature of the study.

INTRODUCTION

Presenteeism, defined as going to work while being ill, is a common organisational behaviour.¹ In the 2010 European Working Conditions Survey, out of 40 000 respondents in 34 countries, 40% indicated that they went to work while being sick during the 12 months prior to the study and the average days of presenteeism was 3.1.² Compared with the general population, the prevalence of presenteeism among doctors was found to be consistently higher.^{3 4} Over 80% of physicians had worked while ill.³ In a German study, about 90% of the 1311 clinicians in surgery from 489 hospitals reported that they worked despite

illness at least once a year, and 65% reported that they sometimes or often worked when feeling sick.⁴

The implications of presenteeism has prompted growing attention in the healthcare institutions. When the concept presenteeism was introduced in 1990, the act was considered as 'a demonstration of work commitment by exhibiting excellent attendance'.¹ However, as the studies about presenteeism continued to roll out, attention has now been shifted to the association of presenteeism with the profound long-term effects on the individual employees' health, as well as the adverse implications to the patients they cared for and the organisations they worked at.¹ According to a systematic review,⁵ presenteeism was a risk factor for future sickness absence and decreased self-rated health. It might also predict poor work ability,^{6,7} physical health complaints⁷ and increased risk of depression⁶ in the future. Especially for these highly invested professionals, such threats to their health status could easily turn into serious workforce problems in the long run. In terms of economic consequences to the organisation, the consequences of presenteeism have been frequently assessed by the cost and the productivity loss. It has been reported that presenteeism among doctors was associated with higher medical errors, productivity loss, higher infectious to the patients and colleagues, and posed negative effect on the health of the coworkers.^{8,9}

Presenteeism has been frequently linked to the mental health of employees in previous studies with anxiety and depression in particular.^{10–14} Depression and anxiety are the most common mental disorders which may occur together.¹⁵ It has been suggested that employees who were depressed might have a higher prevalence of presenteeism. In one study conducted across eight diverse countries, it was found that individuals living in a country with a higher prevalence of depression diagnosis had higher levels of presenteeism.¹⁰ Studies in developed countries also found that employees with depression lost 20% of total worktime with 81% of these losses accrued to presenteeism.¹¹ On the other hand, presenteeism could also increase the risks of depression and anxiety reportedly. In a 2-year follow-up Danish study, reporting eight or more days of presenteeism was associated with an increased risk of depression among initially non-depressed employees.¹² The productivity costs of presenteeism associated with depression across these countries ranged from US\$547 in China to US\$5524 in the USA and US\$5788 in Brazil.¹⁰ According to the researchers, the productivity costs of presenteeism in China was likely to be an underestimate relative to the other countries as it was based on individual income rather than household income as was done for the other countries.

Presenteeism is now projected to bring profound implications to individual doctor's health, patient's quality of care and the costs to the healthcare organisation.^{3,8} Anxiety and depression have become significant health issues especially in the healthcare sector with a possible linkage with presenteeism.^{13,14} Despite the important role of doctors and their profound impact on the patient outcome and the performance of the health institutions

in China, previous studies about presenteeism and its association with anxiety and depression among doctors was limited. Targeting hospital doctors, the study aimed to (1) investigate the prevalence of presenteeism, (2) investigate the association between presenteeism and the states of anxiety and depression and (3) identify actions which may help alleviate presenteeism. The overall goal was to explore measures which may help to mitigate the impact of presenteeism in the workplace.

METHOD

Study design and sampling

A cross-sectional survey study was conducted in Hangzhou city, Zhejiang Province, China between October 2017 and March 2018. Hangzhou is the capital and the most populous city of Zhejiang province and is one of the most economically advanced provinces in the Yangtze River Delta Zone. In 2016, there were 31 548 healthcare institutions in Zhejiang.

The healthcare institutions were categorised into three categories based on the number of beds: category 1 (20–99 beds), category 2 (100–499 beds) and category 3 (>500 beds). Healthcare institutions with fewer than 20 beds were excluded. In this study, within each group, the healthcare institutions were ranked in descending order of population coverage. The top 10 healthcare institutions with the greatest population coverage from each group were selected as sampling sites. The target sample size was set at 1000 doctors in order to optimise the generalisability of the study results. Within each hospital, the doctors were randomly selected from each department. In order to collect sufficient responses to allow meaningful data analysis and to ensure representativeness, a minimum of three doctors from each department were randomly selected to participate in this survey study. If the number of doctors in a particular department was exceptionally high, that is, more than twice the average number of doctors per department at the studied hospital, the number of doctors was then sampled proportionally. The rationale for this sampling method was to minimize the sampling bias by ensuring that the number of doctors sampled from each department correlated with the actual size of doctor workforce at each department, and reducing the risks of under-representation of departments which had larger number of doctors. A trained researcher was onsite to obtain participants' consent to conduct the survey and to clarify any queries participants might raise when completing the self-administered questionnaire.

Questionnaire design

The survey questionnaire was pilot tested by 123 doctors for validity. The English translation of the survey was provided in the online supplementary annex 1. The questionnaire consisted of three parts to collect description information about the participant, to measure the act of presenteeism and to screen depression and anxiety cases among the participants.

In part 1, participants were asked to provide a range of sociodemographic, health, financial, work-related information. According to a previous study,¹³ factors suggested to be associated with presenteeism, included sociodemographic factors (age, gender, marital status, pregnancy for female participants or for the spouse of male participants, number of children, highest education level), health factors (history of chronic diseases in the past year), financial factors (reward system for full attendance, monthly salary) and work-related factors (number of years working at the current hospital,^{16–19} level of seniority,²⁰ people management duty, weekly work hours, ease of replacement, superior's leadership type).²¹ All of this information was collected in part 1. Ease of replacement at work was measured using the method developed by Arosso and Gustafsson.²² The type of superior's leadership was measured based on the leadership theory developed by Lewin.²³

In part 2, a one-question measurement was used to measure the act of presenteeism.¹³ Participants were asked 'Has it happened over the previous 12 months that you have gone to work despite feeling that you should have taken sick leave because of your state of health?' and had to choose one of the four answers: 'never', 'once', '2–5 times' and 'more than 5 times'. In part 3, the 'Hospital Anxiety and Depression Scale (HADS)' originally developed by Zigmond and Snaith was used to screen the doctors for depression and anxiety.²⁴ HADS was originally written in English and the Chinese translation of the tool was validated by Sun *et al.*²⁵ The HADS is a 14-item scale that collects ordinal data. Seven of the items relate to anxiety and seven relate to depression. To each item, there are four scores: 0 (never), 1 (seldom), 2 (often) and 3 (always). The possible scores range from 0 to 21 for anxiety and 0 to 21 for depression. A score between 0 and 7 was considered normal cases, a score of 8–11 identified borderline cases and a score of 12–21 indicated abnormal cases of anxiety or depression.²⁶

Statistical analysis

In this study, presenteeism was set to be the dependent variable and the states of anxiety and depression be the independent variables. The controlled variables selected for the logistic regression analysis were listed in table 1, which included demographic factor, health factors, economic factors and work factors. All the variables used for data analysis was listed in online supplementary annex 2. Descriptive statistics were performed on the data collected from the participants. The logit model for the binary data was used to determine the relationship between presenteeism and the states of anxiety and depression, and to identify the influence factors associated with the behaviour of presenteeism. Logistic regression analysis was conducted by using Stata V.13.0-SE and driven by four theoretical models: Job Demands-Resources Model,²⁷ Job Demand-Control Model,²⁸ The dynamic model of presenteeism and absenteeism¹ and the Human Service Organisations framework.²⁹ As the data of monthly salary was not normally

distributed, the salary data collected was log transformed before conducting regression analysis. Statistical significance was defined as $p < 0.05$. The Bonferroni adjustment was used for multiple comparisons to validate the impact of different cases of anxiety or depression on presenteeism.

Patient and public involvement

Patients and the public were not involved in the design or planning of the study.

RESULTS

A total of 1309 surveys were distributed, 1153 of which were completed giving a response rate of 88.1%. The invited participants who did not participate explained that they did not have the time. As reported by the on-site researchers, doctors who had started answering the questionnaire but failed to complete it indicated that they did not have enough time to go through all the questions or had to stop abruptly to attend to patient care or other urgent matter. Further investigation of the reasons for incompleteness was not possible because the survey was answered anonymously, and follow-up questions were, therefore, not feasible. Among the participants, 42.4% ($n=489$) were female, 76.2% ($n=879$) aged between 20 and 39 years, 70.6% ($n=814$) held at least a master degree. Further descriptive information about the participants is shown in table 1.

The prevalence of presenteeism, and the normal, borderline and abnormal cases of depression and anxiety is shown in table 2. Among all the participants, 66.4% ($n=766$) reported that they had worked when not feeling well twice or more over the previous 12 months. Using the HADS, 68.8% ($n=793$) and 72.3% ($n=834$) of the participants were identified as abnormal cases of anxiety or depression, respectively.

Regression analysis

Logistic regression analysis showed that 10 variables were associated with presenteeism with statistical difference as shown in table 3. Compared with participants with normal cases of anxiety or depression, participants with abnormal cases of anxiety, borderline cases of depression or abnormal cases of depression were more likely to practice presenteeism (all $p < 0.05$). For multiple comparisons, Bonferroni adjustment was used and it was found that the impact of different cases of anxiety or depression on presenteeism was all significant. Data analysis using Stata also showed that there were interactions between anxiety and depression which, however, did not affect the overall finding about the association between abnormal cases of anxiety or depression and presenteeism in this study. For the adjustment for multiple comparisons and determination of statistical interactions, please refer to online supplementary file. In addition to three demographic factors (age, education level, being a parent), four work-related factors were also more likely to result in presenteeism including the time working at the current

Table 1 Descriptive information about the participants (n=1153)

Variables	Types	Counts	Proportions (%)
Gender	Female	489	42.4
	Male	664	57.6
Age (years)	20–29	135	11.7
	30–39	438	38.0
	40–49	441	38.3
	50–59	118	10.2
	60 or above	21	1.8
Highest education level	Junior college	17	1.5
	Bachelor	322	27.9
	Master	603	52.3
	PhD	211	18.3
Marital Status	Never married	137	11.9
	Married or cohabited	858	74.4
	Divorced or widowed	158	13.7
Pregnancy status	Non-pregnant or spouse was not pregnant	1019	88.4
	Pregnancy or spouse was pregnant	134	11.6
No of children	0	385	33.4
	1	483	41.9
	2	237	20.6
	3 or more	48	4.1
History of chronic diseases in the last year	No	1050	91.1
	Yes	103	8.9
People management duty	No	889	77.1
	Yes	264	22.9
Level of seniority	None	152	13.2
	Junior staff	313	27.1
	Middle management	275	23.9
	Sub-top management	271	23.5
	Top management	142	12.3
Weekly work hours	Less than 34	163	14.1
	35–39	125	10.8
	40	475	41.2
	41–45	340	29.5
	46 or more	50	4.3
Reward system for full attendance	No	388	33.7
	Yes	765	66.3
Ease of replacement ('work left undone')	None or only a small proportion	221	19.2
	Somewhat less than half	520	45.1
	Somewhat more than half	334	29.0
	Virtually all	78	6.8
Superior's leadership type	Authoritarian	249	21.6
	Democratic	637	55.2
	Laissez-faire	267	23.2
	Minimum	Maximum	Mean±SD
No of years working at the current hospital	1	50	12.1±8.3
Monthly salary (¥)	2500	16 000	7917.4±2609.9

Table 2 Prevalence of presenteeism, depression and anxiety among the participants (n=1153)

	No of participants	Proportions (%)
Prevalence of presenteeism (no of times having worked despite feeling the need to use sick leave)		
Never or once	387	33.6
Twice or more	766	66.4
Screening results of depression and anxiety using 'Hospital Anxiety and Depression Scale'		
Anxiety score 0–7 (normal cases)	183	15.9
8–11 (borderline cases)	177	15.4
12–21 (abnormal cases)	793	68.8
Depression score 0–7 (normal cases)	191	16.6
8–11 (borderline cases)	128	11.1
12–21 (abnormal cases)	834	72.3

hospital, management duties, lack of ease of replacement and monthly salary (all $p < 0.05$).

DISCUSSION

In this study, the prevalence of presenteeism was high in China with 66.4% of hospital doctors reported to work while they felt the need to use sick leave twice for more in a year. Furthermore, it was also found that 68.8% and 72.3% of the hospital doctors in China had abnormal cases of anxiety and depression, respectively. The association between the practice of presenteeism and these psychological conditions was also found to be statistically significant. While the findings about presenteeism behaviour and the mental health of doctors are worth further discussion in its own right, the combination of these findings also prompt a need to explore the act and implications of presenteeism in the context of mental health among the doctors.

Although the prevalence of presenteeism among hospital doctors in China identified in this study (66.4%) appears to be lower than what was previously reported about doctors in New Zealand (88%)⁸ and some European countries (70%–86%),³⁰ these findings are not meant for direct comparison with accuracy due to the differences in study design. Nevertheless, the common behaviour of presenteeism among doctors has been once again confirmed in this study. While the practice of presenteeism has caused concerns over individuals' health, the quality of patient care and the overall performance of the health institutions,¹ the coexistence of mental problems further adds to the burden associated with presenteeism act. In a study conducted in the USA involving 3127 resident physicians, it was found that substantial presenteeism was identified among interns with depressive symptoms and the presenteeism-related cost per resident was significantly higher compared with residents with no

change in depressive symptoms, suggesting an estimation of more than US\$1.2 million added cost attributable to depression-related presenteeism.³¹

Our findings revealed that at least 68.8% and 72.3% of hospital doctors might have abnormal cases of anxiety and depression respectively. Not only is the prevalence of suspected cases of depression higher compared with the overall employees,³² it also appears to be higher than that among doctors in other countries.^{33–38} Compared with the general population, the mental health of Chinese doctors being at particular risk is not surprising as this health profession has become increasingly challenging nowadays. Along with the Chinese economy booming in recent years, the health consciousness among this huge population has greatly improved which is translated into an increasing demand for quality medical services. According to the doctor workforce statistics in 2012, China had only 1.6 physicians per 1000 population which was much lower than the OECD average (3.2 physicians).³⁹ The growing demand of medical care thus resulted in mounting workload for the doctors. The stress to address the overwhelming medical needs could easily add to the tension between doctors and patients. Medical disputes, deteriorating doctor–patient relationship and even violence against doctors have become a serious problem in China.^{40–42} The severity of these issues in China can also help to explain why Chinese doctors were more likely to suffer from depression as the prevalence of depressive symptoms among doctors only ranged from 10% to 29% in the USA, the UK, Norway, Japan and the Netherlands,^{34–38} and the anxiety symptoms was only prevalent in 24% of doctors.³⁸ As reported in a literature review, only around 30% of residents screened positive for depression.⁴³

When comparing with previous studies conducted in China, it seems that the participants in this study were more prone to mental health problems. In a study carried out in the northeast of China, it was found that up to 65.3% doctors working in national hospitals had depressive symptoms.⁴² In another study conducted in southern China, an estimated 25.67% of doctors working in public hospitals had anxiety symptoms and 28.1% had depressive symptoms.¹⁴ Although these findings were not for direct comparison and the tool used in this study was only for screening purposes, the mental health problems of doctors in China call for serious attention and efficient interventions to help them cope with the mounting stress at work. It has been suggested that coping strategies and social support are both important for maintaining and improving doctors' mental health, which should be further explored in future studies.^{42 44 45}

The association of presenteeism with anxiety and depression identified in this study worth further investigation. Due to the nature of the cross-sectional research design used in this study, no causal relationships between presenteeism and mental health conditions can be inferred. As such, it remains unclear whether this unhealthy trend in the workplace may contribute to the mental health problems or in fact is a consequence of depression or anxiety. Nevertheless, presenteeism can be conceptualised as a possible indicator

Table 3 Logistic regression analysis of factors associated with presenteeism

	OR	P value	95%CI
Borderline cases of anxiety	2.046	0.100	0.872 to 4.802
Abnormal cases of anxiety	5.370	0.000	2.096 to 13.760
Borderline cases of depression	3.319	0.005	1.427 to 7.717
Abnormal cases of depression	5.350	0.000	2.214 to 12.925
Gender	1.072	0.705	0.748 to 1.537
Age (years)			
30–39	1.067	0.863	0.510 to 2.235
40–49	2.791	0.040	1.047 to 7.435
50–59	5.126	0.033	1.142 to 22.999
60 or above	0.562	0.622	0.057 to 5.558
Highest education level			
Bachelor	0.984	0.981	0.246 to 3.925
Master	1.380	0.651	0.342 to 5.569
PhD	5.622	0.023	1.264 to 25.010
Marital status			
Married or cohabited	0.858	0.687	0.407 to 1.808
Divorced or widowed	0.657	0.376	0.259 to 1.667
Pregnancy status	1.735	0.064	0.969 to 3.105
No of children			
1	1.432	0.167	0.861 to 2.383
2	2.620	0.004	1.357 to 5.060
3 or more	9.359	0.195	0.319 to 274.485
History of chronic diseases in the past year	0.887	0.707	0.476 to 1.656
People management duty	0.269	0.000	0.162 to 0.445
Level of seniority			
Junior staff	0.733	0.329	0.393 to 1.368
Middle management	0.598	0.161	0.291 to 1.228
Sub-top management	1.507	0.435	0.538 to 4.219
Top management	0.874	0.826	0.262 to 2.909
Weekly work hours			
35–39 hours	0.467	0.100	0.189 to 1.157
40 hours	0.455	0.060	0.201 to 1.033
41–45 hours	0.441	0.062	0.187 to 1.040
46 hours or more	0.409	0.124	0.131 to 1.278
Reward system for full attendance	0.833	0.394	0.547 to 1.268
Ease of replacement ('work left undone')			
Somewhat less than half	0.728	0.220	0.438 to 1.209
Somewhat more than half	0.390	0.001	0.224 to 0.679
Virtually all	1.117	0.805	0.462 to 2.701
Superior's leadership type			
Democratic	1.195	0.451	0.753 to 1.896
Laissez-faire	0.855	0.542	0.516 to 1.416
Time working at the current hospital	1.089	0.003	1.029 to 1.153
Monthly salary (log*)	0.043	0.004	0.05 to 0.362

Continued

Table 3 Continued

	OR	P value	95%CI
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Statistical significance was defined as $p < 0.05$.

*Log (monthly salary) was used to enhance the relationship between the variable and presenteeism.

that helps to identify hidden cases of mental health problems among doctors. The challenging clinical setting and the competitive work environment were great sources of stressor for doctors contributing to their increasing psychological distress.⁴⁶ There is also mounting evidence that physicians are at risk for depression and deterioration of the condition.⁴⁶ Moreover, it has been shown that presenteeism shows strong associations with psychosocial workload.⁴ However, doctors reportedly were not proactive about seeking help or only did so later in the course of disease compared with other groups.³ In particular, they appeared to be reluctant to seek help for psychological health problems due to concerns about confidentiality.³ While mental health is already a major public health issue in its own right, it is proposed that the issue of presenteeism should be dealt with in conjunction of and with special emphasis on the mental health of the doctors. It has been suggested that measurement of presenteeism could be used to predict the risk for emotional problems.⁴⁷

As explained by the conceptual model developed by Aronsson and Gustafsson,²² for doctors go to work while sick involves a highly complicated decision-making process. Contributing factors might include personally related demands (individual boundary lessness and private-financial demands) and work-related demands (replaceability, sufficient resources, conflicting demands, control and time pressure).²¹ Among various contributing factors, time pressure, the worker's replaceability,²¹ workload,⁴⁸ organisational and other work-related factors⁴ have been linked to presenteeism behaviour. In this study, it was reconfirmed that doctors who had to take up management duties, or worked at an environment where it was not easy to find replacement were more incline to practice presenteeism. Although there are little data that determine the cost and productivity loss due to presenteeism in China, the implication of presenteeism among medical staff on risks to the patients, the cost and productivity loss to the healthcare institutions has been demonstrated in other countries.^{3 5 31} The predisposing factors identified in this study should be considered important implications for the management personnel in the healthcare institutions in China. Attention and strategies to mitigate presenteeism at the management level might be prompted to prevent organisation suffering in the long run. Supervisory support for people who have management duties, being able to make work adjustments, health interventions and organisational support for a healthy lifestyle have been shown to mitigate the impact of presenteeism on productivity. Human resource arrangement which allows needing physicians taking short spells of time off work may allow individuals who are ill or stressed to recover, so that more serious conditions are avoided.⁴⁹ The ability to

recover from work appears to be important as it was found that employees who rarely recovered from work during free weekends had an increased risk of death through cardiovascular disease.⁵⁰ Mental health support for doctors and workplace management are also important. Initiatives include improving access to free, confidential mental health treatment and structural changes to reduce clerical burden and work compression hold the promise to improve depression rates.

Limitation

There are several limitations to our study. First, the recall period of 12 months might be a period too long for the participants to remember clearly which might result in inaccuracy in self-reporting due to memory loss. Second, the influence of hospital category, which may influence doctors' presenteeism behaviour due to the different intensity of service and severity of illness of patients in the hospitals by category, was not evaluated in this study. This unanswered question will be addressed in a future study as a part of a bigger project requiring a bigger sample size and more complicated research methods. Third, presenteeism and the states of anxiety and depression were measured using self-assessment. Other objective assessments in future studies might be needed. Furthermore, while the prevalence and characteristics of presenteeism among doctors in China were investigated using a cross sectional analysis in this study, future studies may be considered to further derive, if any, the causal relationships between presenteeism and anxiety/depression. Finally, the subjects in this study were comprised exclusively of hospital doctors. Future studies targeting doctors working at different settings might enhance the understanding of presenteeism within the overall workforce.

CONCLUSIONS

Presenteeism is highly prevalent among doctors in China and the association between presenteeism and anxiety or depression has been verified. In order to mitigate the impact of presenteeism on individual doctors and at workplace, it is important to have appropriate measures at the healthcare institutions to support doctors' mental health, help them develop and reinforce management skills, and ensure appropriate manpower in order to alleviate the practice of presenteeism. This will in turn help to ensure the quality of patient care and benefit the overall performance of the health institutions.

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Contributors XX and QL planned and designed the study. QL, TW, PP and GL were responsible for data management and analysis. COLU and HH drafted the manuscript. All authors contributed to interpretation of study results, critical revision of the paper and approval of final version, and agree to be accountable for all aspects of this article.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Ethical approval was obtained from the Ethics Committee of the China Pharmaceutical University (Project number: CPU2018016).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement The de-identified data set related to this study could be made available with the approval of the Ethics Committee of the China Pharmaceutical University if necessary.

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