Depression and relevant influencing factors among elderly adults with different sleep quality in pension institutions in Northeastern China

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Abstract

Objective

This study aimed to assess depression among elderly adults with different sleep quality in pension institutions and to clarify its factors.

Methods

We conducted a cross-sectional study using a staged sampling method in six pension institutions located in Northeastern China from May to September 2017. Our study population comprised all elderly adults willing to participate in this study, who were not suffering from dementia and had lived in these pension institutions for six months or longer. All the participants were interviewed using a questionnaire that explored cognitive function, demographic characteristics, and factors influencing depression. The questionnaire also made use of the Pittsburgh Sleep Quality Index (PSQI) and Geriatric Depression Scale (GDS). After screening for cognitive function, we chose 507 elderly adults without cognitive defects as our participants. We used logistic regression to analyze the factors influencing depression among elderly adults with poor or good sleep quality.

Results

The overall depression rate among elderly adults was 21.7%. The depression rates among elderly adults with good and poor sleep quality were 12.3% and 31.1%, respectively. The logistic regression analysis revealed that, after adjustment for age, depression was significantly associated with multiple influencing factors only among elderly adults with good sleep quality.

Conclusion

The prevalence of depressive symptoms among elderly adults with different sleep
quality in pension institutions in Northeastern China was insignificant. However, different factors influenced depression among elderly adults depending on their sleep quality. Therefore, the risk factors of depression among elderly adults should be analyzed separately.

Introduction
Population aging is becoming an increasingly serious issue globally, posing serious challenges to the maintenance and/or improvement of human health and socioeconomic development, particularly in China\(^1\). China has the largest aged population—it is the only country in the world with over 100 million elderly adults (aged 60 years and above) \(^2\). With aging population and changing family structures, traditional home-based care in China has gradually weakened, and an increasing number of elderly people are inclined to receive long-term care in pension institutions\(^1\). Elderly adults who live in pension institutions rather than in their own homes are unable to receive care from their adult children. Accordingly, they are more likely to suffer from mental disorders than other elderly adults.

Depression is one of the most important indicators of mental health. Among elderly adults, depression has become the second largest mental disorder after Alzheimer's disease \(^3\). It is also the only mental disorder that ranks among the top in terms of disease burden in both high and low income countries (high-income countries: rank 2; low and middle-income countries: rank 4) \(^4\). It has been reported that about 80\% of elderly adults who commit suicide do so as a result of depression \(^4\). Therefore, it is imperative to analyze depression among elderly adults living in pension institutions.
Sleep is a physiological need of the human body. Numerous studies have shown that the quality of sleep among the elderly is closely related to mental disorders, such as depression and anxiety. Elderly adults' sleep quality certainly affects their lives, work, and mental status to varying degrees, and as such affects their quality of life. Therefore, it is necessary to conduct targeted research on the characteristics of the elderly population with different sleep quality. To date, there have been some studies on the relationship between sleep and depression among elderly adults. However, most of them focus on the correlation between sleep and depression among elderly adults who are either hospitalized or reside in a community; there are few studies on elderly adults living in pension institutions.

In addition, previous studies in China have relied on different methods of measuring depression, making comparison of depression levels among elderly adults difficult. Moreover, research conclusions from developed countries cannot be directly applied to elderly adults in China because of differences in race, culture, income level, and lifestyle. Most previous studies also did not screen for cognitive impairment among elderly adults, leading to insufficient reduction of information bias and decreasing the generalization of previous conclusions.

This study attempted to analyze depression and factors influencing depression among elderly adults with different sleep quality living in pension institutions in Northeastern China. We used the Geriatric Depression Scale (GDS), which is widely used in China and abroad, to investigate depression among elderly adults living in pension institutions. Furthermore, we comprehensively analyzed and compared the depression levels among elderly adults according to their sleep quality and examined their correlation with demographic information and health status. Through
this study, we provide rational prevention and intervention measures for elderly adults with different sleep quality that were suffering from depression.

Methods

Ethics approval

The study protocol and informed consent form received ethics approval from the Committee on Human Experimentation at the China Medical University (Code: AF-SOP-07- 1.1-01). Written informed consent concerning the conduct of the survey was obtained from each participant.

Study area and subjects

This cross-sectional study was performed in Northeastern China. A list of pension institutions in Northeastern China was taken from the website of the Liaoning Provincial Civil Affairs Bureau. A staged sampling method was carried out from May to September 2017. Six public pension institutions were selected as research objects: two in Shenyang, two in Anshan, one in Tieling, and one in Benxi. Our study population comprised all elderly willing to participate in this study, who were not suffering from dementia and had lived in these pension institutions for six months or longer. All the participants were interviewed using a questionnaire exploring cognitive function, demographic characteristics, and influencing factors. The questionnaire also made use of the Pittsburgh Sleep Quality Index (PSQI) and Geriatric Depression Scale (GDS). A total of 553 valid questionnaires were obtained, for an effective response rate of 84.04%. After screening for the cognitive function using the Mini-Mental State Examination (MMSE) \(^{10}\), 507 elderly adults without cognitive defects were chosen as participants.
Survey and quality control

Survey scales

The GDS \(^{11}\) is a 30-item self-report assessment used to identify depression among the elderly. In the GDS, 20 questions are answered “yes” (scored 1) or “no” (scored 0), while the remain 10 questions are evaluated the opposite way (where “yes” is scored 0 and “no” is scored 1). The total score of the GDS ranges from 0 to 30, with a score of ≥ 11 indicating depression.

The PSQI \(^{12}\) is a self-report questionnaire that assesses sleep quality over a one-month time interval. The measure scale consists of seven components, including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication, and daytime dysfunction. The score for each component ranges from 0 to 3, where 0 indicates “no difficulty” and 3 indicates “very difficult.” The total score of the PSQI ranges from 0 to 21, with a score of > 7 denoting poor sleep quality or having a sleep disorder.

The MMSE has been widely used to screen for cognitive defects among the elderly\(^{10}\). The total score of the MMSE ranges from 0 to 30. Combined with the educational level of the elderly, the diagnostic criteria for cognitive impairment among the elderly are as follows: illiteracy is ≤ 17 points, primary school is ≤ 20 points, secondary school (including technical secondary school) is ≤ 22 points, and university is ≤ 23 points.

We also used a self-designed questionnaire for baseline information including age, sex, marital status, pension, economic status, chronic disease, self-care, body aches, chewing ability, ability to go out alone, exercise, regular diet, smoking, filial piety, and loneliness.
Quality control

All the surveyors were trained uniformly. While conducting the investigation, they had to ensure that the respondents could grasp and understand the meaning of each question, avoid inducement of any bias as far as possible, and ensure the reliability of the information collected.

Statistical analysis

Items for which over 95% of participants had the same answers were excluded from the data analysis; these items included race (“Han” accounted for 96.8%) and medical insurance (“Have” accounted for 98.9%).

In addition, the proportion of missing items was < 5% among elderly adults with poor or good sleep quality. No missing items were processed. We performed a statistical analysis of the data using SPSS Statistics 20.0. We conducted a univariate analysis using the chi-square test, and a multivariate analysis using binary logistic regression analysis. A P < 0.05 was considered statistically significant.

Results

Sample Characteristics

Among the 507 eligible participants, 253 had good sleep quality (71.6 ± 5.5 years old). This group comprised 125 females (49.9%) and 128 males (50.6%). Among them, 75 persons (29.6%) were aged < 75 years and 178 persons (70.4%) were aged > 75 years. Furthermore, 235 elderly adults (92.9%) were married/cohabiting and 18 (7.1%) were divorced/widowed/unmarried. Two hundred six (81.4%) participants had pensions and 47 (18.6%) did not. On the other hand, 254 elderly adults had poor sleep quality (71.9 ± 4.8 years old). This group included 129
females (50.8%) and 125 males (49.2%). Among them, 61 participants (24.0%) were aged < 75 years and 193 (86.0%) were aged > 75 years. Further, 194 participants (76.4%) were married/cohabiting and 60 (23.6%) were divorced/widowed/unmarried. One hundred eighty-five participants (72.8%) had pensions and 69 (27.2%) did not. The overall prevalence of depression was 21.7%; the ratios among elderly adults with good and poor sleep quality were 12.3% and 31.1%, respectively. The results of the chi-square test showed a significant difference in the depression rate between the two groups of elderly adults (P < 0.05).

Univariate analysis of factors influencing depression among the elderly living in pension institutions

The results of the univariate analysis of factors influencing depression among elderly adults living in pension institutions are reported in Table 1. Marital status, pension, economic status, chronic illness, self-care, body aches, chewing ability, ability to go out alone, regular exercise, and regular diet were significantly related to the prevalence of depression among all elderly adults (P < 0.05). For elderly adults with good sleep quality, marital status, pension, economic status, chronic illness, self-care, body aches, chewing ability, ability to go out alone, regular exercise, eating patterns, smoking, and filial piety were significantly related to depression (P < 0.05). As for elderly adults with poor sleep quality, marital status, pension, chronic illness, self-care, chewing ability, ability to go out alone, regular exercise, diet, and loneliness were related to the detection rate of depression (P < 0.05).
Table 1
Univariate analysis of the factors influencing depression among elderly adults living in pension institutions

| Factors                      | Total  | Good sleep quality | Poor sleep quality |
|------------------------------|--------|--------------------|--------------------|
|                              | n      | Depression (%)     | OR (95%CI)         | n      | Depression (%) | OR (95%CI) |
| Age                         |        |                    |                    |        |                |            |
| ≥ 75 years                  | 371    | 25.0               | 1.29 (0.8, 1.206)  | 178    | 13.3            | 1.15 (1.258) |
| 60–74 years                 | 136    | 20.5               | 1.30 (0.8, 2.011)  | 75     | 11.8            | 1.73 (0.374) |
| Sex                         |        |                    |                    |        |                |            |
| Female                      | 254    | 24.0               | 1.38 (0.9, 0.211)  | 125    | 15.2            | 1.73 (0.374) |
| Male                        | 253    | 19.0               |                    | 128    | 9.4             |            |
| Marital status              |        |                    |                    |        |                |            |
| Divorce/d/widowed/unmarried | 429    | 15.4               | 235                | 8.9     | 194             | 23.2       |
| Married/cohabiting          |        |                    |                    |        |                |            |
| Pension                     |        |                    |                    |        |                |            |
| No                          | 116    | 37.9               | 1.9 (0.4, 4.76)    | 47     | 29.8            | 4.72 (2.1, 10.48) |
| Yes                         | 391    | 16.9               |                    | 206    | 8.3             |            |
| Economic status             |        |                    |                    |        |                |            |
| Bad                         | 52     | 34.6               | 2.0 (1.1, 3.386)   | 34     | 32.4            | 4.76 (2.0, 11.17) |
| Good                        | 454    | 20.3               |                    | 219    | 9.1             |            |
| Chronic disease             |        |                    |                    |        |                |            |
| Yes                         | 283    | 35.0               | 10.42 (4.2, 11.96) | 114    | 24.6            | 14.76 (4.3, 5.79) |
| No                          | 224    | 4.9                | 139                | 2.2     | 85              | 9.4        |
| Self-care                   |        |                    |                    |        |                |            |
| No                          | 297    | 34.0               | 11.5 (5.6, 23.4)   | 134    | 20.9            | 10.21 (3.01, 34.5) |
| Yes                         | 210    | 4.3                | 119                | 2.5     | 91              | 6.6        |
| Body aches                  |        |                    |                    |        |                |            |
| Yes                         | 68     | 38.2               | 2.6 (1.5, 1.49)    | 34     | 32.4            | 4.76 (2.0, 31.17) |
| No                          | 438    | 19.2               | 219                | 9.1     | 219             | 29.2       |
| Chew ing ability            |        |                    |                    |        |                |            |
| Poor                        | 224    | 38.8               | 7.18 (4.3, 11.88)  | 100    | 21.0            | 3.80 (1.7, 18.47) |
| Good                        | 283    | 8.1                | 153                | 6.5     | 130             | 10.0       |
| Ability to go out alone     |        |                    |                    |        |                |            |
| No                          | 186    | 37.1               | 4.0 (2.5, 9.627)   | 75     | 28.0            | 6.53 (2.9, 14.73) |
| Yes                         | 321    | 12.8               | 178                | 5.6     | 143             | 21.7       |
| Regular Exercise            |        |                    |                    |        |                |            |
| No                          | 281    | 33.8               | 7.19 (4.0, 12.82)  | 105    | 24.8            | 9.41 (3.4, 25.48) |
| Yes                         | 226    | 6.6                | 148                | 3.4     | 78              | 12.8       |
| Regular diet                |        |                    |                    |        |                |            |
| No                          | 201    | 35.3               | 3.74 (2.4, 5.83)   | 71     | 19.7            | 2.38 (1.1, 15.14) |
| Yes                         | 306    | 12.7               | 182                | 9.3     | 124             | 17.7       |
| Smoking                     |        |                    |                    |        |                |            |
| Yes                         | 145    | 22.1               | 73                 | 5.5     | 182             | 28.0       |
| No                          | 362    | 21.5               | 180                | 15.0    | 72              | 38.9       |
| Filial piety                |        |                    |                    |        |                |            |
| No                          | 125    | 28.0               | 1.59 (1.0, 0.253)  | 79     | 22.8            | 3.65 (1.6, 9.79) |
| Yes                         | 382    | 19.6               | 174                | 7.5     | 208             | 29.8       |
| Loneliness                  |        |                    |                    |        |                |            |
| Yes                         | 130    | 43.1               | 5.78 (2.4, 13.91)  | 42     | 17.6            |            |
| No                          | 377    | 20.0               | 211                | 19.4    | 296             | 21.6       |

Note: OR: Odds ratio; CI: confidence interval.
adults living in pension institutions

The results of the multivariate analysis of factors influencing depression among elderly adults in pension institutions are reported in Table 2. After adjustment for age, the significant factors \((P < 0.05)\) from the univariate analysis were entered into the binary logistic model for all participants. The factors significantly influencing depression among elderly adults were ranked (in descending order of effect size) as follows: marital status, smoking, chronic illness, chewing ability, regular exercise, economic status, and child filial piety.

| Factor                        | OR    | 95% confidence interval | P     |
|-------------------------------|-------|-------------------------|-------|
| Age \(^a\)                    | 1.02  | 0.96–1.08               | 0.47  |
| Marital status (divorced/widowed/unmarried vs. married/cohabiting) | 9.07  | 2.69–30.58              | < 0.01|
| Smoking (Yes vs. No)          | 5.22  | 2.10–12.96              | < 0.01|
| Chronic disease (Yes vs. No)  | 4.46  | 2.03–9.80               | < 0.01|
| Chewing ability (Yes vs. No)  | 4.08  | 2.25–7.38               | < 0.01|
| Regular exercise (No vs. Yes) | 2.96  | 1.46–5.99               | < 0.01|
| Economic status (bad vs. good) | 2.95  | 1.33–6.53               | < 0.01|
| Sleep quality (bad vs. good)  | 2.36  | 1.29–4.31               | < 0.01|
| Filial piety (No vs. Yes)     | 2.19  | 1.16–4.12               | 0.02  |

\(^a\)Fixed in the model.

Multivariate analysis of the interaction between factors influencing depression and sleep quality among elderly adults living in pension institutions

Considering the significant difference in prevalence of depression among elderly adults with good and poor sleep quality, we wanted to examine the interaction between sleep quality and the factors influencing depression among elderly adults living in the pension institutions. As seen in Table 3, after adjustment for age, regular exercise and child filial piety significantly interacted with sleep quality to
influence depression (P < 0.05). Therefore, we went forward with analyzing the specific factors influencing depression among elderly adults according to their sleep quality (good or poor).

### Table 3
Multivariate analysis of the interaction between factors influencing depression and sleep quality among elderly adults living in pension institutions

| Factor                                      | OR    | 95% confidence interval | P    |
|---------------------------------------------|-------|-------------------------|------|
| Agea                                        | 1.02  | 0.91–1.08               | 0.52 |
| Chronic disease (Yes vs. No)                | 4.06  | 1.92–8.58               | < 0.01|
| Smoking (Yes vs. No)                        | 3.77  | 1.72–8.30               | < 0.01|
| Chewing ability (Yes vs. No)                | 3.74  | 2.07–6.73               | < 0.01|
| Sleep quality (bad vs. good) × Regular exercise (No vs. Yes) | 3.72  | 1.34–10.32             | 0.01 |
| Marital status (divorced/widowed/unmarried vs. married/cohabiting) | 2.95  | 1.59–5.45              | < 0.01|
| Sleep quality (poor vs. good) × Filial piety (No vs. Yes) | 2.52  | 1.19–5.34              | 0.02 |
| Economic status (poor vs. good)             | 2.44  | 1.10–5.45              | 0.03 |

*Fixed in the model; age was set as a continuous variable in the multivariate analysis.*

Multivariate analysis of risk factors of depression according to sleep quality among elderly adults living in pension institutions

The results of the multivariate analysis of risk factors for depression among elderly adults with different sleep quality living in pension institutions are reported in Table 4. After adjusting for age as a fixed factor in the model, the logistic regression analysis revealed that the factors influencing depression among elderly adults with good sleep quality were ranked (in descending order of effect size) as follows: marital status, chronic disease, regular exercise, body aches, child filial piety, and chewing ability (P < 0.05). By contrast, the factors influencing depression among elderly adults with poor sleep quality were ranked as follows: loneliness, regular diet, chewing ability, and chronic disease (P < 0.05; Table 4).
Table 4
Multivariate analysis of factors influencing depression among elderly adults with different sleep quality living in pension institutions

| Factor                                      | OR   | 95% confidence interval | P     |
|---------------------------------------------|------|-------------------------|-------|
| Good sleep quality (n = 253)                |      |                         |       |
| Agea                                        |      |                         |       |
| Marital status (divorced/widowed/un married vs. married/cohabiting) | 6.91  | 1.79-26.79              | <0.01 |
| Chronic disease (Yes vs. No)                | 6.66  | 1.64-26.96              | <0.01 |
| Regular exercise (No vs. Yes)               | 5.11  | 1.56-16.67              | <0.01 |
| Body aches (Yes vs. No)                     | 4.10  | 1.30-12.97              | 0.02  |
| Filial piety (No vs. Yes)                   | 3.79  | 1.34-10.73              | 0.01  |
| Chewing ability (Yes vs. No)                | 2.74  | 1.00-7.51               | 0.05  |
| Poor sleep quality (n = 254)                |      |                         |       |
| Agea                                        | 0.96  | 0.89-1.04               | 0.32  |
| Loneliness (Yes vs. No)                     | 8.77  | 2.37-32.54              | <0.01 |
| Self-care (No vs. Yes)                      | 7.00  | 2.25-21.75              | <0.01 |
| Chewing ability (Yes vs. No)                | 5.31  | 2.47-11.40              | <0.01 |
| Chronic disease (Yes vs. No)                | 4.40  | 1.64-11.83              | <0.01 |

*Fixed in the model; age is set as a continuous variable in the multivariate analysis.*

Discussion

This study conducted a cognitive function screening for elderly adults living in pension institutions, and adopted the highly valid and reliable GDS as the main assessment tool for evaluating depression and its influencing factors among elderly adults without cognitive dysfunction. The findings of this study can be characterized as a good representation of the population (and thus bearing high information reliability). The conclusions drawn also have strong generalizability. The results of this study showed that the depression rate among elderly adults without cognitive dysfunction living in pension institutions in Northeastern China was 21.7%, which is much lower than that in Beijing 13 (n = 107, 32.71%) and Guangdong Province 14 (n = 379, 38.5%). The depression rate among elderly adults with poor sleep quality was 31.1%, which was significantly higher than that among elderly adults with good
sleep quality (12.3%). The results were similar to those pertaining to elderly adults living in pension institutions in Beijing\textsuperscript{13}.

Elderly adults showed significant differences in depression, marital status, economic status, chronic disease, self-care, chewing ability, ability to go out alone, regular exercise, regular diet, filial piety, and loneliness according to sleep quality. Similarly, Dai and Li et al. \textsuperscript{5,13} found a significant negative correlation between sleep quality and depression. Poor sleep quality in elderly adults can trigger feelings of irritability, listlessness, fatigue, weakness, and even deepen their negative experiences of the aging process, thereby leading to the emergence of depression. Moreover, the interactions between sleep quality and other factors influencing depression had significant effects on elderly depression. These findings further indicated that the factors influencing depression in elderly adults differ according to sleep quality. Therefore, the risk factors of depression in elderly adults with good and poor sleep quality were analyzed separately, enabling us to propose specific recommendations to reduce the incidence of depression among elderly adults and thereby improve their quality of life.

Marital status is an important risk factor for depression among elderly adults with good sleep quality. Spousal support and care can reduce the incidence of depression: indeed, the incidence of depression in widowed elderly adults was significantly higher than that among married elderly adults\textsuperscript{15}. Divorced elderly adults or those in poor marriages are also more likely to suffer from mental health problems and increased depression\textsuperscript{16}. The elderly population is a high-risk group in terms of the incidence of various chronic diseases, which harm the physical and mental health of elderly adults and impact their normal lives and social
communication, thus triggering depression\textsuperscript{17}. Regular exercise can strengthen the body and increase the opportunity to communicate with others while exercising, thereby sustaining feelings of pleasure among elderly adults\textsuperscript{18}. Appropriate exercise can also promote elderly adults’ sleep quality. Therefore, elderly adults living in pension institutions should be encouraged to exercise more. In this study, elderly adults who often experienced body aches had a higher risk of depression. Body aches are likely to increase discomfort among elderly adults, which in turn can affect their daily activities and increase their negative emotions. Furthermore, children’s filial piety can increase feelings of comfort and warmth among elderly adults, which can greatly reduce the occurrence of depression\textsuperscript{19}. Therefore, elderly adults in pension institutions would require more attention from their children. In addition, chewing ability was found to have an impact on depression among participants. Good chewing ability can ensure adequate intake of nutrition, thus ensuring that elderly adults can enjoy good health and a pleasant mood. For elderly adults with poor sleep quality, loneliness is an important risk factor of depression. Insomnia can increase elderly adults’ sense of loneliness, which is likely to cause depression\textsuperscript{13}. As for self-care, researchers have found that self-care ability can sufficiently reflect elderly adults’ basic degree of self-care as well as their general health status. Additionally, one study\textsuperscript{20} showed that depression and self-care ability have a mutual causal relationship, such that a decline in self-care ability will lead to the aggravation of depression. Similarly, chewing ability and chronic diseases also have an impact on depression among elderly adults with poor sleep quality. Therefore, we should pay close attention to the chewing ability and physical health of elderly adults. Pension institutions should make soft food
available to elderly adults (depending on their chewing ability. These institutions should also conduct regular physical examinations of elderly adults, supervise the rational and timely use of drugs among elderly adults with chronic diseases, and formulate measures to reduce disease-related psychological burdens for elderly adults, thereby reducing the incidence of depression among elderly adults living in pension institutions.

There were some limitations in our study. First, measures for some of the factors, such as smoking and chewing ability, were simplistic and broad, and therefore could have weakened our assessments of their effects. Second, although the present study was a population-based study on depression among elderly adults with different sleep quality in pension institutions in Northeastern China, it was limited by its cross-sectional design. Therefore, all conclusions drawn from this study should be confirmed in a future prospective study.

In conclusion, this study is the first to assess depression among elderly adults with different sleep quality in pension institutions in Northeastern China and to clarify its associated factors. Our results revealed that the prevalence of depression differed among elderly adults according to their sleep quality. Marital status, chronic disease, regular exercise, body aches, filial piety, and chewing ability had considerable effects on depression among elderly adults with good sleep quality. By contrast, loneliness, self-care, chewing ability, and chronic disease had considerable effects on depression among elderly adults with poor sleep quality. Our findings suggest that there should be a focus on the maintenance of health status and psychological factors to reduce the incidence of depression among elderly adults in pension institutions.
Abbreviations

PSQI: Sleep Quality Index; GDS: Geriatric Depression Scale; MMSE: Mini-Mental State Examination.

Declarations

Ethics approval and consent to participate

We strictly followed the ethical principles.

Consent for publish

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Competing interests

The authors declare they have no competing interests.

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Authors’ contributions

JZ and APW designed the research protocol, performed and analyzed the research. JZ, YYZ and HRJ performed the search. Where questions arose, YYZ, ZGL and XJZ advised. JZ and APW designed the Tables. JZ wrote the manuscript. JZ, APW, YYZ, ZGL, XJZ and HRJ read and revised the manuscript. All authors read and approved
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Declarations

Ethics approval and consent to participate

We strictly followed the ethical principles.

Consent for publish

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Competing interests

The authors declare they have no competing interests.

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Authors’ contributions

JZ and APW designed the research protocol, performed and analyzed the research. JZ, YYZ and HRJ performed the search. Where questions arose, YYZ, ZGL and XJZ advised. JZ and APW designed the Tables. JZ wrote the manuscript. JZ, APW, YYZ, ZGL, XJZ and HRJ read and revised the manuscript. All authors read and approved the final manuscript.

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