Research Paper

Distress management in cancer patients: Guideline adaption based on CAN-IMPLEMENT

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ABSTRACT

Objective: This study aimed to adapt relevant clinical practice guidelines for distress management in cancer patients based on A Guideline Adaptation and Implementation Planning Resource (CAN-IMPLEMENT), and develop Cancer-related Distress Management Guidelines in the context of the research site.

Methods: According to CAN-IMPLEMENT, the symptoms of cancer patients in Shanghai were investigated, and a work plan was formulated to adapt cancer-related distress management guidelines. The relevant clinical practice guidelines for distress management in cancer patients were searched, screened and assessed, the contents of the included clinical practice guidelines were screened, extracted and integrated, and the Cancer-related Distress Management Guidelines was developed. After peer review, the Cancer-related Distress Management Guidelines was finally formed.

Results: The physical symptom distress score was higher than the psychological symptom distress score among cancer patients in Shanghai. Two clinical practice guidelines related to distress management in cancer patients were included after searching, screening, assessment and selection systematically. The domain scores of the draft Cancer-related Distress Management Guidelines on Appraisal of Guidelines for Research and Evaluation II (AGREE II) were 73.75%–87.50%, respectively. The scores of most recommendations on feasibility, appropriateness, meaningfulness and effectiveness were at least 90%. The final guidelines included 13 recommendations.

Conclusions: The quality of the draft Cancer-related Distress Management Guidelines based on two included guidelines was well-accepted. The final Cancer-related Distress Management Guidelines needs to be further verified in clinical practice for feasibility, suitability and effectiveness.

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What is known?

- Almost all cancer patients experience some level of distress, significantly reducing their quality of life.
- Clinical practice guidelines are essential evidence-based resources for performing evidence-based practice. However, most clinical practice guidelines cannot be directly applied to clinical practice, with possible reasons including unclear recommendations, inapplicable recommendations, and imperfect evaluation recording tools.

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A Guideline Adaptation and Implementation Planning Resource (CAN-IMPLEMENT) was developed by Harrison, M.B. and van den Hoek, J. for the Canadian Guideline Adaptation Study Group of the Canadian Partnership Against Cancer (the ‘Partnership’) based on the ADAPTE methodology using a mixed-methods, case-study design.

What is new?

- The symptom burden of cancer patients in Shanghai was high. The physical symptom distress score was higher than the psychological symptom distress score. Even so, psychological symptoms and physical symptoms were both worthy of attention.
- Guided by the CAN-IMPLEMENT, the Cancer-related Distress Management Guidelines was formed, including 13 recommendations. The guideline adaptation was proved feasible in the hospital in China.

1. Introduction

With the progress of cancer treatment, the survival time of cancer patients is prolonged [1,2]. The prolongation of survival time places higher demands on existing health care services, with a view to better improving the quality of life (QoL) in cancer patients. It is well known that cancer patients always have a series of physiological symptoms and/or psychological symptoms due to the disease and/or related treatment, such as distress, sleep disturbance, fatigue, lack of appetite and so on [3–5]. A literature review revealed that the symptom burden of cancer patients has a great negative impact on the patients’ QoL [6–8]. At the beginning of the study, the current results were inconsistent on frequency, severity, distress of physical and psychological symptoms in different studies [3,4,9].

In view of the large scope of symptom management for cancer patients, it was not easy to determine the research topic. As a result, a cross-sectional survey was conducted to clarify the status of symptom burden among cancer patients in the research site [10]. The Memorial Symptom Assessment Scale Short Form (MSAS-SF) was chosen as the instrument in the investigation because its items are comprehensive (covering both physical and psychological symptoms) and convenient (only the distress or frequency of symptoms is evaluated), which is easy for cancer patients to fill in [10,11]. Finally, distress was identified as the research theme based on the investigation, literature review and professional judgment. It is reported that the positive rate and severity of distress were both high in cancer patients [12,13], which significantly reduced their QoL [14]. Distress management can clarify the patient’s distress status, understand their experience of distress, and effectively alleviate their distress through relevant management strategies [12,15,16]. Thus, it is necessary to carry out distress management in cancer patients under the guidance of appropriate theories, models, frameworks, methods and so on.

Nowadays, there is increasing understanding and implementation of evidence-based practice in various fields of health care, and it has played an important role in regulating clinical practice, improving patient outcomes, optimizing resource allocation and so on. To date, many evidence-based practice models, frameworks and methods have been launched by different organizations worldwide. For example, the JBI Model of Evidence-based Healthcare developed by the Joanna Briggs Institute [17,18], the Ottawa Model of Research Use reported by Logan and Graham [19], the Promoting Action on Research Implementation in Health Service Framework published by Kitson et al. [20–22], the Knowledge-to-Action Framework by Graham et al. [23], and A Guideline Adaptation and Implementation Planning Resource (CAN-IMPLEMENT) presented by Harrison and her colleagues [24,25].

Different models, frameworks and methods are suitable for different situations, and healthcare professionals can choose the appropriate model, framework or method according to the actual situation. CAN-IMPLEMENT is guided by the Knowledge-to-Action Framework, which also includes two parts of knowledge creation and action cycle. The action cycle part is divided into three stages: identification and clarification of the practice issue, solution building and implementation, evaluation and sustainability [24], aiming to facilitate the translation of existing guidelines into clinical practice by adaptation, alignment, application and evaluation. Therefore, CAN-IMPLEMENT is different from other evidence-based practice models, frameworks, and methods, emphasizing the primary evidence resource of clinical practice guidelines (including systematic reviews) rather than all types of complex evidence resources. This helps to simplify the process of evidence synthesis, and facilitates clinical practitioners to master the method, thereby promoting the clinical translation of guidelines more conveniently and quickly.

We carried out guideline adaptation and implementation for distress management in cancer patients based on CAN-IMPLEMENT and guided by the Knowledge-to-Action Framework. The total study consisted of three phases: 1) integrating relevant clinical practice guidelines on the distress management in cancer patients to form the Cancer-related Distress Management Guidelines (identification and clarification of the practice issue); 2) aligning the Cancer-related Distress Management Guidelines into clinical practice among gastric cancer patients receiving chemotherapy (solution building); 3) monitoring, evaluating and maintaining the implementation of the Cancer-related Distress Management Guidelines in clinical practice (implementation, evaluation and sustainability). The adaptation process (Phase 1 of the entire study) is reported in this paper. The Adaptation Part was to clarify the theme of guideline adaptation, integrate relevant clinical practice guidelines on distress management in cancer patients, and develop the Cancer-related Distress Management Guidelines. The specific objectives of the present study were as follows: 1) To investigate the status of related symptoms in cancer patients; 2) To search and screen existing relevant clinical practice guidelines on distress management in cancer patients systematically and comprehensively; 3) To assess and select relevant clinical practice guidelines on distress management in cancer patients rigidly and normatively; 4) To draft the Cancer-related Distress Management Guidelines by selecting, extracting and integrating the included clinical practice guidelines on distress management in cancer patients; 5) To revise and endorse the final Cancer-related Distress Management Guidelines by peer review.

2. Methods

Ethics approval for this study was obtained from School of Nursing Fudan University (IRB#2017-9-3) and Fudan University Shanghai Cancer Centre (1710177-23). From May 2017 to June 2019, the study ‘Guideline Adaptation and Implementation for Distress Management in Cancer Patients’ was conducted in School of Nursing, Fudan University and three medical oncology units of Fudan University Shanghai Cancer Center, China. The main contents of the above study were translating relevant guidelines on distress management into clinical practice, which was based on CAN-IMPLEMENT and guided by the Knowledge-to-Action Framework. The translation and application of CAN-IMPLEMENT in China were authorized by the principal investigator of CAN-IMPLEMENT.
According to CAN-IMPLEMENT, Phase 1 Identification and clarification of the practice issue: guideline adaptation Consists of Steps 1 to 5.

2.1. Step 1: Call to action

To clarify the theme of this guideline adaptation, a cross-sectional study was carried out to investigate patients’ symptoms from September 25, 2017 to December 28, 2017. The Simplified Chinese Version of the Memorial Symptom Assessment Scale Short Form (MSAS-SF-SC) was distributed to 384 adult cancer patients in three medical oncology units of Fudan University Shanghai Cancer Center.

2.2. Step 2: Guideline development plan

The health problem of this guideline adaptation was articulated based on PIPOH (P-Population, I-Intervention, P-Professional/Patients, O-Outcomes, H-Health Care Setting). The feasibility was confirmed through a preliminary search for existing guidelines on distress management. A multidisciplinary panel of guidelines adaptation was set up to manage this guideline adaptation. The consensus process and the work plan were determined by the guideline adaptation panel using the expert meeting method.

2.3. Step 3: Search and screen

Three researchers (a professor skilled with evidence-based practice methodologies, a doctoral candidate and a postgraduate student of nursing science) searched and screened all guidelines including distress management for cancer patients using the literature search method, which was published on guidelines website, professional website and medical database from April 1, 2013 to March 31, 2018. Additional references were identified through an examination of the references from included guidelines. Only references in Chinese and English were searched. Two researchers were invited to screen and record the references. For disputed references, the consensus among researchers was required or a third researcher was invited to identify.

2.4. Step 4: Assess and select

Four appraisers (a doctoral candidate and three postgraduate students of nursing science) evaluated guidelines using the literature evaluation method with Appraisal of Guidelines for Research and Evaluation II (AGREE II). A professor and an associate professor skilled with evidence-based practice methodologies were involved if there were disagreements among the four appraisers. The included guidelines were selected by the guideline adaptation panel. Only de novo clinical practice guidelines were included in this guideline adaptation.

2.5. Step 5: Draft, revise and endorse

The draft of adapted guidelines was written based on the guideline adaptation method by the guideline adaptation panel. The fundamental principles of this guideline adaptation were as follow: 1) the recommendations in different guidelines are consistent, then the original recommendations are accepted. 2) the recommendations in different guidelines are not consistent, or the recommendations are not clear, then certain original recommendations are accepted or new adapted recommendations are formed by comparing and analyzing the original guidelines’ evidence descriptions, evidence sources, quality of evidence, strength of recommendation and so on, combined with professional judgments.

Ten stakeholder representatives (an associate professor skilled with evidence-based practice methodologies, a chief physician of psychological medicine, a chief physician of palliative care, a chief physician of clinical epidemiology, a professor and a supervisor nurse of oncology nursing, an associate physician of oncology, an associate professor of psychological care, a social worker, a breast cancer patient and her husband) were invited to review the draft adapted guidelines on June 11, 2018. The on-site expert review method was adopted with AGREE II and self-designed recommendations review form (Based on The JBI Model of Evidence-based Healthcare) [17,18] (Appendix A). The final guidelines were revised and formed by the guideline adaptation panel, and a renewal plan was established.

3. Results

Results of Phase 1 Identify issue/problem: guideline adaptation including Steps 1 to 5 were reported accordingly.

3.1. Step 1: Call to action

Totally 359 (93.5%) of 384 patients provided full informed consent and completed the MSAS-SF-SC. The top ten symptoms of cancer patients were lack of energy (53.8%, 193/359), dry mouth (44.0%, 158/359), numbness/tingling in hands and feet (39.3%, 141/359), feeling irritable (38.2%, 137/359), hair loss (36.5%, 131/359), pain (35.7%, 128/359), worrying (35.1%, 126/359), difficulty sleeping (34.0%, 122/359), lack of appetite (33.4%, 120/359), and feeling sad (31.2%, 112/359). The distress score of physical symptom 0.47 (0.13, 0.87) was higher than the distress score of psychological symptom 0.33 (0.00, 0.87).

3.2. Step 2: Guideline development plan

The health problem was P (cancer patients), I (screening, assessment, care, referral and treatment), P (professionals and patients), O (professionals and patients) O-H (tumor hospital, oncology department and so on). Several related guidelines were found in the preliminary search, such as the Distress Management Guidelines of National Comprehensive Cancer Network (NCCN) [13]. The guideline adaptation panel consisted of a professor and two associate professors skilled with evidence-based practice methodologies, a chief physician and an associate chief physician of oncology, a professor, two associate professors, four supervisor nurses and a nurse practitioner of oncology nursing, an associate physician of palliative care, an attending doctor of psychological medicine, a social worker, a doctoral candidate and a postgraduate student of nursing science. The determined consensus methods were consensus conference and voting.

A work plan for adapting the Cancer-related Distress Management Guidelines was written, including background, the health problem, the multidisciplinary panel, consensus methods, evidence sources, methodology for reporting clinical practice guidelines, methods of guideline adaptation, conflicts of interest statement and so on.

3.3. Step 3: Search and screen guidelines

The search initially retrieved 1,864 references from guidelines websites \( n = 105 \), professional agency websites \( n = 145 \) and medical databases \( n = 1,614 \) (Appendix B). Other eight references were identified by tracing the references of including references. After excluding 725 duplicates, 1,147 were screened by title and abstract. Following title and abstract screening, 138 references continued on to full-text screening. Finally, two clinical practice
guidelines related to distress management in cancer patients were found after searching and screening (Fig. 1). The two obtained guidelines were Distress Management [13] and Chinese Psychosocial Oncology Therapy Guidelines for Cancer Patients [26] (Table 1).

3.4. Step 4: Assess and select guidelines

Distress Management was developed by Jimmie C. Holland’s team and published by NCCN on February 23, 2018. Another obtained guidelines were Chinese Psychosocial Oncology Therapy Guidelines for Cancer Patients, developed by Lili Tang et al. and published by China Anti-Cancer Association on June 18, 2016. The scores of each AGREE II domain were 54.17%–81.94% and 44.27%–88.89%, respectively. The overall quality scores of the two obtained guidelines were 3–6 (Table 2). The guideline adaptation panel decided to include the two guidelines based on the assessment results with consensus.

| Guidelines | Organization | Author | Release time | Country |
|------------|--------------|--------|--------------|---------|
| Distress Management | National Comprehensive Cancer Network | Jimmie C. Hollan... | February 2018 | America |
| Chinese Psychosocial Oncology Therapy Guidelines for Cancer Patients | Cancer Psycho-social Oncology Society of China Anti-Cancer Association | Lili Tang et al. | June 2016 | China |

Table 2
Assessment of the included guidelines based on AGREE II.

| Guidelines | Scope and Purpose | Stakeholder Involvement | Rigour of Development | Clarity and Presentation | Applicability | Editorial Independence | Overall Quality | Recommendations |
|------------|-------------------|-------------------------|-----------------------|-------------------------|--------------|-----------------------|----------------|-----------------|
| A          | 81.94%            | 75.00%                  | 56.25%                | 54.17%                  | 59.38%       | 70.83%                | 6, 3, 4, 6     | 1               |
| B          | 88.89%            | 59.72%                  | 44.27%                | 86.11%                  | 53.13%       | 87.50%                | 6, 5, 6, 4     | 3               |

Note: A – Distress Management. B – Chinese Psychosocial Oncology Therapy Guidelines for Cancer Patients. Y – Yes. YM – Yes, with modifications. N – No.
The scores on feasibility, appropriateness, meaningfulness and effectiveness of recommendations in the adapted guidelines were the same with the draft guidelines, and minor revisions were made based on the recommendations from stakeholder representatives. Firstly, Chinese characters “心理痛苦” (xīnlǐ tòngkǔ) was adopted as the formal translation for “distress,” distinguished from “心理困扰” (xīnlǐ kūnrǎo), “心理逆境” (xīnlǐ nìjìng) and so on. Secondly, one recommendation in the draft version was excluded, namely “According to the results of further clinical evaluations, it is recommended to refer patients to mental health professionals, social workers, chaplains, medical staff for further diagnosis and treatment”. Therefore, only 13 recommendations were included in the final version. In addition, it is recommended to replaced “chaplaincy and spiritual care” by “life meaning support.” The Cancer-related Distress Management Guidelines will be updated in five years using the same methods presented in this paper.

### 4. Discussion

The symptom burden of cancer patients in Shanghai was high [10]. The physical symptom distress score was higher than the psychological symptom distress score. Even so, psychological symptoms and physical symptoms were both noteworthy. Distress is a multifactorial unpleasant experience of a psychological (i.e., cognitive, behavioral, emotional), social, spiritual, and/or physical nature [13], which includes both physical and psychological symptoms, and coincides with the results of this study. Meanwhile, the definition of distress is clear, and mature scales for measuring are available [13]. Finally, distress was identified as the theme of this guideline adaptation.

The multidisciplinary panel wrote the work plan of guideline adaptation to guide the practice of this guideline adaptation. In order to retrieve the clinical practice guidelines related to distress management of cancer patients as comprehensively as possible, the

### Table 3
The recommendations in the draft Cancer-related Distress Management Guidelines.

| Number | Recommendations                                                                                     | Feasibility | Appropriateness | Meaningfulness | Effectiveness |
|--------|------------------------------------------------------------------------------------------------------|-------------|-----------------|---------------|--------------|
| 1      | All patients should be assessed prior to clinical visits using the Distress Thermometer, and immediate screenings should be provided during the vulnerable period. | 100         | 100             | 97            | 100          |
| 2      | If the patient’s distress is mild (thermometer score <4), the primary oncology team should assess the possible distress related symptoms of the patient. | 100         | 90              | 97            | 100          |
| 3      | According to the assessment results of possible distress-related symptoms, the primary oncology team manages the symptoms associated with the patient’s distress. | 100         | 100             | 97            | 100          |
| 4      | After the primary oncology team manages the symptoms associated with the patient’s distress, the Distress Thermometer is used again for follow-up screening. | 100         | 90              | 97            | 100          |
| 5      | If the patient’s distress is moderate or severe (thermometer score ≥4), the oncology team should provide further clinical evaluations, including clinical interviews, anxiety/depression assessment, etc. | 100         | 90              | 97            | 100          |
| 6      | According to the results of further clinical evaluations, it is recommended to refer patients to mental health professionals, social workers, chaplains, medical staff for further diagnosis and treatment. | 100         | 90              | 97            | 100          |
| 7      | Mental health professionals provide psychoeducation for patients in need. | 100         | 90              | 97            | 100          |
| 8      | Mental health professionals provide cognitive behavioral therapy for patients in need. | 100         | 90              | 97            | 100          |
| 9      | Mental health professionals provide supportive psychotherapy for patients in need. | 100         | 90              | 97            | 100          |
| 10     | Mental health professionals provide family and couples therapy for patients in need. | 100         | 90              | 97            | 100          |
| 11     | Social workers provide support and counseling to patients in need. | 100         | 90              | 97            | 100          |
| 12     | Chaplains provide spiritual and chaplaincy care for patients in need. | 100         | 90              | 97            | 100          |
| 13     | Medical staff provide palliative care for patients in need. | 100         | 90              | 97            | 100          |
| 14     | Patients who were referred or not referred to mental health professionals, social workers, chaplains, medical staff were further screened using the Distress Thermometer. | 100         | 90              | 97            | 100          |

### Table 4
The scores on feasibility, appropriateness, meaningfulness and effectiveness of recommendations in the adapted guidelines (n = 10).

- **Number 1**: All patients should be assessed prior to clinical visits using the Distress Thermometer, and immediate screenings should be provided during the vulnerable period.
- **Number 2**: If the patient’s distress is mild (thermometer score <4), the primary oncology team should assess the possible distress related symptoms of the patient.
- **Number 3**: According to the assessment results of possible distress-related symptoms, the primary oncology team manages the symptoms associated with the patient’s distress.
- **Number 4**: After the primary oncology team manages the symptoms associated with the patient’s distress, the Distress Thermometer is used again for follow-up screening.
- **Number 5**: If the patient’s distress is moderate or severe (thermometer score ≥4), the oncology team should provide further clinical evaluations, including clinical interviews, anxiety/depression assessment, etc.
- **Number 6**: According to the results of further clinical evaluations, it is recommended to refer patients to mental health professionals, social workers, chaplains, medical staff for further diagnosis and treatment.
- **Number 7**: Mental health professionals provide psychoeducation for patients in need.
- **Number 8**: Mental health professionals provide cognitive behavioral therapy for patients in need.
- **Number 9**: Mental health professionals provide supportive psychotherapy for patients in need.
- **Number 10**: Mental health professionals provide family and couples therapy for patients in need.
- **Number 11**: Social workers provide support and counseling to patients in need.
- **Number 12**: Chaplains provide spiritual and chaplaincy care for patients in need.
- **Number 13**: Medical staff provide palliative care for patients in need.
- **Number 14**: Patients who were referred or not referred to mental health professionals, social workers, chaplains, medical staff were further screened using the Distress Thermometer.

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The symptom burden of cancer patients in Shanghai was high [10]. The physical symptom distress score was higher than the psychological symptom distress score. Even so, psychological symptoms and physical symptoms were both noteworthy. Distress is a multifactorial unpleasant experience of a psychological (i.e., cognitive, behavioral, emotional), social, spiritual, and/or physical nature [13], which includes both physical and psychological symptoms, and coincides with the results of this study. Meanwhile, the definition of distress is clear, and mature scales for measuring are available [13]. Finally, distress was identified as the theme of this guideline adaptation.

The multidisciplinary panel wrote the work plan of guideline adaptation to guide the practice of this guideline adaptation. In order to retrieve the clinical practice guidelines related to distress management of cancer patients as comprehensively as possible, the
search of related websites and professional institutions was added to the common databases of evidence-based medicine. Distress Management and Chinese Psychosocial Oncology Therapy Guidelines for Cancer Patients were included after searching, screening, assessment and selection, providing the best evidence sources for the guideline adaptation. Several clinical practice guidelines were excluded because they were not de novo clinical practice guidelines. AGREE II was used to assess the included guidelines’ quality in this guideline adaptation. The guidelines’ currency was assessed by the publication date. The content was assessed in the screening. The acceptability and applicability of recommendations were assessed in the next step because the clinical context in the guideline implementation site should be taken into consideration.

Generally, most clinical practice guidelines cannot be directly applied to clinical practice. Possible reasons include unclear recommendations, inapplicable recommendations, and imperfect evaluation recording tools. There are no clear recommendations in the Distress Management of the NCCN. Therefore, the guideline adaptation team must first form corresponding recommendations based on the evidence description. Although the Chinese Psychosocial Oncology Therapy Guidelines for Cancer Patients has clear recommendations, their recommendations mainly focus on medical treatment, different from the research questions of this guideline adaptation. The recommendations in the adapted guidelines involved the screening, assessment, care, referral and treatment of distress. At the same time, the first draft of the Cancer-related Distress Management Guidelines was sent to the members of the guideline adaptation panel. Next, the guideline adaptation panel members reviewed the first draft and gave specific suggestions for revision independently. Then, all revision suggestions were summarized, discussed and analyzed by the panel. Afterwards, corresponding revisions were made to the first draft of the adapted guidelines according to the specific suggestions for the revisions. The quality of the draft Cancer-related Distress Management Guidelines was high, and the feasibility, appropriateness, meaningfulness and effectiveness of most recommendations included were good. The guideline adaptation panel discussed and analyzed the recommendations proposed by the stakeholders one by one, revised the first draft guidelines, and formed the final version of the Cancer-related Distress Management Guidelines.

5. Strength and limitations

The main strength of this study was that the framework CAN-IMPLEMENT was strictly followed to carry out the guideline adaptation. Meanwhile, the study was conducted by a multidisciplinary team to ensure professionalism in clinical practice, evidence-based methodology and leadership. This study has the following limitations. Firstly, researchers only searched guidelines in English and Chinese. Some guidelines with high quality in other languages may not be included. Secondly, the adapted guidelines were only endorsed by multidisciplinary experts in related fields. Further endorsement from formal professional bodies may be necessary to promote the application of adapted guidelines in other contexts.

6. Conclusions

The symptom burden of cancer patients in Shanghai was high, and the physical symptom distress score was higher than the psychological symptom distress score. Both psychological symptoms and physical symptoms were worthy of attention. Based on CAN-IMPLEMENT and guided by the Knowledge-to-Action Framework, the adapted Cancer-related Distress Management Guidelines was formed and could be taken as a reference to carry out distress management of cancer patients in health care settings in China.

Declaration of competing interest

The authors declared that they have no conflicts of interest to this work.

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CRediT authorship contribution statement

Liang Fu: Conceptualization, Methodology, Investigation, Formal analysis, Writing - original draft. Yang Yang: Methodology, Investigation, Resources, Writing - review & editing. Yan Hu: Conceptualization, Methodology, Supervision, Writing - review & editing. Zhenqi Lu: Methodology, Supervision, Writing - review & editing. Xiaoju Zhang: Methodology, Resources, Writing - review & editing. Mingzhu Huang: Methodology, Resources, Writing - review & editing. Yuanyuan Li: Methodology, Resources, Writing - review & editing. FuZhong Zhu: Methodology, Resources, Writing - review & editing. Yang Wang: Methodology, Investigation, Resources, Writing - review & editing. Zhe Huang: Methodology, Resources, Writing - review & editing.

Data availability statement

The datasets used and analyzed during the current study are available from the corresponding authors on reasonable request.

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Appendices. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jnns.2021.12.005.

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