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Postprint of a Systematic Review of Guidelines and Expert Consensuses on Pain Management in Endometriosis

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Abstract

Background: With the deepening understanding of pain management for endometriosis, relevant domestic and international guidelines/expert consensuses have gradually increased, providing important guidance and reference for clinical practice, but their quality is uneven, requiring systematic evaluation to guide clinical practice.

Objective: To systematically evaluate the quality of guidelines/expert consensuses related to endometriosis pain management, providing a basis for formulating pain management protocols.

Methods: Computerized searches were conducted in CNKI, CBM, Wanfang Data, VIP, PubMed, Embase, Cochrane Library, Web of Science, CINAHL, Guideline Central, GIN database, and official websites of ACOG, NICE, SIGN, WHO, IASP, APS, BPS, and other sources, from database inception to November 12, 2024. The Appraisal of Guidelines for Research and Evaluation II (AGREE II) was used to evaluate the quality of guidelines/expert consensuses related to endometriosis pain management, and relevant recommendations were summarized.

Results: A total of 15 guidelines/expert consensuses were included, of which 9 were guidelines and 6 were expert consensuses; 7 were from China and 8 from abroad; published between 2018 and 2024. In the 6 domains of AGREE II, the mean scores of the 15 guidelines/expert consensuses were: scope and purpose 83.15%, stakeholder involvement 71.11%, rigor of development 44.79%, clarity of presentation 65.74%, applicability 35.55%, and editorial independence 87.78%. Among the included 15 guidelines/expert consensuses, 1 had Grade A recommendation and 14 had Grade B recommendations. A total of 33 recommendations related to endometriosis pain management were extracted from the

15 guidelines/expert consensus, involving 6 aspects: general principles of pain management, pain assessment, pharmacological management, surgical management, non-pharmacological/non-surgical management, and health education.

Conclusion: The quality of the included guidelines/expert consensus is at a medium level, providing reference basis for clinical practice, but still needs further improvement in the domains of rigor and applicability.

Full Text

A Systematic Review of Guidelines and Expert Consensus Related to Endometriosis Pain Management

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Abstract

Background: As understanding of endometriosis pain management deepens, an increasing number of related domestic and international guidelines and expert consensus have emerged, providing important guidance and reference for clinical practice. However, the quality of these guidelines and consensus is inconsistent, necessitating a systematic review to guide clinical practice. **Objective:** To systematically evaluate the quality of guidelines and expert consensus related to pain management in endometriosis, thereby providing an evidence base for the development of pain management protocols. **Methods:** Computerized searches were conducted in CNKI, SinoMed, Wanfang Data, VIP, PubMed, Embase, Cochrane Library, Web of Science, CINAHL, Guideline Central, the Guidelines International Network (GIN) database, and official websites of the American College of Obstetricians and Gynecologists (ACOG), National Institute for Health and Care Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN), WHO, International Association for the Study of Pain (IASP), American Pain Society (APS), and British Pain Society (BPS), supplemented by manual searches of reference lists. The search period was from database inception to November 12, 2024. The Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument was used to assess the quality of guidelines and expert consensus related to endometriosis pain management, and relevant recommendations were summarized. **Results:** A total of 15 guidelines/expert consensus were ultimately included, of which 9 were guidelines and 6 were expert consensus; 7 were from China and 8 from abroad; publication dates ranged from 2018 to 2024. Among the 6 domains of AGREE II, the mean scores of the 15 guidelines/expert consensus were as follows: scope and

purpose 83.15%, stakeholder involvement 71.11%, rigor of development 44.79%, clarity of presentation 65.74%, applicability 35.55%, and editorial independence 87.78%. Among the 15 included guidelines/expert consensus, 1 received an A-level recommendation and 14 received B-level recommendations. A total of 33 recommendations related to endometriosis pain management were extracted from the 15 guidelines/expert consensus, covering 6 domains: general principles of pain management, pain assessment, medication management, surgical management, non-pharmacologic/surgical management, and health education. **Conclusion:** The quality of the included guidelines/expert consensus is at a moderate level and provides a reference point for clinical practice, but further improvement is needed in the areas of rigor of development and applicability.

Keywords: Endometriosis; Pain; Management; Guideline; Expert consensus; Quality appraisal

1. Methods

1.1 Literature Sources Computerized searches were conducted in databases and guideline websites: CNKI, SinoMed, Wanfang Data, VIP, PubMed, Embase, Cochrane Library, Web of Science, CINAHL, Guideline Central, the Guidelines International Network (GIN) database, and official websites of ACOG, NICE, SIGN, WHO, IASP, APS, and BPS, supplemented by manual searches of reference lists. The search period was from database inception to November 12, 2024.

1.2 Literature Search Strategy Based on database characteristics, a combination of subject headings and free-text terms was used. Chinese search terms included “endometriosis,” “endometrioma,” “pain,” “dyspareunia,” “pelvic pain,” “dysmenorrhea,” “abdominal pain,” “defecation pain,” “anal heaviness,” “pain hypersensitivity,” “central pain,” “guidelines,” “statements,” “recommendations,” “expert opinions,” and “consensus.” English search terms included “endometriosis,” “Endometrioses,” “Endometrioma,” “Endometriomas,” “Pains,” “Suffering, Physical,” “Physical Suffering,” “Physical Sufferings,” “Sufferings, Physical,” “Ache,” “Aches,” “painful intercourse,” “dysmenorrhea,” “menstrual cramps,” “Dysmenorrhea,” “Painful Menstruation,” “painful bowel movements,” “Pain Management,” “Management, Pain,” and “Managements, Pain.” Taking Wanfang Data as an example, the search strategy was: Subject: (“endometriosis” OR “endometrioma” OR “ovarian endometrioma”) AND Subject: (“pain” OR “dyspareunia” OR “pelvic pain” OR “dysmenorrhea” OR “abdominal pain” OR “defecation pain” OR “anal heaviness” OR “pain hypersensitivity” OR “central pain” OR “management”) AND Subject: (“guidelines” OR “statements” OR “recommendations” OR “expert opinions” OR “consensus”).

1.3 Inclusion and Exclusion Criteria **Inclusion criteria:** (1) Guideline literature involving pain management in endometriosis patients, including clinical guidelines and expert consensus; (2) Guidelines/expert consensus containing relevant recommendations for endometriosis pain management; (3) For revised guidelines, the latest version was included; (4) Language: Chinese or English. **Exclusion criteria:** (1) Guidelines/expert consensus for which full text could not be obtained; (2) Guidelines/expert consensus that had been repeatedly published; (3) Literature translating, commenting on, or interpreting guidelines/expert consensus; (4) Guidelines/expert consensus evaluated as C-level by AGREE II.

1.5 Quality Evaluation of Included Guidelines/Expert Consensus

The Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument was used for independent literature quality evaluation. The evaluation includes 6 domains: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence, comprising 23 key items plus 2 overall assessment items. Each item is scored from 1 to 7, where 1 indicates completely non-compliant and 7 indicates completely compliant. The standardized score for each domain = (actual score - minimum possible score) / (maximum possible score - minimum possible score) × 100%. Based on the scoring results, if a guideline or expert consensus has standardized percentages >60% in all 6 domains, it is strongly recommended (A-level); if standardized percentages are 30%-60% in most domains (≥3), it is recommended (B-level); if standardized percentages are <30% in most domains (<3), it is not recommended (C-level). Two researchers independently evaluated the quality of included guidelines using AGREE II. To test consistency of evaluation, SPSS 25.0 was used to analyze intraclass correlation coefficient (ICC); ICC ≥ 0.80 indicated acceptable consistency for evaluation.

2 Results

2.1 Guideline/Expert Consensus Screening Process and Results Initial search yielded 1,936 articles. Based on inclusion and exclusion criteria, 15 evidence-based guidelines/expert consensus were ultimately included [11-25]. The screening process and results are shown in Figure 1 [Figure 1: see original paper].

2.2 Basic Characteristics of Included Guidelines/Expert Consensus

Among the 15 included guidelines/expert consensus, 9 [11-13, 17-20, 22, 25] were guidelines and 6 [14-16, 21, 23-24] were expert consensus; 7 [11-15, 23-24] were from China and 8 [16-22, 25] from abroad; publication dates ranged from 2018 to 2024. Among the 15 guidelines/expert consensus, 8 [11-13, 17-18, 22-23, 25] explicitly described evidence grading, and 7 [11, 13, 17-18, 22-23, 25]

specified recommendation strength. Information on included guidelines/expert consensus is shown in Table 1 .

2.3 Quality Evaluation Results of Included Guidelines/Expert Consensus In the 6 domains of AGREE II, the mean scores of the 15 guidelines/expert consensus were: scope and purpose 83.15%, stakeholder involvement 71.11%, rigor of development 44.79%, clarity of presentation 65.74%, applicability 35.55%, and editorial independence 87.78%. Among the included 15 guidelines/expert consensus, 1 [19] was A-level recommendation and 14 [11-18, 20-25] were B-level recommendations. Details are shown in Table 2 .

2.4 Consistency Test of Guideline/Expert Consensus Evaluation In this study, the consistency of evaluation by 2 reviewers for all guidelines/expert consensus was >0.8 , indicating good consistency between the two reviewers. Results are shown in Table 3 .

2.5 Summary of Main Recommendations A total of 33 recommendations related to endometriosis pain management were extracted from the 15 guidelines/expert consensus, covering 6 aspects: general principles of pain management, pain assessment, medication management, surgical management, non-pharmacologic/surgical management, and health education. Specific recommendations are shown in Table 4 .

3 Discussion

3.1 Quality Analysis of Guidelines/Expert Consensus The overall quality of guidelines/expert consensus was at a moderate level. Among the 6 domains, the highest mean scores were for editorial independence and scope and purpose, followed by stakeholder involvement and clarity of presentation; scores for rigor of development and applicability were slightly lower.

In the “applicability” domain, 8 guidelines/expert consensus [11-16, 20, 24] had standardized scores below 30%. Analysis revealed this was because they did not detail barriers to application or cost considerations. Barrier factors and related costs are particularly critical for long-term management of endometriosis, as endometriosis not only poses significant health threats but is also associated with substantial social and economic burden, causing \$22 billion in productivity losses and direct healthcare costs annually to the U.S. economy [26]. In China, endometriosis also brings significant consumption of social resources [27] and major impacts on patients, their families, and economy [28]. Only 1 guideline [19] reported medication dosages and prices; 4 guidelines/expert consensus [14, 16-17, 22] mentioned the need to consider costs but did not specify details. It is recommended that future guideline development consider these economic and social factors to ensure feasibility and cost-effectiveness of recommendations, reducing economic pressure on patients and society. One guideline [22]

scored below 60% only in applicability, reporting medication dosages and prices but not explaining monitoring and/or audit criteria. If improved in this aspect, it could potentially be elevated to A-level recommendation.

In the “rigor of development” domain, 5 guidelines/expert consensuses [14-16, 23-24] had standardized scores below 30%. Analysis revealed this was because they did not provide detailed search methods, evidence strengths and limitations, recommendation formulation processes, or external review procedures, making it difficult to assess the completeness and systematic nature of included evidence and the scientific validity and impartiality of recommendations, thereby affecting the rigor, objectivity, authority, and continued applicability of guidelines and limiting clinicians’ and patients’ trust and application of recommendations. Only 4 guidelines [18-19, 22, 25] mentioned search methods, but some only mentioned databases searched without specific search strategies. It is recommended that future guideline development processes detail and transparentize search strategies, including databases used, search strategies, screening processes, etc., to ensure comprehensiveness and systematic nature of evidence, while conducting quality assessment of all included evidence and clearly reporting evidence strengths and limitations. Additionally, external review should be implemented, inviting external experts to review guideline drafts and reporting review processes and results in final guidelines, as well as developing clear update plans including mechanisms for monitoring new evidence, update frequency, and procedures to ensure guideline timeliness and effectiveness and improve guideline quality and credibility [29].

In the “clarity of presentation” domain, 2 guidelines [11, 13] had standardized scores below 40%. Analysis revealed this was because key recommendations were not easily identifiable; only 1 guideline [22] used pictures and tables to highlight important recommendations. Using pictures to present content can help readers more intuitively understand complex information, enhance visualization effects, thereby improving information transmission efficiency and persuasiveness [30]. To improve guideline clarity and operability, it is recommended that future guideline development use more intuitive display methods such as charts to improve information transmission efficiency and effectiveness.

3.2 Analysis of Recommendations As a chronic disease requiring long-term management, endometriosis has pain as one of its debilitating symptoms that often severely impacts women’s quality of life and work capacity [19], making pain management particularly important [31]. Analysis revealed that recommendations from included guidelines were generally consistent, all emphasizing the importance of medication management for endometriosis pain. Overall, medication management for endometriosis pain must comprehensively consider efficacy, safety, and patient quality of life. However, current guidelines have deficiencies in lacking clear long-term management strategies, including duration of medication management and post-discontinuation management. Endometriosis medication management must be long-term; pain recurrence rates are high

after stopping medication [32]. It is recommended that future guidelines provide clearer guidance and recommendations. Meanwhile, controversy remains regarding preoperative medication use. Some studies suggest preoperative hormone use may help reduce intraoperative bleeding and postoperative adhesions, while others worry it may affect lesion identification and complete resection [32]. Three guidelines [17, 19-20] do not recommend preoperative medication; further research is needed.

Additionally, relevant recommendations are mostly limited to measures taken by healthcare professionals. Support for non-pharmacologic/surgical management is also crucial for improving pain in endometriosis patients. Six guidelines [11-12, 17-20] mentioned non-pharmacologic/surgical management. The guideline published by NICE [19] stated that no high-quality studies have been found on the effectiveness of lifestyle interventions such as diet or exercise in reducing pain. Some guidelines included non-pharmacologic/surgical management, but some measures were not evidence-based. To successfully self-manage endometriosis pain, patients need evidence-based, easily accessible information about the disease and non-pharmacologic/surgical management methods. It is recommended that future high-quality related research be conducted to provide more scientific evidence supporting the effectiveness of non-pharmacologic/surgical management methods and help patients better manage pain.

3.3 Current Status and Optimization Suggestions for Chinese Endometriosis Pain Management Guidelines This study included 7 Chinese guidelines related to endometriosis pain management. These guidelines demonstrate significant advantages in multiple aspects. In terms of professional authority, the expert panels involved in compilation were strong, covering authoritative experts in obstetrics and gynecology from renowned hospitals nationwide. In terms of content comprehensiveness, guidelines detailed the incidence, types, and characteristics of endometriosis-related pain, comprehensively covering various pain symptoms including dysmenorrhea, chronic pelvic pain, and dyspareunia, with special attention to pain management in adolescent endometriosis patients, detailing their clinical characteristics, diagnosis, and long-term management, demonstrating attention to individual differences in special populations. Chinese guidelines related to endometriosis pain management have made significant progress, but compared with foreign guidelines, there is still room for optimization and improvement.

First, Chinese guidelines related to endometriosis pain management need further improvement in systematic evidence-based medicine. Although domestic clinical research has gradually increased, the number of systematic reviews and high-quality randomized controlled trials is still in the accumulation stage, making the evidence base for some recommendations need further enrichment. Additionally, foreign guidelines provide more detailed and specific recommendations in medication selection and surgical options, including dosages, treatment courses, indications, and contraindications for different drugs. In contrast, domestic

guidelines' recommendations in these aspects are relatively general, not providing similarly detailed treatment course guidance and specific information on applicable populations. This may be because domestic guidelines focus more on comprehensiveness and general applicability to adapt to different medical environments and resource conditions. Finally, domestic and foreign guidelines have relatively less discussion on multidisciplinary management. Studies show that patients managed through multidisciplinary approaches have significantly reduced pain levels [33]. With continuous development of clinical practice, this area is expected to be further enhanced.

To build high-quality Chinese guidelines for endometriosis pain management and better help endometriosis patients manage pain, it is recommended to increase systematic reviews and conduct high-quality randomized controlled trials to improve scientific validity and reliability of evidence, which can be supported through national research projects to promote high-quality research and detail evidence sources and quality levels for each recommendation in guidelines. In terms of guideline recommendations, detailed medication plans should be listed, including drug selection, dosage, treatment course, indications, and contraindications. It is recommended that domestic guideline writing teams deeply study foreign advanced guidelines, such as the 2024 NICE updated guideline [19], learn from its detailed medication plans and surgical indications, and organize multidisciplinary expert seminars to make precise recommendations on drug dosage and treatment courses based on domestic medical conditions, reducing uncertainty in clinical doctors' independent judgment and improving treatment standardization and effectiveness. In multidisciplinary management, it is recommended that guidelines clearly define the composition and roles of multidisciplinary teams and workflow, coordinate various medical resources, and integrate multidisciplinary opinions [34] to provide clearer guidance for clinical practice and help medical institutions more effectively establish and manage multidisciplinary teams.

3.4 Limitations This study has limitations. The AGREE II guideline evaluation tool only evaluates the quality of guidelines/expert consensus but does not deeply analyze the reasonableness of evidence levels and recommendation strengths in guidelines, and the evaluation process may be subject to some subjective factors. More than half of included guidelines/expert consensus were from abroad, making results potentially not specific and limiting applicability of research findings in China, requiring appropriate adjustment and localization to ensure applicability and effectiveness.

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Author Contributions

XIE Wan proposed the research idea, designed the research plan, and proposed research questions, design, and methods; TU Xulian, LIU Xia, LI Xiaoyan, LENG Mingyue, YANG Xueqing, and LI Li were responsible for data collection, acquisition, cleaning, statistical analysis, and chart preparation; XIE Wan and TU Xulian drafted the manuscript; WU Liping and LIU Xia were responsible for final version revision and accountability for the manuscript.

Conflict of Interest

This article has no conflict of interest.

Note: Figure translations are in progress. See original paper for figures.

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