

A Narrative Review and Risk-Stratification Framework for Preventing LNG-IUS Expulsion in Adenomyosis

Jin Zhao*, Jianliang Chen*, Xiaoe Wang*, Huabin Wang*

Department of Obstetrics and Gynecology, the First People's Hospital of Xiaoshan District, Xiaoshan Affiliated Hospital of Wenzhou Medical University, Hangzhou, Zhejiang, People's Republic of China

*These authors contributed equally to this work

Correspondence: Huabin Wang, Department of Obstetrics and Gynecology, the First People's Hospital of Xiaoshan District, Xiaoshan Affiliated Hospital of Wenzhou Medical University, Hangzhou, Zhejiang, People's Republic of China, Email genical@sina.com

Abstract: Levonorgestrel-releasing intrauterine system (LNG-IUS) expulsion rates are markedly elevated (15–37.5%) in patients with adenomyosis compared to those with normal uteri (3–10%), significantly compromising treatment efficacy and adherence. Existing evidence on risk factor mitigation is fragmented, lacking a structured management framework. This narrative review synthesizes current literature to identify key determinants of expulsion—including uterine enlargement, intracavitary lesions, and insertion techniques—and evaluates preventive strategies such as GnRH-agonist pretreatment and imaging-guided placement. Its primary aim is to propose a novel, three-tiered risk-stratification model that tailors management (conventional, augmented, or advanced fixation approaches) to individual patient profiles based on anatomical, procedural, and clinical factors. This structured approach seeks to optimize LNG-IUS retention and resource allocation. Prospective validation through randomized controlled trials remains essential to establish evidence-based, personalized protocols.

Keywords: LNG-IUS, uterine enlargement, intrauterine device displacement, gonadotropin-releasing hormone agonists, ultrasonography, therapeutic effectiveness

Introduction

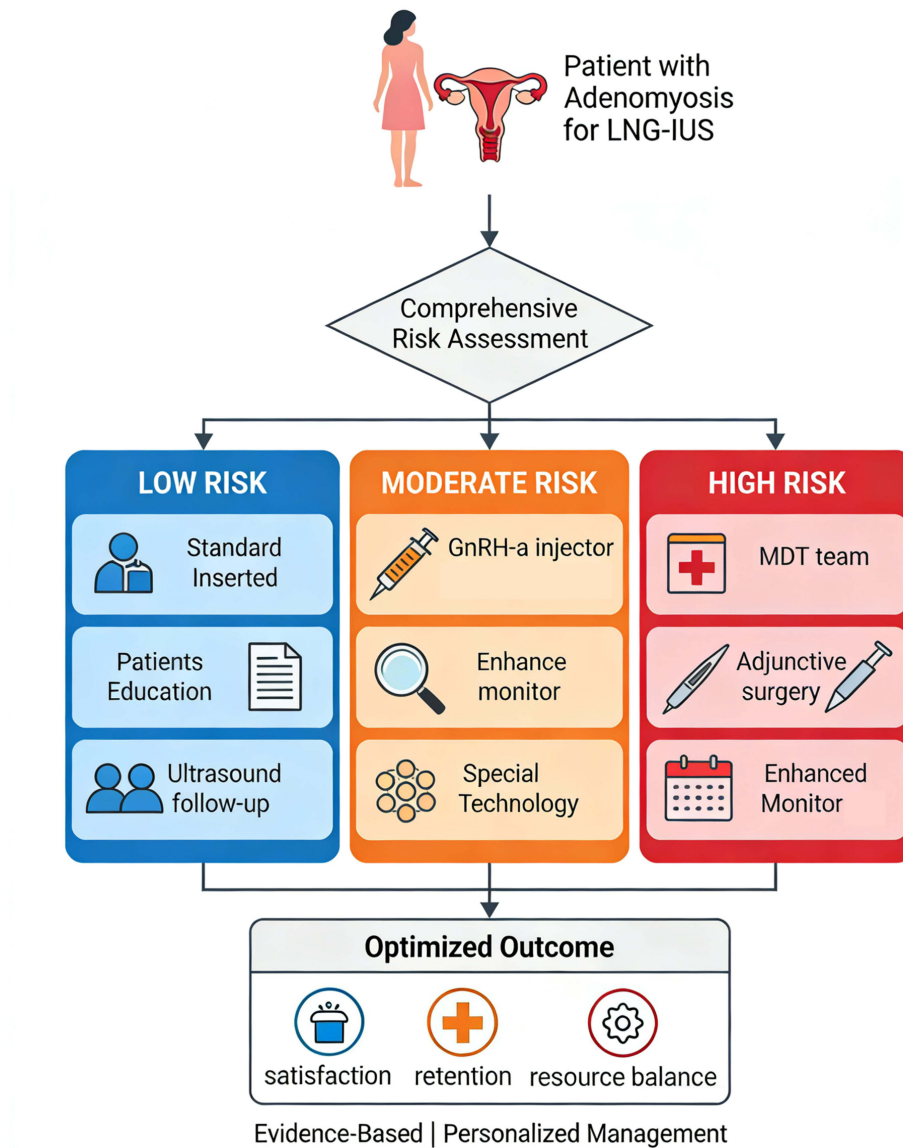
Adenomyosis, a common gynecological condition, significantly impairs patients' quality of life. The levonorgestrel-releasing intrauterine system (LNG-IUS) represents an effective non-surgical therapeutic option through continuous progestogen release.^{1,2} However, patients with this condition face special challenges: anatomical variations and extensive lesions lead to LNG-IUS expulsion rates as high as 9–37.5%, significantly higher than the 3–10% observed in women without this condition.^{3,5} This undermines treatment efficacy, reduces compliance, and sometimes necessitates premature surgical intervention. However, current clinical guidelines lack personalized, risk-stratified management recommendations for LNG-IUS expulsion specifically in adenomyosis patients.

Research has identified key factors affecting device expulsion, including uterine enlargement, morphological abnormalities, lesion extent, symptom severity, and placement techniques.^{3–7} Recent chronic disease management increasingly emphasizes risk stratification approaches, potentially applicable to adenomyosis treatment beyond traditional “one-size-fits-all” methods.^{8,9} Preventive strategies such as pharmacological pretreatment, image-guided insertion, and hysteroscopic fixation have shown promising results in high-risk populations.^{10–13}

This narrative review synthesizes evidence from selective literature searches in PubMed, Web of Science, Cochrane Library, and Embase (January 2000–June 2025) using comprehensive keyword combinations regarding risk factors for LNG-IUS expulsion in adenomyosis and proposes a risk stratification management strategy. Given the limited availability of high-quality RCTs, we primarily integrated insights from observational studies to develop a practical clinical

Graphical Abstract

Risk-Stratified Management Model for LNG-IUS in Adenomyosis



framework, while emphasizing the importance of prospective validation. This review aims to address this gap by synthesizing available evidence to propose a structured three-tier risk-stratification management framework, assisting clinicians in optimizing decision-making based on individual risk.

LNG-IUS in the Treatment of Adenomyosis: Clinical Efficacy and Shedding Issues

The clinical value of LNG-IUS in adenomyosis management has been widely established. Multiple prospective studies have confirmed its significant therapeutic efficacy. Randomized controlled trials by Ozdegirmenci et al demonstrated that both LNG-IUS and hysterectomy significantly improve VAS pain scores and quality of life in adenomyosis patients. Importantly, LNG-IUS offers the advantage of fertility preservation as a non-surgical treatment option.¹³ Shaaban et al further quantified this therapeutic effect, showing that patients experienced substantial relief of dysmenorrhea and menorrhagia within six months after LNG-IUS implantation, with superior outcomes compared to low-dose combined oral contraceptives.¹⁴ Kang et al confirmed through MRI and ultrasound assessments that LNG-IUS treatment not only alleviates symptoms but also reduces uterine volume and junctional zone thickness, suggesting a direct therapeutic effect on adenomyosis lesions.^{11,15,16}

Despite these favorable outcomes in symptom control, the clinical utility of LNG-IUS is substantially limited by high expulsion rates. This issue has garnered considerable clinical attention and represents a major challenge in adenomyosis management. A prospective cohort study (n=1,100) by Li L et al documented a time-dependent pattern of device expulsion in symptomatic adenomyosis patients, with cumulative expulsion rates of 13.8% at 12 months and 20.0% at 36 months. The researchers observed that expulsion events predominantly occurred within the first year post-implantation, though long-term monitoring revealed persistent risk, with a cumulative expulsion rate reaching 43.8% at 60 months.¹⁷ This temporal distribution of expulsion events underscores the necessity for structured long-term follow-up strategies in adenomyosis patients receiving LNG-IUS therapy. When expulsion occurs, patients typically experience rapid symptom recurrence, necessitating additional interventions or device reinsertion. This phenomenon not only increases healthcare utilization and treatment costs but also significantly impacts patient satisfaction and long-term treatment adherence, potentially compromising the overall management effectiveness in this patient population.

Risk Factors for LNG-IUS Expulsion in Adenomyosis

Anatomical and Disease-Related Factors

The unique anatomical features of the uterus and structural alterations induced by adenomyosis constitute the primary risk basis for LNG-IUS expulsion. Uterine volume is widely recognized as a crucial predictor of device retention success. Clinical evidence indicates that as uterine volume increases, device stability progressively diminishes, with this trend becoming particularly pronounced when volume exceeds 150 mL.¹⁸ Multiple investigations by Park et al have further established that uterine enlargement secondary to adenomyosis is significantly associated with higher treatment discontinuation rates.^{5,6,13,19} The enlarged uterine cavity reduces the device-to-cavity proportionality while simultaneously increasing intrauterine mechanical pressure. Coupled with adenomyosis-induced myometrial abnormalities that may precipitate irregular uterine contractions, these factors collectively elevate expulsion risk.

Beyond adenomyosis itself, concomitant gynecological pathologies additionally increase expulsion susceptibility. A study involving 481 women demonstrated significantly higher cumulative expulsion rates in patients with uterine fibroids (14.5%, 15.8%, and 15.8% at 1, 2, and 3 years, respectively) compared to those with isolated adenomyosis (9.1%, 10.6%, and 11.1%) and normal uteri (3.6%, 4.1%, and 4.6%) (P=0.008).³ Notably, patients with submucosal fibroids exhibited particularly elevated expulsion risk (15.4%), substantially exceeding that of other fibroid types (7.9%). This heightened risk primarily relates to fibroid-induced uterine cavity distortion and deformation, which compromise device retention.⁶ Additionally, these uterine pathologies frequently provoke severe menorrhagia or dysmenorrhea, leading to frequent uterine contractions and flushing effects that further promote device displacement. Current evidence regarding the influence of adenomyosis-specific pathological characteristics remains limited. Theoretically, diffuse adenomyosis may confer higher expulsion risk than focal disease,¹⁰ though insufficient clinical data exist to substantiate correlations between junctional zone thickening, myometrial heterogeneity, and expulsion rates.¹⁷

Surgical History and Procedure-Related Factors

Previous uterine surgeries, insertion techniques, and perioperative management significantly influence LNG-IUS retention success. Clinical observations indicate that improper insertion methods or suboptimal positioning frequently result in device displacement or expulsion.^{20,21} Inaccurate positioning may place the device excessively distant from the uterine fundus or misaligned with the uterine cavity axis, increasing biomechanical expulsion risk. Inadequate preoperative preparation, insufficient intraoperative position verification, or irregular postoperative follow-up may also delay identification of potential complications.²²

Insertion timing represents another critical consideration. Evidence suggests significantly higher expulsion risk when insertion occurs within 8 days preceding the menstrual cycle compared to day 9 or later.²³ This temporal pattern primarily relates to thinner endometrial lining and more active uterine contractions during menses and early proliferative phase, which compromise device stabilization.

Implementation of preoperative intervention strategies for high-risk patients can substantially improve retention outcomes. Research by Zhang's team demonstrates that GnRH analogue pretreatment creates a more favorable retention environment by reducing uterine volume (from $311.4 \pm 32.3 \text{ cm}^3$ to $276.6 \pm 32.1 \text{ cm}^3$) and suppressing abnormal uterine contractions, thereby decreasing expulsion rates to 14%.²⁴

Symptom-Related Factors

A clear association exists between clinical symptom severity and device expulsion. Research by Youm et al indicates higher cumulative expulsion rates in patients with severe menorrhagia (11.0%, 12.7%, and 13.4%) and those with dysmenorrhea (8.1%, 9.0%, and 10.0%).³ Li et al further confirmed that severe dysmenorrhea ($\text{VAS} \geq 7$) increases LNG-IUS expulsion risk.²⁵

This correlation may operate through several mechanisms: First, symptom severity typically reflects the extent of adenomyosis lesions, including enhanced abnormal myometrial contractility; Second, severe menorrhagia may compromise initial LNG-IUS placement and fixation efficacy; Third, severe dysmenorrhea associates with aberrant uterine contraction patterns. These strongly uncoordinated uterine contractions directly elevate device displacement risk. Consequently, symptom assessment proves important not only for treatment selection but also for expulsion risk stratification.

Individual Patient Factors

Individual patient characteristics also significantly influence LNG-IUS treatment success. Literature confirms that previous expulsion history constitutes an important risk factor. Studies demonstrate that patients experiencing spontaneous LNG-IUS expulsion exhibit significantly elevated recurrence risk. In one investigation, 30% of participants with spontaneous expulsion opted for reinsertion, among whom approximately 57% experienced recurrent expulsion.¹⁸ This "expulsion tendency" may relate to specific uterine morphology, unique myometrial contraction patterns, or endometrial characteristics.

Regarding age and reproductive status effects on expulsion risk, most studies indicate that younger age (≤ 24 years) and nulliparity associate with higher IUD expulsion risk,^{26,27} though some investigations have failed to confirm this association.¹⁸ Despite evidence limitations and inconsistent findings, these factors should still receive consideration as auxiliary parameters when formulating individualized management strategies.

Patient psychological status and treatment attitudes additionally affect treatment adherence. Patients with previous adverse LNG-IUS experiences may demonstrate heightened sensitivity to minor discomforts, potentially leading to premature intervention or self-removal.^{28,29} Through comprehensive evaluation of these multidimensional individual factors, clinicians can more accurately predict expulsion risk and develop personalized preventive measures.

Preventive Strategies and Technological Improvements

The high expulsion rate of LNG-IUS in adenomyosis patients has remained a persistent clinical concern, significantly impacting treatment efficacy and causing unnecessary patient distress. In response to this challenge, various evidence-

based strategies have emerged, focusing on preoperative preparation, insertion techniques, timing optimization, and follow-up protocols.

Preoperative pharmacological intervention represents a promising approach for improving device retention. Gonadotropin-releasing hormone (GnRH) agonists or mifepristone create a more favorable implantation environment by inhibiting endometrial proliferation and reducing uterine volume.^{30–32} A large prospective cohort study (n=1,100) demonstrated that three cycles of GnRH agonist pretreatment significantly reduced the 60-month cumulative LNG-IUS expulsion rate (36.4% vs 50.6% in controls; HR 0.60, 95% CI 0.40–0.80; P<0.001).²⁵ This approach particularly benefits patients with uterine enlargement (≥ 10 weeks' gestational size) or heavy menstrual bleeding (PBAC>200). A smaller investigation (n=21) reported only 14.3% expulsion rate at 12 months following 3–4 GnRH agonist injections, with sustained uterine volume reduction.²⁴ However, potential adverse effects—including menopause-like symptoms, decreased bone density, and symptom recurrence after drug discontinuation—suggest that routine pretreatment should be reserved for patients with specific risk factors.

Advanced insertion technology significantly enhances device retention rates. Ultrasound-guided or hysteroscopic-assisted implantation facilitates more precise positioning. A systematic review and meta-analysis encompassing 7 randomized controlled trials (total 1,267 patients) indicated that transabdominal ultrasound-guided implantation not only significantly reduced intraoperative pain scores (MD = -1.91, 95% CI -3.08 to -0.73, P = 0.001) but also substantially decreased the risk of IUD displacement/expulsion (RR = 0.36, 95% CI 0.16–0.78, P = 0.01).²¹ For patients with anatomical abnormalities or recurrent expulsion risks, innovative techniques such as hysteroscopic suture fixation show potential, though high-quality randomized controlled studies supporting these methods remain limited, and such procedures require considerable operator expertise.

Insertion timing requires careful consideration. Clinical observations indicate that insertion on or after day 9 of the menstrual cycle can reduce early expulsion rates by approximately 30% compared to insertion within the first 8 days.²³ Determining optimal insertion timing based on individual menstrual cycle characteristics can significantly enhance treatment success rates.^{7,13,33–36}

Standardized follow-up protocols are crucial for maintaining LNG-IUS therapeutic efficacy. Regular imaging assessments and symptom evaluations facilitate early identification and management of potential complications. The high-standard clinical pathway recommendation from the University Hospital of Zurich, Switzerland, includes regular follow-up at 6 weeks, 6 months post-implantation, and annually thereafter, with transvaginal ultrasound measurement of IUD-ED (distance from the IUD upper edge to the endometrium-uterine cavity junction) at each visit to detect malposition early.²⁰ Bachofner et al's data indicate that approximately half of malpositions were identified during the 6-week follow-up. Timely intervention maintains the one-year unintended pregnancy rate at an exceptionally low level (<1%).²⁰ However, patient compliance varies considerably, and follow-up processes often lack standardized protocols, underscoring the necessity for enhanced patient education and innovative monitoring approaches.

Risk-Stratified Management Approach for LNG-IUS Treatment in Adenomyosis Patients

Foundation of Multidisciplinary Integration and Stratification Concept

The complexity of adenomyosis necessitates a comprehensive management approach that transcends single-specialty care.³⁷ The multidisciplinary team (MDT) model, which has demonstrated success in chronic pelvic pain and endometriosis management, offers valuable insights for adenomyosis treatment by effectively integrating expertise from gynecologists, imaging specialists, pain management physicians, and psychologists.^{38–40} Within this framework, gynecologists coordinate disease assessment and treatment implementation; imaging specialists analyze lesion characteristics through ultrasound and MRI; mental health professionals address disease-related psychological issues; and pain specialists provide comprehensive solutions for chronic pelvic pain.⁴¹ Multiple clinical observations and cohort studies have confirmed that the MDT model significantly enhances diagnostic accuracy,^{38,39} improves patient experience,⁴⁰ and reduces misdiagnosis risk.³⁹

Personalized management constitutes the cornerstone of successful LNG-IUS treatment for adenomyosis. Vannuccini and Petraglia noted that adenomyosis represents a heterogeneous group of conditions, emphasizing “patient-centered individualized long-term management” as a core principle.⁴² Similarly, Chapron et al proposed that “modern treatment should focus on patient preferences, fertility plans, and lesion phenotype rather than solely on lesion excision”⁴¹ This personalized approach naturally evolves toward risk stratification strategies, a concept successfully applied in cardiovascular disease (ASCVD scoring) and oncology (TNM staging).^{43,44}

The essence of risk stratification lies in identifying high-risk patients, optimizing resource allocation, and avoiding overtreatment of low-risk patients.⁴⁵ In adenomyosis LNG-IUS therapy, comprehensive assessment incorporates multi-dimensional factors including patient age, fertility desires, previous expulsion history, uterine volume, imaging characteristics, and psychological status^{41,42,46} High-risk patients (eg, those with previous LNG-IUS expulsion, uterine volume >150 mL, or significant myometrial heterogeneity) may benefit from GnRH-a or HIFU pretreatment to reduce uterine volume and improve device retention.^{42,46} For patients with significant psychological distress, enhanced health education and intensive follow-up are necessary.⁴² Additionally, treatment strategies and follow-up protocols should be tailored according to imaging-based classifications (such as Bazot-Darai’s internal, external, and adenomyoma subtypes).^{41,42,46}

Based on these concepts, we propose an evidence-based risk stratification model for adenomyosis patients receiving LNG-IUS treatment and corresponding targeted intervention strategies (Table 1). This comprehensive approach achieves individualized management through systematic assessment of anatomical features, procedural factors, and patient-specific variables, thereby optimizing device retention rates across different patient populations. Our approach is grounded in the recognition that LNG-IUS expulsion in adenomyosis patients stems from complex interactions among multiple factors, addressing the multifactorial nature of expulsion by systematically integrating procedure-related factors (operator experience and insertion timing), patient anatomical features (uterine cavity changes and adenomyosis invasion degree), and other key parameters (uterine volume and cavity morphology).

Evidence-Based Risk Stratification Framework

Based on published literature and clinical practice, we recommend a three-tiered stratified intervention approach (Table 1). Risk assessment should be based on imaging findings, patient history, and gynecological examination. In

Table 1 Three-Tiered Risk Stratification Model for LNG-IUS Treatment in Adenomyosis

Risk Level	Stratification Criteria	Management Strategy	Supporting Evidence (Level) ^a
Low Risk	<ul style="list-style-type: none"> • Uterine volume <12 gestational weeks • Regular uterine cavity • No fibroids /intracavitary lesions • No expulsion history 	<ul style="list-style-type: none"> • Standard insertion technique • patient education • Ultrasound follow-up (1, 3, 6, 12 months) 	14,17,47 (B/Strong)
Moderate Risk	<ul style="list-style-type: none"> • Single risk factor: <ul style="list-style-type: none"> - Uterine volume ≥12 weeks - Cavity length ≥8cm - Mild abnormality - Previous expulsion 	<ul style="list-style-type: none"> • GnRH-a pretreatment • Ultrasound / hysteroscopy-guided • Enhanced monitoring (1–3 months) • Special insertion techniques 	3,18,23,24,33 (B/Strong)
High Risk	<ul style="list-style-type: none"> • Multiple risk factors (≥2) • Complex presentations: <ul style="list-style-type: none"> - Uterus >150 mL - Severe deformity - Recurrent expulsion - With fibroids 	<ul style="list-style-type: none"> • Multidisciplinary team approach • Advanced fixation techniques (suturing/cold knife) • Consider adjunctive surgery • Enhanced monitoring 	5,7,13,34–36,48 (B/Strong)

Notes: ^aEvidence levels: A=High-quality RCTs/systematic reviews; B=Well-designed cohort studies; C=Case series/expert opinions. Recommendation strength: Strong=Benefits outweigh risks; Weak=Benefit-risk uncertain.

this narrative review, we employ a simplified evidence grading system (Levels A, B, C) and recommendation strength assessment (strong, weak) to reflect the quality of existing evidence and reliability of clinical recommendations.⁴⁹ Level A represents high-quality randomized controlled trials or systematic reviews, Level B represents well-designed cohort studies, and Level C represents case series or expert opinions. The detailed supporting evidence for each risk-stratified management strategy is comprehensively summarized in Table 2, which provides an overview of key studies

Table 2 Supporting Evidence Assessment for Risk-Stratified Management Strategies

Author (Year)	Study Design	Sample Size (n)	Key Findings	Evidence Level ^a	Applicable Risk Level
Ozdegirmenci et al (2011) ¹⁴	Prospective randomized trial	75 (43 LNG-IUS vs 32 hysterectomy)	To compare the efficacy and quality of life improvement of LNG-IUS versus hysterectomy in patients with adenomyosis. The dropout rate in the LNG-IUS group was only 2.3% (1/43), with a continuation rate of 97.7%. Improvement in Hb and quality of life was comparable to the hysterectomy group. No serious complications.	A	Low risk
Bragheto et al (2007) ¹⁷	Prospective descriptive study	29	To evaluate the effectiveness of LNG-IUS in MRI-confirmed adenomyosis patients and its impact on symptoms and uterine morphology. No LNG-IUS expulsions were observed. Significant pain relief and 24% reduction in junctional-zone thickness ($p < 0.0001$) were achieved. Uterine volume remained stable (142.6→136.4 mL, $p = 0.21$).	B	Low risk
Fedele et al (1997) ⁴⁷	Prospective, open, non-comparative study	25	To investigate the feasibility and efficacy of LNG-IUS in treating adenomyosis-associated menorrhagia. A 4% expulsion rate (1/25) and 92% continuation rate were observed at 12 months. Hb and ferritin levels increased significantly. Slight uterine volume reduction occurred (348→314 mL, $p < 0.05$).	B	Low risk
Youm et al (2014) ³	Retrospective cohort study	481 (total cohort), 198 (with adenomyosis)	To identify and compare factors (including adenomyosis) associated with spontaneous LNG-IUS expulsion across different uterine conditions. Adenomyosis was an independent risk factor for expulsion, with a 1-year cumulative expulsion rate of 11.1%. Heavy menstrual bleeding, dysmenorrhea, and pre-insertion GnRH agonist use further increased the risk.	B	Moderate risk
Lee et al (2016) ¹⁸	Retrospective cohort study	171	To determine if uterine volume is an independent predictor of LNG-IUS treatment failure (expulsion or removal due to side effects) in adenomyosis patients. Uterine volume ≥ 150 mL was an independent predictor of treatment failure (OR 5.38, failure rate 21.6%).	B	Moderate risk
Harris et al (2021) ²³	Retrospective cohort study	176	To investigate the association between uterine cavity length, timing of insertion, and expulsion risk in patients using LNG-IUS for non-contraceptive indications. Uterine cavity length ≥ 8.5 cm and insertion on menstrual cycle days 1–8 were independently associated with a higher expulsion rate (22% overall).	B	Moderate risk

(Continued)

Table 2 (Continued).

Author (Year)	Study Design	Sample Size (n)	Key Findings	Evidence Level ^a	Applicable Risk Level
Zhang et al (2013) ²⁴	Retrospective cohort study	21	To evaluate the effect of GnRH agonist (GnRHa) pre-treatment on reducing uterine volume and subsequent LNG-IUS retention in patients with adenomyosis. GnRHa pre-treatment significantly reduced uterine volume (from 311.4±32.3 to 220.6±17.2 cm ³). Expulsion rate was 14.3% (3/21) at 12 months. Significant symptom improvement was achieved.	B	Moderate risk
Peng et al (2010) ³³	Retrospective cohort study	273	To compare the efficacy of a modified insertion technique ("Yang's method") versus the conventional method in reducing LNG-IUS expulsion rates in adenomyosis patients. The modified "Yang's method" significantly reduced the expulsion rate to 10.2% compared to 25.3% with the conventional method. No significant difference in symptom relief was found.	B	Moderate risk
Park et al (2015) ⁵	Retrospective cohort study	48	To assess the clinical efficacy and device retention of LNG-IUS in patients with large adenomyotic uteri (≥12 gestational weeks). In patients with large uteri (median 253.5 mL), the LNG-IUS expulsion rate was high (37.5%), primarily within 6 months. Significant symptom improvement was achieved despite the high expulsion risk.	B	High risk
Lv et al (2024) ⁷	Retrospective case series	79	To evaluate the feasibility and effectiveness of hysteroscopic suture fixation of LNG-IUS to the uterine fundus for preventing expulsion in adenomyosis. Hysteroscopic suture fixation resulted in a low expulsion rate (2.6%) and significant improvements in dysmenorrhea, menstrual bleeding, hemoglobin, and CA125 levels over 12 months.	B	High risk
Zhang et al (2022) ¹³	Prospective case series	12	To explore the feasibility and preliminary outcomes of suture fixation using a hysteroscopic cold knife surgery system for LNG-IUS in adenomyosis. Suture fixation using the cold knife system was feasible, with one expulsion (8.3%) in 12 months. Significant improvements in menstrual flow, dysmenorrhea, and quality of life were observed.	B	High risk
Mao et al 2024) ³⁴	Prospective observational study	21	To prospectively observe the effectiveness of hysteroscopic suture fixation of LNG-IUS in preventing expulsion in adenomyosis patients at high risk of device expulsion. No expulsions occurred during the 12-month observation period. Significant improvements in menstrual bleeding, dysmenorrhea, and hemoglobin levels were documented.	B	High risk

(Continued)

Table 2 (Continued).

Author (Year)	Study Design	Sample Size (n)	Key Findings	Evidence Level ^a	Applicable Risk Level
Yu et al (2025) ³⁵	Prospective study	31	To assess the clinical application and short-term efficacy of a novel hysteroscopic non-suture fixation technique for LNG-IUS at the uterine fundus. The non-suture fixation technique prevented expulsion (0%) over 6 months and led to significant improvements in menstrual bleeding, dysmenorrhea, endometrial thickness, and uterine volume.	B	High risk
Lai et al (2025) ³⁶	Retrospective study	39	To retrospectively evaluate the long-term (6–24 months) effectiveness of hysteroscopic cold-knife-assisted suture fixation of LNG-IUS in adenomyosis patients. No expulsions were observed during the follow-up period (6–24 months). Significant and sustained improvements in menorrhagia and dysmenorrhea were achieved.	B	High risk
Lou et al (2019) ⁴⁸	Retrospective study	66	To compare the outcomes of second-generation endometrial ablation (NovaSure) combined with LNG-IUS versus LNG-IUS alone in treating adenomyosis. The combined treatment (ablation + LNG-IUS) resulted in a lower expulsion rate and higher patient satisfaction compared to LNG-IUS alone, alongside significant improvements in menorrhagia and dysmenorrhea.	B	High risk

Notes: ^aEvidence levels: A=High-quality randomized controlled trials or systematic reviews; B=Well-designed cohort or case-control studies; C=Case series, expert opinions, or observational studies.

underpinning our framework. Our stratification framework (Figure 1) provides clinicians with a clear decision pathway to help formulate management plans suitable for individual patients.

Individualized Management Strategies Based on Risk Categories

The risk stratification model presented in Table 1 provides a framework for tailoring management approaches according to patient-specific factors. Management recommendations can be stratified based on the assessed risk level for LNG-IUS expulsion.

For patients meeting low-risk criteria, standard insertion procedures combined with comprehensive patient education and systematic follow-up protocols have demonstrated favorable outcomes. In a prospective study of 29 patients with relatively normal uterine volumes (142.6 mL), Bragheto et al observed no LNG-IUS expulsions throughout the follow-up period.¹⁷ Similarly, Fedele et al documented a 4% expulsion rate and 92% continuation rate in 25 patients with uterine volumes below 348 mL.⁴⁷ These findings support the implementation of standard management protocols in this population subset without need for additional interventions.

Patients presenting with moderate risk factors require enhanced interventional strategies. A large-scale retrospective analysis (n=481) by Youm et al established adenomyosis as an independent risk factor for LNG-IUS expulsion, with a documented one-year cumulative expulsion rate of 11.1%.³ When addressing isolated risk factors such as uterine volume ≥ 150 mL¹⁸ or uterine cavity length ≥ 8.5 cm,²³ pre-insertion GnRH-agonist administration has demonstrated efficacy in reducing uterine volume from 311.4 to 220.6 cm³ (p<0.001).²⁴ Additionally, modified insertion techniques have shown potential to reduce expulsion rates from 25.3% to 10.2%.³³ These interventions may significantly improve device retention in patients with intermediate risk profiles. However, global clinical practice varies regarding the optimal timing and patient selection for interventions such as GnRH-agonist pretreatment or advanced fixation techniques, reflecting the evolving nature of this field and the need for more consensus.

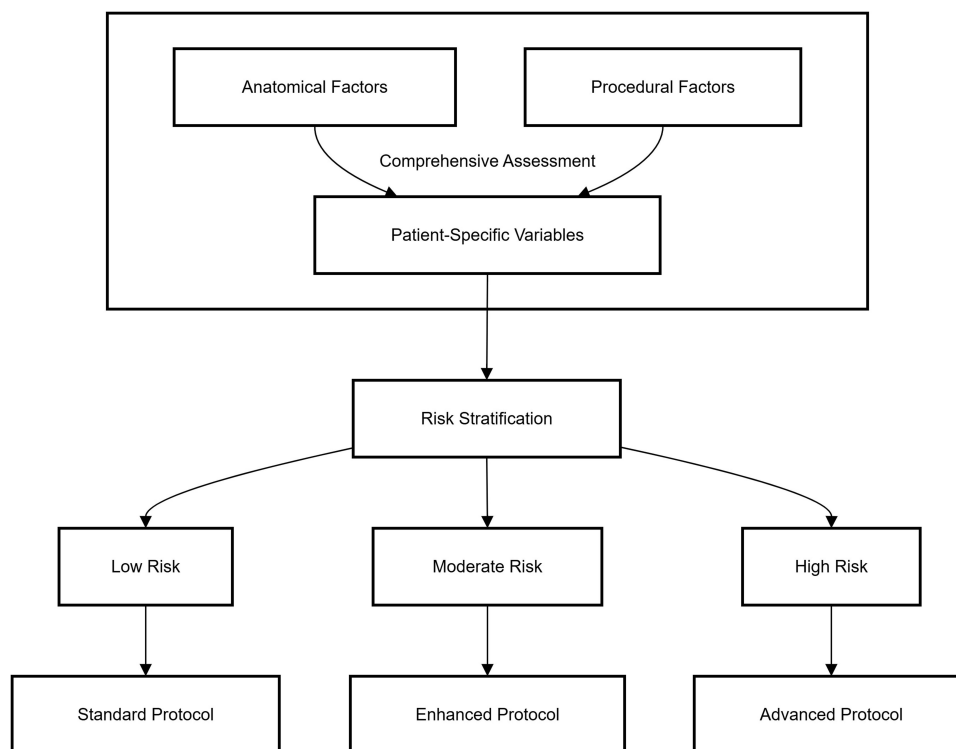


Figure 1 Comprehensive decision pathway for risk assessment and management of LNG-IUS expulsion in adenomyosis. This flowchart illustrates the sequential process for determining patient risk and appropriate clinical management. Key anatomical and procedural risk factors are first evaluated. These inputs undergo a comprehensive assessment that incorporates additional patient-specific variables to determine a collective risk profile. Patients are subsequently stratified into one of three risk categories (Low, Moderate, or High), which directly informs the recommended clinical management protocol (Standard, Enhanced, or Advanced).

The management of high-risk cases necessitates multidisciplinary approaches and advanced technical interventions. Park et al reported a 37.5% expulsion rate in patients with adenomyosis measuring ≥ 12 gestational weeks,⁵ underscoring the need for more intensive intervention in this cohort. Recent literature has documented the efficacy of hysteroscopic fixation techniques in high-risk patients: suture fixation methods demonstrated expulsion rates of 2.6%⁷ and 8.3%¹³ in separate investigations, while several studies reported no expulsions during defined follow-up periods.^{34–36} The combination of second-generation endometrial ablation with LNG-IUS has also been associated with improved retention rates and enhanced patient satisfaction.⁴⁸

This stratified management approach, supported predominantly by level B evidence, provides clinicians with evidence-based guidance tailored to individual risk profiles. The stratification model facilitates optimal resource allocation while potentially improving LNG-IUS retention rates and therapeutic outcomes compared to standardized management protocols. Prospective validation through randomized controlled trials would further strengthen the evidence base for this personalized approach to LNG-IUS management in adenomyosis.

Evidence Assessment and Limitations

The evidence supporting our risk stratification framework derives predominantly from retrospective and prospective cohort studies rather than randomized controlled trials. Analysis of studies summarized in Table 2 indicates level B evidence across all risk categories, with notable variations in methodological rigor and sample size. Studies supporting low and moderate-risk management strategies generally demonstrate greater methodological consistency and larger sample sizes, as exemplified by Youm et al (n=481)³ and Peng et al (n=273).³³ Conversely, high-risk management evidence, while showing promising results with substantially reduced expulsion rates through advanced fixation techniques, often relies on smaller cohorts ranging from 12¹³ to 79 participants.⁷

Key limitations of the current evidence include: methodological heterogeneity across studies; limited follow-up duration beyond 12–24 months; post-hoc analysis of studies not specifically designed to evaluate risk-stratified

approaches; and potential publication bias favoring positive outcomes, particularly for novel interventional techniques. Future research should prioritize prospective validation of risk stratification models, standardization of outcome measures, and comparative studies of interventions within defined risk categories.

Conclusions

The three-tiered risk stratification model provides a clinically applicable framework for individualizing levonorgestrel-releasing intrauterine system (LNG-IUS) management in adenomyosis patients. Integration of available evidence supports differentiated management strategies according to patient risk profiles, potentially optimizing both resource allocation and clinical outcomes. This approach systematically incorporates anatomical, procedural, and patient-specific variables into clinical decision-making, addressing the multifactorial nature of LNG-IUS expulsion.

Current evidence provides reasonable support for risk-specific interventions, though opportunities exist to strengthen this evidence base through rigorous prospective validation. Development of standardized risk assessment tools and implementation of comparative trials would advance clinical practice in this domain. The risk-stratified approach represents a step toward precision medicine in adenomyosis management. Current evidence supports its implementation as a promising approach to clinical decision-making.

Data Sharing Statement

This narrative review is based on previously published studies cited in the reference list.

Ethical Approval Statement

Ethical approval was not required for this narrative review as it did not involve human participants or original data collection.

Disclosure

The authors declare no conflicts of interest in this work.

References

- Lazaridis A, Grammatas AL, Spencer S, Hirsch M. Nonsurgical management of adenomyosis: an overview of current evidence. *Curr Opin Obstet Gyn.* 2022;34:315–323. doi:10.1097/GCO.0000000000000810
- Etrusco A, Barra F, Chiantera V, et al. Current medical therapy for adenomyosis: from bench to bedside. *Drugs.* 2023;83(17):1595–1611. doi:10.1007/s40265-023-01957-7
- Youm J, Lee HJ, Kim SK, Kim H, Jee BC. Factors affecting the spontaneous expulsion of the levonorgestrel-releasing intrauterine system. *Int J Gynecol Obstet.* 2014;126(2):165–169. doi:10.1016/j.ijgo.2014.02.017
- Hong Y, Wang S, Fu X, Lan R, Gong H. Effect of modified levonorgestrel-releasing intrauterine system in human adenomyosis with heavy menstrual bleeding. *J Obstet Gynaecol Re.* 2021;48:161–168.
- Park DS, Kim M, Song T, et al. Clinical experiences of the levonorgestrel-releasing intrauterine system in patients with large symptomatic adenomyosis. *Taiwanese J Obstet Gynecol.* 2015;54(4):412–415. doi:10.1016/j.tjog.2014.05.009
- Magalhaes J, Ferreira-Filho ES, Soares-Junior JM, Baracat EC. Uterine volume, menstrual patterns, and contraceptive outcomes in users of the levonorgestrel-releasing intrauterine system: a cohort study with a five-year follow-up. *Euro J Obstet Gynecol Reprod Biol.* 2022;276:56–62. doi:10.1016/j.ejogrb.2022.06.029
- Lv N, Guo J, Yuan Q, Shen S, Chen Q, Tong J. Feasibility and effectiveness of hysteroscopic suture fixation of the levonorgestrel-releasing intrauterine system in the treatment of adenomyosis. *J Minimally Invasive Gynecol.* 2024;31(1):57–63. doi:10.1016/j.jmig.2023.10.012
- Valdés-Bango M, Ros C, Daza M, et al. Internal and external adenomyosis phenotypes: ultrasound features and association with clinical outcomes. *Human Reproduct.* 2024;39(7):1471–1480. doi:10.1093/humrep/deae105
- Cozzolino M, Pellicer N, Galliano D, Pellicer A. Pituitary suppression with GnRH agonists before ART may be insufficient to treat women with severe adenomyosis. *Reproduct BioMed Online.* 2023;46(1):150–155. doi:10.1016/j.rbmo.2022.09.023
- Struble J, Reid S, Bedaiwy MA. Adenomyosis: a clinical review of a challenging gynecologic condition. *J Minim Invas Gyn.* 2016;23(2):164–185. doi:10.1016/j.jmig.2015.09.018
- Zheng Z, Wang N, Wang J, Gan X, Zheng Q, Ke P. Effect of levonorgestrel-releasing intrauterine system combined with GnRH analogue for treatment of large adenomyosis. *Nan Fang Yi Ke Da Xue Xue Bao.* 2010;30(3):541–543,546.
- Kang Y, Sang C, Zhao L, Ding K, Zhao S. High-intensity focused ultrasound combined with hysteroscopic insertion of levonorgestrel-releasing intrauterine system for intrinsic adenomyosis: a retrospective observational study. *Int J Hyperther.* 2025;42(1):2531028. doi:10.1080/02656736.2025.2531028
- Zhang H, Cao B, Tong J, et al. An innovative surgical approach: suture fixation of the levonorgestrel-releasing intrauterine system in the treatment of adenomyosis. *BMC Women's Health.* 2022;22(1):451. doi:10.1186/s12905-022-01932-6

14. Ozdegirmenci O, Kayikcioglu F, Akgul MA, et al. Comparison of levonorgestrel intrauterine system versus hysterectomy on efficacy and quality of life in patients with adenomyosis. *Fertility Sterility*. 2011;95(2):497–502. doi:10.1016/j.fertnstert.2010.10.009
15. Shaaban OM, Ali MK, Sabra AMA, Abd El Aal DEM. Levonorgestrel-releasing intrauterine system versus a low-dose combined oral contraceptive for treatment of adenomyotic uteri: a randomized clinical trial. *Contraception*. 2015;92(4):301–307. doi:10.1016/j.contraception.2015.05.015
16. Hai N, Hou Q, Guo R. Ultrasound-guided transvaginal radiofrequency ablation combined with levonorgestrel-releasing intrauterine system for symptomatic uterine adenomyosis treatment. *Int J Hyperther*. 2021;38(1):65–69. doi:10.1080/02656736.2021.1874063
17. Braghetto AM, Caserta N, Bahamondes L, Petta CA. Effectiveness of the levonorgestrel-releasing intrauterine system in the treatment of adenomyosis diagnosed and monitored by magnetic resonance imaging. *Contraception*. 2007;76(3):195–199. doi:10.1016/j.contraception.2007.05.091
18. Lee KH, Kim JK, Lee MA, et al. Relationship between uterine volume and discontinuation of treatment with levonorgestrel-releasing intrauterine devices in patients with adenomyosis. *Arch Gynecol Obstet*. 2016;294(3):561–566. doi:10.1007/s00404-016-4105-y
19. Abbas AM, Samy A, Atwa K, et al. The role of levonorgestrel intra-uterine system in the management of adenomyosis: a systematic review and meta-analysis of prospective studies. *Acta Obstetrica et Gynecologica Scandinavica*. 2020;99(5):571–581. doi:10.1111/aogs.13798
20. Bachofner M, Blickenstorfer K, Huttmacher J, Wehrle L, Leeners B, Merki-Feld G. Intrauterine device continuation rates and reasons for discontinuation in a central European clinic with a high standard of care and ultrasound follow-up: a retrospective cohort study. *Eur J Contracep Repr*. 2018;23:407–414.
21. Baradwan S, Alshahrani MS, Alnoury A, et al. Does ultrasound guidance provide pain relief during intrauterine contraceptive device insertion? A systematic review and meta-analysis of randomized controlled trials. *J Ultrasound Med*. 2023;42(7):1401–1411. doi:10.1002/jum.16166
22. Harvey C, Bateson D, Wattimena J, Black KI. Ease of intrauterine contraceptive device insertion in family planning settings. *Aust New Zealand J Obstet Gynaecol*. 2012;52:534–539. doi:10.1111/ajo.12007
23. Harris S, Kaneshiro B, Ahn HJ, Saito-Tom L. Timing of insertion affects expulsion in patients using the levonorgestrel 52 mg intrauterine system for noncontraceptive indications. *Contraception*. 2021;103(3):185–189. doi:10.1016/j.contraception.2020.11.012
24. Zhang P, Song K, Li L, Yukuwa K, Kong B. Efficacy of combined levonorgestrel-releasing intrauterine system with gonadotropin-releasing hormone analog for the treatment of adenomyosis. *Med Principles Prac*. 2013;22(5):480–483. doi:10.1159/000351431
25. Li L, Leng J, Jia S, Lang J. Treatment of symptomatic adenomyosis with the levonorgestrel-releasing intrauterine system. *Int J Gynecol Obstet*. 2019;146(3):357–363. doi:10.1002/ijgo.12887
26. Madden T, McNicholas C, Zhao Q, Secura GM, Eisenberg DL, Peipert JF. Association of age and parity with intrauterine device expulsion. *Obstet Gynecol*. 2014;124(4):718–726. doi:10.1097/AOG.0000000000000475
27. Aoun J, Dines VA, Stovall DW, Mete M, Nelson CB, Gomez-Lobo V. Effects of age, parity, and device type on complications and discontinuation of intrauterine devices. *Obstet Gynecol*. 2014;123(3):585–592. doi:10.1097/AOG.0000000000000144
28. Higgins JA, Kramer RD, Everett B, Wright KQ, Turok DK, Sanders JN. Association between patients' perceptions of the sexual acceptability of contraceptive methods and continued use over Time. *JAMA Internal Med*. 2021;181(6):874–876. doi:10.1001/jamainternmed.2021.1439
29. Gomez AM, Hartofelis EC, Finlayson S, Clark JB. Do knowledge and attitudes regarding intrauterine devices predict interest in their use? *Women's Health Issues*. 2015;25(4):359–365. doi:10.1016/j.whi.2015.03.011
30. Khan KN, Kitajima M, Hiraki K, et al. Changes in tissue inflammation, angiogenesis and apoptosis in endometriosis, adenomyosis and uterine myoma after GnRH agonist therapy. *Human Reproduct*. 2010;25(3):642–653. doi:10.1093/humrep/dep437
31. Zhang B, Shi J, Gu Z, et al. The role of different LNG-IUS therapies in the management of adenomyosis: a systematic review and meta-analysis. *Reproduct Biolog Endocrinol*. 2025;23(1):23. doi:10.1186/s12958-025-01349-4
32. Stratopoulou CA, Donnez J, Dolmans M. Conservative management of uterine adenomyosis: medical vs. *Surg Approach J Clin Med*. 2021;10.
33. Peng F, Wu M, Yang J, Chen S, Ho H, Yang Y. Insertion of the Mirena intrauterine system for treatment of adenomyosis-associated menorrhagia: a novel method. *Taiwanese J Obstet Gynecol*. 2010;49(2):160–164. doi:10.1016/S1028-4559(10)60034-4
34. Mao M, Gou Y, Luo Z, Li Y, Tong Y. The suture fixation of the levonorgestrel-releasing intrauterine device with hysteroscope for the treatment of adenomyosis in patients at high risk of device expulsion—a prospective observational study. *BMC Women's Health*. 2024;24(1):556. doi:10.1186/s12905-024-03390-8
35. Yu Y, Zhang H, Sui L, Chen L. Clinical application of a novel hysteroscopic LNG-IUS non-suture fixation at the uterine fundus. *Front Med*. 2025;12:1563888. doi:10.3389/fmed.2025.1563888
36. Lai Z, Dong J, Zhang Y, Wu J. Suture fixation of levonorgestrel-releasing device using the hysteroscopic surgery system. *JSLS-J Soc Laparoend*. 2025;29.
37. Burla L, Kalaitzopoulos DR, Samartzis N, et al. Recommendations for the implementation and conduct of multidisciplinary team meetings for those providing endometriosis and adenomyosis care – a Delphi consensus of the European endometriosis league (EEL). *Facts Views Vision ObGyn*. 2024;16(3):337–350. doi:10.52054/FVVO.16.3.038
38. Fang QY, Campbell N, Mooney SS, Holdsworth-Carson SJ, Tyson K. Evidence for the role of multidisciplinary team care in people with pelvic pain and endometriosis: a systematic review. *Aust New Zealand J Obstet Gynaecol*. 2024;64(3):181–192. doi:10.1111/ajo.13755
39. Duncan J, Delara R, Ranieri G, Wasson M. Management of endometriosis: a call to multidisciplinary approach. *J Osteopath Med*. 2025;125(6):305–313. doi:10.1515/jom-2024-0105
40. Staudt MD. The multidisciplinary team in pain management. *Neurosurg Clin North Ame*. 2022;33(3):241–249. doi:10.1016/j.nec.2022.02.002
41. Chapron C, Marcellin L, Borghese B, Santulli P. Rethinking mechanisms, diagnosis and management of endometriosis. *Nat Rev Endocrinol*. 2019;15(11):666–682. doi:10.1038/s41574-019-0245-z
42. Vannuccini S, Petraglia F, El Moshy S. Recent advances in understanding and managing adenomyosis. *F1000Res*. 2019;8:8. doi:10.12688/f1000research.17047.1
43. Colivicchi F, Di Fusco SA. Cardiovascular risk stratification: from algorithms to clinical phenotype. *Gital Cardiol*. 2025;26:e1–e5.
44. Shen Q, Shan Y, Xu W, et al. Risk stratification of thymic epithelial tumors by using a nomogram combined with radiomic features and TNM staging. *Euro Radiol*. 2021;31(1):423–435. doi:10.1007/s00330-020-07100-4
45. Wetwittayakhleng P, Kotri G, Bessissow T, Lakatos PL. How close are we to a success stratification tool for improving biological therapy in ulcerative colitis? *Expert Opinon Biolog Therapy*. 2024;24(6):433–441. doi:10.1080/14712598.2024.2371049

46. Vannuccini S, Luisi S, Tosti C, Sorbi F, Petraglia F. Role of medical therapy in the management of uterine adenomyosis. *Fertility Sterility*. 2018;109(3):398–405. doi:10.1016/j.fertnstert.2018.01.013
47. Fedele L, Bianchi S, Raffaelli R, Portuese A, Dorta M. Treatment of adenomyosis-associated menorrhagia with a levonorgestrel-releasing intrauterine device. *Fertility Sterility*. 1997;68(3):426–429. doi:10.1016/S0015-0282(97)00245-8
48. Lou J, Huang X, Zhang L, Xu P, Zhang X, Chen Z. The second generation endometrial ablation (NovaSure) improves efficacy of levonorgestrel-releasing intrauterine system in management of adenomyosis. *Zhejiang da xue Xue Bao Yi Xue Ban*. 2019;48(2):136–141. doi:10.3785/j.issn.1008-9292.2019.04.03
49. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ-Brit Med J*. 2008;336(7650):924–926. doi:10.1136/bmj.39489.470347.AD

Therapeutics and Clinical Risk Management

Publish your work in this journal

Therapeutics and Clinical Risk Management is an international, peer-reviewed journal of clinical therapeutics and risk management, focusing on concise rapid reporting of clinical studies in all therapeutic areas, outcomes, safety, and programs for the effective, safe, and sustained use of medicines. This journal is indexed on PubMed Central, CAS, EMBase, Scopus and the Elsevier Bibliographic databases. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/therapeutics-and-clinical-risk-management-journal>

Dovepress
Taylor & Francis Group