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Vaginal Estrogen for Urinary Tract Infection Prevention: A Narrative Review of Evidence, Guidelines, and Regulatory Gaps

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Short Title: Vaginal Estrogen in Recurrent Urinary Infection Prevention
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Abstract

Background: Recurrent urinary tract infections (rUTIs) are common in peri- and postmenopausal women and impose substantial symptom, quality of life, and antimicrobial stewardship burdens, with particularly high incidence and hospitalization costs documented in England and UK primary care populations. Vaginal estrogen, by restoring urogenital epithelium and the lactobacillus-dominant microbiome, is recommended in several guidelines for preventing rUTI; including UK antimicrobial prescribing guidance for rUTIs and European Association of Urology recommendations. However, most formulations are licensed only for genitourinary syndrome of menopause, not for UTI prophylaxis. This creates a mismatch between the growing clinical evidence base and the absence of a specific regulatory indication for rUTI prevention across major regulatory agencies, including the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which may contribute to underuse and clinician uncertainty. **Objectives:** To review and summarize the evidence on vaginal estrogen for prevention of recurrent urinary tract infections in peri- and postmenopausal women, with a particular focus on its use alone and in combination with antibiotic therapy, and on the gap between clinical guideline recommendations and regulatory product labelling. **Methods:** We conducted a structured narrative review focusing on randomized controlled trials and clinical practice guidelines that evaluate intravaginal estrogen for the prevention of rUTI in peri- and postmenopausal women. PubMed and Embase searches were performed using key terms for estrogen, urinary tract infection, and menopause, and were supplemented with targeted searches of major guidelines. Data were described in terms of study design, participant characteristics, estrogen formulations and dosing regimens, timing of initiation, comparators, outcome measures, and reported safety outcomes. **Outcome:** Evidence from five RCTs reported that low-dose vaginal estrogen, administered as creams, tablets, rings, or gels, reduced culture-confirmed rUTI episodes and improved vaginal health indices, with **no** head-to-head trials comparing estrogen formulations directly, precluding conclusions about the relative superiority of any single preparation, and a favorable local safety profile. One trial found estriol pessaries less effective than antibiotic prophylaxis for rUTI prevention, suggesting that estrogen alone may be insufficient in some women and that combined regimens warrant further investigation, although no trial has directly evaluated concurrent antibiotic and estrogen therapy. Initiation was predominantly prophylactic or post-antibiotic, and no identified trial evaluated co-initiation of vaginal estrogen with antibiotics at the onset of acute UTI, highlighting a persisting evidence gap regarding optimal timing of therapy. **Conclusions and Outlook:** Vaginal estrogen is an evidence-based yet underutilized strategy for rUTI prevention in peri- and postmenopausal women, supported by RCT data and guideline recommendations, but not recognized in current FDA-approved indications for vaginal estrogen products. Closing this evidence licensing gap will require regulatory reconsideration informed by existing trial data, alongside new pragmatic studies to refine timing, dosing, and formulation choices, to evaluate co-administration with antibiotics, and to refine timing, dosing, and formulation choices, and to evaluate the efficacy of combined estrogen and antibiotic co-administration; patient-centred research on women's preferences, acceptability, and shared decision-making should follow once optimal therapeutic parameters have been established, as the nature of treatment will determine patient experience and response.

Background

Urinary tract infections (UTIs) place a substantial burden on patients and healthcare systems. Approximately 189,756 hospital admissions related to UTI in England were reported in 2023-2024, accounting for around 1.2 million bed-days and costing over £604 million [1]. The risk of UTIs increases with age, and among adults aged 65 and older, 21 % experienced at least one clinically diagnosed UTI over a 10-year primary care period [2]. Specifically in women, this incidence rose progressively from 9–11 per 100 person-years (ages 65–74) to 11–14 (75–84), and 15–20 (>85) per 100 person-years [2], reflecting the vulnerability of postmenopausal women. Furthermore, recurrent urinary tract infections (rUTIs), typically defined as ≥2 infections within 6 months or ≥3 within 12 months, are particularly common in this population and substantially impair quality of life and increase the overall healthcare burden [3, 4]. Beyond economic costs, rUTIs contribute to clinical challenges, including frequent symptoms, increased antibiotic use with associated risks of resistance, and overlap with menopause-related urogenital symptoms complicating management [3, 4].

Beyond economic costs, rUTIs contribute to clinical and psychosocial challenges, including frequent symptoms, increased antibiotic use with associated resistance risks, and impacts on quality of life including anxiety, reduced social interactions, and impaired sexual wellbeing] [5]. A large UK survey of 1096 women with recent UTIs identified that recurrent infections were linked to increased urinary incontinence, urgency, and persistent discomfort, resulting in marked impairment of daily functioning (OR 1.93, 95% CI 1.52–2.44 for symptom severity; OR 1.68, 95% CI 1.32–2.14 for impact on daily life) [6]. These findings highlight the burden of rUTIs in postmenopausal women and the need for improved preventive strategies to meet the needs of this population. Existing evidence suggests that the decline of estrogen post-menopause disrupts the vaginal microbiome, increasing susceptibility to urinary pathogens such as E. coli and Klebsiella [7]. Consequently, vaginal estrogen therapy is frequently used to prevent rUTIs in postmenopausal women. By restoring estrogen levels in the vaginal mucosa, these treatments promote the rebuilding of the vaginal microbiome, notably increasing the presence of beneficial lactobacilli, which help protect against infections [8]. This shift contributes to maintaining an acidic vaginal environment by lowering pH to premenopausal levels, thereby inhibiting the proliferation of pathogenic microorganisms [9].

The clinical practice guidelines recommend vaginal estrogen for UTI prevention, based on strong evidence that it restores mucosal defense and reduces infection rates by up to 50–75% in some trials [10-12]. Commonly used formulations in clinical practice include local preparations such as tablets, creams, and rings [13]. Importantly, several studies have confirmed the safety of these formulations due to their minimal systemic absorption [14-16]. However, these treatments currently lack a specific regulatory indication for the prevention of rUTIs. Vaginal estrogen products remain approved primarily for genitourinary syndrome of menopause under the regulatory frameworks of the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the UK Medicines and Healthcare Products Regulatory Agency (MHRA), despite recommendations in clinical guidelines for rUTI prevention [17-19]. Notably, in 2025, the FDA convened an expert panel that recommended removing outdated black box warnings on vaginal estrogen products, citing minimal systemic risk and positive clinical benefits, including UTI prevention [20]. This misalignment between guideline-endorsed practice and regulatory indications may contribute to underuse in women's healthcare settings and to uncertainty among gynecologists and primary care clinicians. Therefore, the aim of this review is to summarize (i) evidence from RCTs on the efficacy and timing of vaginal estrogen therapy for rUTI prevention, (ii) current clinical guideline recommendations, and (iii) gaps between guideline recommendations and regulatory labelling.

Methods

Study design and eligibility criteria

We conducted a structured narrative review to summarize the clinical evidence on intravaginal estrogen for the prevention of rUTI in peri- and postmenopausal women, rather than performing a formal quantitative analysis. We included studies of peri- or postmenopausal women with a history of rUTI in whom local or intravaginal estrogen was used as a preventive strategy, when UTI-related outcomes were reported. Eligible evidence comprised RCTs addressing vaginal estrogen in the context of rUTI. Searches were limited to human subjects, with no date restriction, and to English-language publications. We supplemented database searches by screening the reference lists of relevant studies and by hand-searching key guideline and regulatory agency websites. While we excluded studies of systemic menopausal hormone therapy without a local estrogen component, studies without UTI-related or urogenital outcomes, pediatric or pregnant populations, and non-human or purely mechanistic laboratory work.

Search strategy and study selection

A focused literature search was conducted in MEDLINE (PubMed) and Embase to identify studies evaluating intravaginal or topical estrogen in peri- and postmenopausal women with acute or recurrent UTI. Searches were conducted from database inception to September 2025. The search combined terms for estrogen and intravaginal administration (e.g., estradiol, estriol, vaginal cream, tablets, rings, gels), urinary tract infection (e.g., UTI, cystitis, recurrent UTI, bladder infection), and menopause (perimenopause, postmenopause). Using comprehensive MeSH terms ("Estrogens"[Mesh] OR "Vaginal Creams"[Mesh] OR "Administration, Intravaginal"[Mesh] OR vaginal[tiab] OR intravaginal[tiab] OR Oestrogen*[tiab] OR Estrogen*[tiab] OR Estradiol[tiab] OR Estriol[tiab] OR "Conjugated Estrogens"[tiab] OR Estrace[tiab] OR Estrofem[tiab] OR Estring[tiab] OR Ovestin[tiab] OR Vagifem[tiab] OR Estrogel[tiab] OR Ethinylestradiol[tiab] OR Diethylstilbestrol[tiab] OR Divigel[tiab] OR Premarin[tiab] OR Prempro[tiab] OR Climara[tiab] OR "Transvaginal Estrogen"[tiab] OR "Topical Estrogen"[tiab]) AND ("Urinary Tract Infections"[Mesh] OR UTI[tiab] OR rUTI[tiab] OR "Recurrent Urinary Tract Infection"[tiab] OR Cystitis[tiab] OR "Bladder infection"[tiab] OR "Urethral infection"[tiab] OR Pyelonephritis[tiab]) AND ("Menopause"[Mesh] OR "Perimenopause"[Mesh] OR "Postmenopause"[Mesh] OR Menopaus*[tiab] OR Perimenopaus*[tiab] OR Postmenopaus*[tiab]).

Data extraction and synthesis

Data extraction focused on study characteristics, effectiveness outcomes, and safety. For each included study, we recorded design, setting, sample size, population (including menopausal status and rUTI definition), estrogen formulation and dose, route and timing of initiation (prophylactic, post-treatment, or started during an acute UTI), comparators, follow-up duration, and any concurrent preventive strategies. Effectiveness and safety information were extracted as reported by the original authors, recognizing that specific outcome measures and definitions varied substantially between studies. Given clinical and methodological heterogeneity, findings are presented descriptively, with particular attention to estrogen formulation, dose, and timing, and to whether concurrent antibiotic prophylaxis or other non-antibiotic strategies were used.

Results

Randomized controlled trials from 1993 onwards generally demonstrate that low-dose vaginal estrogen reduces culture-confirmed rUTI in postmenopausal women, while also improving vaginal ecological markers such as lactobacilli colonization and pH [21-25] **[Table 1]**. In the landmark trial by Raz and Stamm, intravaginal estriol cream (0.5 mg nightly for 2 weeks, then twice weekly) reduced the incidence of UTI from 5.9 to 0.5 episodes per patient-year compared with placebo, and restored lactobacilli in 61% of treated women, versus none in the placebo group [24]. Subsequent trials of estradiol-releasing vaginal rings and low-dose creams or gels have shown similar reductions in recurrence risk relative to placebo, with number-needed-to-treat estimates in the range of 3–4 when evaluated in systematic reviews [13, 25]. One head-to-head trial comparing estriol-containing vaginal pessaries with nitrofurantoin macrocrystals demonstrated that the estrogen-only regimen was less effective than daily antibiotic prophylaxis in preventing rUTI episodes over 9 months, demonstrating superior efficacy of antibiotic prophylaxis [26]. This study highlights that while vaginal estrogen is beneficial, it may not fully replace antibiotic prophylaxis in all women, and that the choice of regimen needs to balance efficacy with antimicrobial stewardship considerations (i.e., the principles guiding judicious antibiotic use to minimize resistance, adverse effects, and preserve long-term antimicrobial effectiveness, including reducing cumulative antibiotic exposure through non-antibiotic alternatives such as vaginal estrogen).

Across trials, adverse events were primarily local (vaginal discharge, pruritus, spotting), and systemic estrogen levels remained low or within the postmenopausal range in most studies, supporting a favorable safety profile in women. These safety data are consistent with broader reviews of low-dose vaginal estrogen, which report minimal systemic absorption and no clear increase in major adverse cardiovascular or thromboembolic events [14, 15, 27]. Nevertheless, caution is advised for women with a history of hormone-sensitive malignancy, in whom the use of vaginal estrogen should be individualized and guided by shared decision-making with oncology or menopause specialists in line with contemporary guidelines and consensus recommendations. Recognized contraindications to vaginal estrogen include: undiagnosed abnormal uterine or vaginal bleeding; known, suspected, or history of hormone-sensitive malignancy (requiring specialist guidance); active thromboembolic disease; known hypersensitivity to any component of the preparation; and active liver disease. In shared decision-making for women with a history of hormone-sensitive cancer, the clinician treating the UTI should present evidence on the minimal systemic absorption of low-dose vaginal estrogen, discuss alternatives (including non-hormonal vaginal moisturizers and antibiotic prophylaxis), and actively involve the oncology team; oncological safety considerations take precedence where genuine uncertainty remains, but the morbidity of frequent rUTIs,

including antibiotic burden, hospitalizations, and quality-of-life impairment should be weighed against the theoretical oncological risk.

Guidelines vs FDA labelling

Major urology and primary care guidelines now clearly endorse vaginal estrogen as a preventive option for rUTI in postmenopausal women. The American Urological Association (AUA)/Canadian Urological Association (CUA)/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) guideline on recurrent uncomplicated UTIs states that clinicians should recommend vaginal estrogen therapy in peri- and postmenopausal women with rUTI, provided there is no contraindication (Moderate recommendation; Grade B)[10]. The EAU urological infections guideline similarly recommends vaginal estrogen replacement in postmenopausal women to reduce recurrence risk, with a strong recommendation rating[28]. NICE antimicrobial prescribing guidance for recurrent UTI also summarizes high and moderate quality evidence supporting estriol cream and estradiol rings in this population [29].**[Figure1]**

FDA label gap

In contrast, FDA-approved vaginal estrogen products commonly used in clinical practice retain indications focused on genitourinary syndrome of menopause[30-32]. The Vagifem 10-µg estradiol vaginal tablet is indicated for the treatment of atrophic vaginitis due to menopause; recurrent UTI prevention is not listed as an indication[32]. The Estring estradiol vaginal ring is similarly indicated for moderate to severe symptoms of vulvar and vaginal atrophy due to menopause, and Premarin vaginal cream is indicated for atrophic vaginitis and related menopausal symptoms, without any mention of rUTI prophylaxis [33, 34]. This divergence between guideline-supported practice and product labelling underscores an “evidence–licensing” gap that may undermine clinician confidence, constrain reimbursement pathways, and ultimately restrict patient access in women’s healthcare settings.

In 2025, federal health authorities and expert panels in the United States moved to reconsider and revise boxed warnings on low-dose vaginal estrogen products, citing data that these preparations achieve serum estradiol levels within the postmenopausal range and are not associated with increased risks of breast cancer, cardiovascular events, or stroke seen with systemic hormone therapy[35, 36]. These emerging labelling changes and calls to remove outdated boxed warnings primarily address safety messaging rather than adding new indications, but by formally recognizing the limited systemic absorption and favorable safety profile of low-dose vaginal estrogen, they may lower barriers to future consideration of rUTI prevention as an explicit, evidence-based indication in peri- and postmenopausal women.

Discussion

The burden of recurrent UTI in postmenopausal women is high in terms of its impact on healthcare costs, morbidity, and quality of life. Current preventive options, such as antibiotics, face issues of resistance and side effects, making alternative approaches like local estrogen clinically important [37]. The management of recurrent UTIs varies according to institutional guidelines and patients' preferences. The recent clinical practice guidelines from the urology associations, including the AUA and the EAU, emphasize a patient-centered approach that considers both the effectiveness of treatment (i.e., evidence-based pharmacological preventive strategies including antibiotic prophylaxis and vaginal estrogen) and antimicrobial stewardship (coordinated programs and principles promoting appropriate selection, dosing, route, and duration of antimicrobial therapy to minimize resistance, adverse effects, and costs, including the use of non-antibiotic alternatives where appropriate)[10]. **Figure 2** summarizes a pragmatic, evidence-informed clinical approach to using low-dose vaginal estrogen for rUTI prevention in peri- and postmenopausal women.

Antibiotic prophylaxis with agents such as nitrofurantoin, cephalexin, and trimethoprim/sulfamethoxazole has demonstrated effectiveness in preventing recurrent UTIs, with reported success rates reaching 94% [10, 38]. However, despite their efficacy, antibiotic prophylaxis carries significant drawbacks, including secondary fungal infections, disruption of gastrointestinal flora, and the development of antibiotic resistance, all of which complicate future treatment [39]. Additionally, prolonged use of these agents has been associated with serious adverse effects such as hepatic and renal toxicity, which may necessitate extended hospitalization and increase healthcare burden [39]. Therefore, alternative preventive strategies, such as local estrogen use, may help reduce this burden. However, the limited literature on the use of vaginal estrogen formulations remains a barrier. This lack of high-quality, contemporary randomized controlled trial data limits our understanding of the effectiveness and optimal dosing of modern vaginal estrogen formulations, particularly regarding whether their combination with antibiotics can improve UTI outcomes. Critically, the optimal duration of local vaginal oestrogen therapy for rUTI prevention has not been established by any RCT. In the available trials, treatment was administered for 6 to 12 months, yet it remains unclear whether protection persists beyond this period, whether indefinite use is

required to sustain benefit, or whether a defined course followed by clinical reassessment is sufficient. Current guidelines do not specify a recommended duration, and clinical practice varies widely in this regard. No trial has systematically evaluated the optimal duration of vaginal estrogen in relation to antibiotic prophylaxis, nor whether the two should be initiated simultaneously or sequentially. In the available RCTs, vaginal estrogen was used as a stand-alone prophylactic strategy over 6–12 months; no trial has evaluated co-tapering or sequential strategies. Based on the biological rationale that vaginal estrogen requires several weeks to restore mucosal defenses, provisional expert-informed guidance suggests that where both therapies are used, vaginal estrogen may be commenced concurrently with antibiotic prophylaxis, with a view to antibiotic de-escalation after approximately 3–6 months once estrogenic mucosal restoration is evident; however, this approach requires prospective validation.

Observational cohort data further support the effectiveness of vaginal estrogen in routine clinical practice [40, 41]. In a retrospective cohort of postmenopausal women offered vaginal estrogen as first-line prophylaxis for rUTI, around 60–70% of participants had a clinically meaningful reduction in recurrence (≥50% fewer culture-confirmed episodes), whereas approximately 30–40% still required additional preventive strategies such as antibiotic prophylaxis or non-antibiotic measures [40]. In a separate cohort of hypoestrogenic women with rUTI, vaginal estrogen use was associated with a statistically significant decrease in documented recurrences, with recurrence rates falling from roughly 2–3 UTIs per woman-year at baseline to around 1 UTI per woman-year on treatment, corresponding to an estimated relative risk reduction in the order of 25–40%, and a parallel reduction in unplanned healthcare visits for UTI [41]. Across these studies, treatment persistence with vaginal estrogen exceeded 70–80% over follow-up, and serious adverse events were rare, supporting its feasibility as a long-term preventive option in appropriately selected women. Taken together, these observational data suggest that vaginal estrogen can substantially lower rUTI burden in a majority of postmenopausal and hypoestrogenic women, while underlining that a sizeable minority will still require additional measures and may benefit from better risk stratification. Notably, these observational studies did not define a fixed duration of vaginal oestrogen use; treatment was typically continued for as long as the patient remained in follow-up (12 months or more), with no protocol-defined stopping rule. Whether a minimum duration of treatment is required to achieve and maintain recurrence reduction, and whether cessation leads to a return of rUTI susceptibility, are important unanswered questions. For clinical practice, in the absence of contraindications, it is reasonable to initiate vaginal oestrogen with the intent of long-term or indefinite use, subject to periodic reassessment of tolerability, adherence, and ongoing benefit. Combined vaginal oestrogen and antibiotic prophylaxis regimens should similarly follow a structured review at 3 to 6 months to determine whether antibiotic de-escalation is appropriate once mucosal restoration is achieved. Proposed stratification levels include: (1) Low risk — postmenopausal women with ≥2 culture-confirmed UTIs in 6 months, no significant comorbidities, and no contraindications to vaginal estrogen, who may be managed with vaginal estrogen as first-line prevention; (2) Intermediate risk — women with higher UTI frequency (≥3/year), antimicrobial resistance, or suboptimal response to estrogen alone, who may benefit from combined estrogen plus antibiotic prophylaxis; and (3) High risk — women with structural urological abnormalities, immunosuppression, or history of hormone-sensitive malignancy, who require specialist involvement and individualized management. Prospective validation of such a framework is needed.

This narrative review has several limitations. First, as a narrative rather than systematic review, the study selection process may be subject to selection bias and does not include a formal risk-of-bias assessment or quantitative meta-analysis. Second, the available randomized trials are relatively small and heterogeneous in terms of populations, estrogen formulations, dosing regimens, outcome definitions, and follow-up duration, which limits direct comparison between studies. Third, only English-language publications were included, which may introduce language bias. Finally, the review focused primarily on randomized trials and major guidelines and may not fully capture all relevant real-world or emerging evidence. Despite these limitations, this review provides a clinically relevant synthesis of evidence, guideline recommendations, and regulatory considerations to support informed decision-making in the prevention of recurrent UTI in peri- and postmenopausal women.

Conclusion

This review highlights that vaginal estrogen represents a potentially underutilized, biologically coherent, and guideline-endorsed strategy that can reduce recurrence rates while potentially lowering cumulative antibiotic exposure in peri- and postmenopausal women with rUTI. Yet the absence of an explicit FDA indication for rUTI prophylaxis, historical safety concerns about hormone therapy, and limited data on women's preferences and adherence all contribute to an implementation gap in routine gynecologic care. Addressing this gap will require regulatory reconsideration of labelling and prioritized RCTs. The most important research questions, in order, are:

first, head-to-head trials comparing vaginal estrogen formulations (e.g., estriol cream versus estradiol tablet versus estradiol ring) for rUTI prevention; second, adequately powered trials of combined vaginal estrogen plus antibiotic prophylaxis versus antibiotic prophylaxis alone; and third, trials evaluating co-initiation of vaginal estrogen at the onset of acute UTI versus prophylactic-only initiation. Patient-centered research on acceptability, adherence, and shared decision-making should be designed after the biological and pharmacological parameters of treatment have been established, as the nature and schedule of treatment will substantially determine patient burden and response.

Statements

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

R.G: Conceptualization, writing, review and editing; A.S: Conceptualization, writing, review and editing; W.M: Conceptualization, writing, review and editing.

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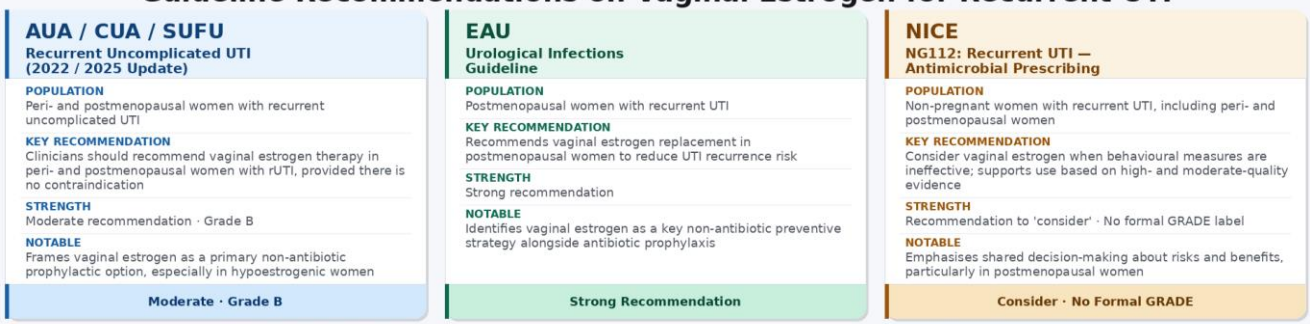
Figures

Figure 1. Guideline recommendations on vaginal estrogen for prevention of recurrent urinary tract infection in peri- and postmenopausal women.

Figure 2. Suggested treatment algorithm for vaginal estrogen in peri- and postmenopausal women with recurrent urinary tract infection, integrating randomized trial evidence and major guideline recommendations reviewed in this article.

Guideline Recommendations on Vaginal Estrogen for Recurrent UTI



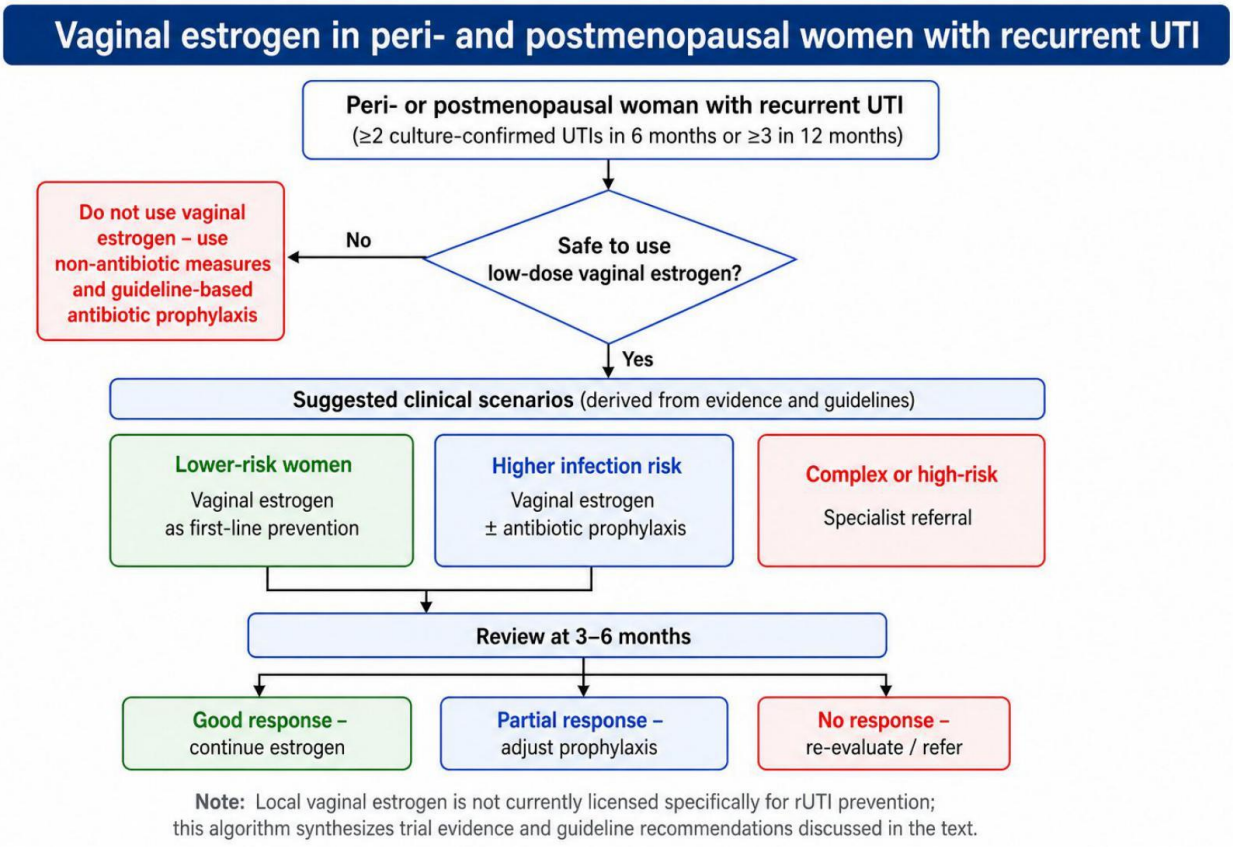


Table 1. ***Randomized controlled trials evaluating vaginal estrogen for prevention of recurrent urinary tract infection***

Study	Title	Year	Sample Size/Population	Study Intervention	Follow-up Duration	Outcomes
Ferrante KL et al. [21]	Vaginal Estrogen for Prevention of Recurrent UTI	2021	Postmenopausal women with rUTI (n=35)	Vaginal estrogen vs. placebo	6 months	Reduced incidence of UTI at 6 months; ITT analysis P=0.041; PP analysis P=0.036
Muiños Fernández N et al. [22]	Ultra-Low-Dose Estriol 0.005% Gel	2024	Postmenopausal with GSM + rUTI history (n=108)	Vaginal estriol 0.005% gel (50 µg estriol) vs. placebo	months 12	Decreased recurrent UTI rates with good safety
Raz R; Stamm WE [24]	Controlled Trial of Intravaginal Estriol	1993	Postmenopausal; ≥3 culture-confirmed UTIs/yr (n=93)	Intravaginal estriol cream (0.5 mg) daily initially, then twice weekly for 8 months vs. placebo	months 8	Significantly fewer UTI episodes
Raz R et al. [26]	Effectiveness of estriol-containing vaginal pessaries and nitrofurantoin macrocrystal therapy in the prevention of recurrent urinary tract infection in postmenopausal women	2003	Postmenopausal with rUTI (n=171)	Vaginal estriol pessary 0.5 mg twice weekly for 9 months vs nitrofurantoin macrocrystals 100 mg once daily for 9 months	9 months	Estriol was significantly less effective: 124 vs 48 UTIs (p = 0.0003); fewer women remained UTI-free (32.6% vs 48.2%)
Eriksen B et al. [25]	Efficacy of an oestradiol-releasing vaginal ring in the treatment of recurrent urinary tract infection	1999	Postmenopausal; recurrent symptomatic UTIs (n=108)	Oestradiol-releasing vaginal ring (Estring®) vs. control group	36 weeks	Significantly fewer UTIs and longer time to recurrence; restoration of lactobacilli; improved vaginal pH

Abbreviations: GSM, genitourinary syndrome of menopause; ITT, intention-to-treat; mg, milligram; n, number of participants; PP, per-protocol; rUTI, recurrent urinary tract infection; UTI, urinary tract infection; vs., versus; yr, year; µg, microgram.