

A rapid review

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Main messages

- 1. This purpose of this rapid review was to assess the evidence for the effectiveness of vaginal oestrogen to prevent primary urinary tract infections in women who are experiencing perimenopause, menopause, or postmenopause, including considering whether benefits outweighed any side effects (search up to 26 February 2024).
- 2. In total, 1,694 records from 6 databases were screened. However, no relevant evidence was identified to answer the review questions.

Purpose

The purpose of this rapid review was to identify and summarise the available evidence on the effectiveness of vaginal oestrogen in women who are experiencing perimenopause, menopause, or postmenopause to prevent primary urinary tract infections (UTIs). If benefits of vaginal oestrogen were identified, a secondary aim was to assess whether these benefits outweighed any side effects.

There were 2 review questions:

- 1. What is the effectiveness of vaginal oestrogen in women who are experiencing perimenopause, menopause, or postmenopause to reduce their risk of primary (non-recurrent) urinary tract infections (UTIs)?
- 2. Do any benefits of using vaginal oestrogen in women who are experiencing perimenopause, menopause, or postmenopause to reduce their risk of primary (non-recurrent) UTIs outweigh any side-effects?

Methods

A rapid review was conducted, following streamlined systematic methods to accelerate the review process (1). A literature search was undertaken to look for all relevant controlled trials or observational studies, published or available as preprint, up to 26 February 2024. The reference lists of relevant reviews were also checked to identify any additional relevant primary studies. Full details of the search are available in the protocol in Annexe A.

Screening on title and abstract was undertaken in duplicate by 2 reviewers for 20% of the eligible studies, with the remainder completed by one reviewer. Screening on full text was undertaken by one reviewer and checked by a second. Studies excluded on full text screening are available with the reasons for exclusion in Annexe B.

A protocol was produced before the literature search was conducted, including the review question, the eligibility criteria, and all other methods. Full details of the methodology are provided in the protocol in <u>Annexe A.</u> There were no deviations from the protocol.

For this review, any dose of any formulation of vaginal oestrogen (such as creams, pessaries, tablets, rings, or gels) was considered relevant to include.

Study definitions of experiencing perimenopause, menopause and postmenopause were used. If the menopause status of the study population was not stated, it was assumed women who were on average at least 65 years of age would be post-menopause and included in the review. Recurrent UTIs were defined as 2 UTIs in 6 months or at least 3 UTIs in one year in non-pregnant women, with non-recurrent (primary) UTIs defined as anything less frequent than this, in line with the European Association of Urology Guidelines (2).

Evidence

In total, 1,694 primary studies were screened at title and abstract, and 38 studies were screened at full text. However, none of these studies met the inclusion criteria. Additionally, citations of 5 systematic reviews identified at full text screening were checked, but no primary studies met the inclusion criteria. The main reasons for exclusion included being the wrong study design (19 studies), not English language (10 studies), and no relevant outcomes (4 studies). Although 19 of the studies were excluded due to wrong study design, they would not have provided information on the effectiveness of vaginal oestrogen, as most were narrative reviews or commentaries.

Health inequalities

Older women and post-menopausal women are at a higher risk of UTIs meaning they can experience more health inequity. However, there was no evidence identified in this review to consider impact on health inequality.

Limitations

This rapid review used streamlined systematic methods to accelerate the review process. Sources of evidence searched included databases of peer-reviewed and preprint research, but an extensive search of other sources was not conducted (such as websites of public health organisations), so it is possible relevant evidence may have been missed. Ten studies written in a language other than English were identified as potentially relevant on title and abstract screening, and so were excluded, but these studies may still have included relevant information to our research question.

Conclusion

The aim of this review was to identify and summarise the available evidence on the effectiveness of vaginal oestrogen to prevent primary UTIs in women who are experiencing perimenopause, menopause, or postmenopause, and to assess whether any benefits of using vaginal oestrogen to prevent primary UTIs outweigh any side effects. However, no relevant evidence was identified and therefore this review is unable to inform on the effectiveness of vaginal oestrogen in this population.

Acknowledgment

We would like to thank colleagues within the Clinical and Public Health Response division who either reviewed or input into aspects of the review.

Disclaimer

UKHSA's rapid reviews aim to provide the best available evidence to decision makers in a timely and accessible way, based on published peer-reviewed scientific papers, unpublished reports and papers on preprint servers. Please note that the reviews:

- use accelerated methods and may not be representative of the whole body of evidence publicly available
- have undergone an internal, but not independent, peer review
- are only valid as of the date stated on the review

In the event that this review is shared externally, please note additionally, to the greatest extent possible under any applicable law, that UKHSA accepts no liability for any claim, loss or damage arising out of, or connected with the use of, this review by the recipient or any third party including that arising or resulting from any reliance placed on, or any conclusions drawn from, the review.

References

- 1. Tricco AC and others. 'Rapid reviews to strengthen health policy and systems: a practical guide' 2017
- 2. Bonkat G and others. '<u>EAU Guidelines on Urological Infections</u>' European Association of Urology 2023
- 3. Borissov N and others. 'Reducing systematic review burden using Deduklick: a novel, automated, reliable, and explainable deduplication algorithm to foster medical research' Systematic Reviews 2022: volume 11, issue 1, page 172
- 4. Sterne JAC and others. 'RoB 2: a revised tool for assessing risk of bias in randomised trials' British Medical Journal 2019: volume 366, page I4898
- 5. Sterne JA and others. 'ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions' BMJ 2016: volume 355, page i4,919
- 6. Academy of Nutrition and Dietetics. '<u>Evidence Analysis Manual: Steps in the Academy Evidence Analysis Process</u>' Academy of Nutrition and Dietetics 2016

Annexe A. Protocol

Review question

There are 2 review questions:

- 1. What is the effectiveness of vaginal oestrogen in women who are experiencing perimenopause, menopause, or postmenopause to reduce their risk of primary (non-recurrent) urinary tract infections (UTIs)?
- 2. Do any benefits of using vaginal oestrogen in women who are experiencing perimenopause, menopause, or postmenopause to reduce their risk of primary (non-recurrent) UTIs outweigh any side-effects?

Vaginal oestrogen can be used in any dose or formulation, for example, creams, pessaries, tablets, rings, or gels. No specific age cut off for women will be used to define women who are experiencing perimenopause, menopause, or postmenopause, although if not otherwise stated, it will be assumed women who are at least 65 years of age would be postmenopause. Recurrent UTIs are defined here as 2 UTIs in 6 months or at least 3 UTIs in one year in non-pregnant women, with non-recurrent UTIs defined here as anything less frequent than this, in line with the European Association of Urology Guidelines.

Eligibility criteria

	Included	Excluded
Population	Women who are experiencing perimenopause, menopause, or postmenopause (including women at least 65 years of age, if menopause status is not otherwise stated), who do not have recurrent UTIs (defined as 2 UTIs in 6 months or at least 3 UTIs in one year in non-pregnant women)	Women who are premenopause (or under 65 years of age, if menopause status is not otherwise stated) or have recurrent UTIs (defined as 2 UTIs in 6 months or at least 3 UTIs in one year in non-pregnant women)
Settings	All	
Context	All	
Intervention	Vaginal oestrogen in any dose or formulation (for example, creams, pessaries, tablets, rings, or gels)	Any other treatment
Outcomes	Effectiveness and side effects of vaginal oestrogen when used to prevent primary (non-recurrent) UTIs, including, but not limited to: • incidence of adverse events, complications, safety, and tolerability • ability to carry out activities of daily living • patient experience • health and social care related quality of life, if considering side effects, including long term harm or disability • health and social care utilisation, including length of stay, planned and unplanned contacts • cost-effectiveness • mortality	
Language	English	Non-English language studies
Date of publication	Up to 26 February 2024	

	Included	Excluded
Study design	Controlled trials (including randomised controlled trials, quasi-experimental trials) Observational studies (including cohort studies, case control studies)	Systematic or narrative reviews (except when searching reviews for relevant studies) Guidelines Opinion pieces Laboratory studies Modelling studies
Publication type	Published and preprint	Conference abstracts

Identification of studies

OVID Medline, OVID Embase, CINAHL complete, Cochrane Central Register of Randomised Controlled Trials (CENTRAL), Web of Science Preprint Citation Index (1990 to current), and WHO International Clinical Trials Registry Platform will be searched for studies published up to 26 February 2024. The search strategy will be checked by another information specialist. Duplicate references will be removed using Deduklick (3).

Screening

Screening on title and abstract will be undertaken in duplicate by 2 reviewers for at least 10% of the eligible studies, with the remainder completed by one reviewer. Disagreement will be resolved by discussion.

Screening on full text will be undertaken by one reviewer and checked by a second.

Relevant reviews (systematic or otherwise) may be searched for primary studies.

Data extraction

Summary information for each study will be extracted and reported in tabular form. Information will include country, study period, study design, participants, results, and any relevant contextual data, including how the primary UTIs were diagnosed, for example by a clinician using urinary symptoms, urine cultures, or urine dipsticks. This will be undertaken by one reviewer and checked by a second.

Risk of bias of included primary studies will be assessed using the Cochrane RoB 2 tool for randomised controlled trials (4), the ROBINS-I tool for non-randomised studies of interventions

 $(\underline{5})$, or the QCC tool for other observational studies $(\underline{6})$. Risk of bias will be assessed by one reviewer and checked by a second.

Synthesis

Where suitable to pool, a narrative synthesis of the results for each outcome across studies will be presented, including the number of studies, the number of participants in each study, the range of effect sizes and their imprecision in each study, and a summary of the risks of bias across studies. If appropriate, a meta-analysis pooling effect estimates for possible outcomes will be conducted, although studies will need to be similar enough in their populations, methods, and statistical analyses, and comprehensive enough in their reporting, for meta-analysis to be possible. If the included studies are too diverse for narrative synthesis, studies will be summarised individually.

Variations across populations and subgroups, for example cultural variations or differences between ethnic or social groups will be considered, where evidence is available.

Search strategy

Ovid MEDLINE(R) ALL (1946 to 27 February 2024)

- 1. (exp Vagina/ or Administration, Intravaginal/) and (exp Estrogens/ or exp Hormone Replacement Therapy/)
- 2. (vagina* adj7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)).tw,kf.
- 3. (intravagina* adj7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)).tw,kf.
- 4. (transvagina* adj7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)).tw,kf.
- 5. (vagina* adj7 (pessar* or ring* or tablet* or cream* or gel*)).tw,kf.
- 6. (intravagina* adj7 (pessar* or ring* or tablet* or cream* or gel*)).tw,kf.
- 7. (transvagina* adj7 (pessar* or ring* or tablet* or cream* or gel*)).tw,kf.
- 8. ((topical* or local*) adj3 hormon*).tw,kf.
- 9. ((topical* or local*) adj3 (estrogen* or oestrogen* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)).tw,kf.
- 10. (Vagifem or Vagirux or Estring or Imvaggis or Blissel or Ovestin).tw,kf.
- 11. or/1-10
- 12. exp Urinary Tract Infections/
- 13. exp Cystitis/
- 14. (UTI or UTIs).tw,kf.
- 15. cystitis.tw,kf.
- 16. bacteriuria.tw,kf.

- 17. ((bladder* or genitourinar* or kidney* or pyelo* or renal* or ureter* or ureth* or urin* or urolog* or urogen*) adj7 infect*).tw,kf.
- 18. (bladder* adj5 (inflamm* or ulcer* or ulcus)).tw,kf.
- 19. ((bacteria* or microb*) adj5 (bladder* or genitourin* or kidney* or renal* or ureter* or ureth* or urin* or urolog* or urogen*)).tw,kf.
- 20. exp Urologic Diseases/
- 21. proteinuri*.tw,kf.
- 22. albuminuri*.tw,kf.
- 23. ((protein* or albumin*) adj5 urin\$).tw,kf.
- 24. (pyelonephriti* or pyonephrosi* or pyelocystiti* or pyelitis).tw,kf.
- 25. or/12-24
- 26. 11 and 25

Embase (1974 to 27 February 2024)

- 1. (exp vagina/ or intravaginal drug administration/) and (exp estrogen/ or exp hormone substitution/) 5329
- 2. (vagina* adj7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)).tw,kf. 5884
- 3. (intravagina* adj7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)).tw,kf. 498
- 4. (transvagina* adj7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)).tw,kf.446
- 5. (vagina* adj7 (pessar* or ring* or tablet* or cream* or gel*)).tw,kf. 7130
- 6. (intravagina* adj7 (pessar* or ring* or tablet* or cream* or gel*)).tw,kf.1089
- 7. (transvagina* adj7 (pessar* or ring* or tablet* or cream* or gel*)).tw,kf. 109
- 8. ((topical* or local*) adj3 hormon*).tw,kf. 3539
- 9. ((topical* or local*) adj3 (oestrogen* or estrogen* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)).tw,kf.3627
- 10. (Vagifem or Vagirux or Estring or Imvaggis or Blissel or Ovestin).tw,kf. 609
- 11. or/1-10 22896
- 12. exp urinary tract infection/ 143813
- 13. exp cystitis/ 29537
- 14. (UTI or UTIs).tw,kf. 29582
- 15. cystitis.tw,kf. 20409
- 16. bacteriuria.tw,kf. 8288
- 17. ((bladder* or genitourinar* or kidney* or pyelo* or renal* or ureter* or ureth* or urin* or urolog* or urogen*) adj7 infect*).tw,kf. 142283
- 18. (bladder* adj5 (inflamm* or ulcer* or ulcus)).tw,kf. 3309
- 19. ((bacteria* or microb*) adj5 (bladder* or genitourin* or kidney* or renal* or ureter* or ureth* or urin* or urolog* or urogen*)).tw,kf. 15476
- 20. exp *urinary tract disease/ 866954
- 21. proteinuri*.tw,kf. 77747

- 22. albuminuri*.tw,kf. 22561
- 23. ((protein* or albumin*) adj5 urin\$).tw,kf. 58598
- 24. (pyelonephriti* or pyonephrosi* or pyelocystiti* or pyelitis).tw,kf. 18551
- 25. or/12-24 1077485
- 26. 11 and 25 1625
- 27. limit 26 to conference abstracts 507
- 28. 26 not 27 1118

CINAHL Complete

Date run: 28 February 2024

- S32 S17 AND S31 296
- S31 S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 170,200
- S30 (pyelonephriti* or pyonephrosi* or pyelocystiti* or pyelitis) 2,037
- S29 ((protein* or albumin*) N5 urin*) 7,452
- S28 albuminuri* 5,565
- S27 proteinuri* 9,459
- S26 (MH "Urologic Diseases+") 155,018
- S25 ((bacteria* or microb*) N5 (bladder* or genitourin* or kidney* or renal* or ureter* or ureth* or urin* or urolog* or urogen*)) 3,777
- S24 (bladder* N5 (inflamm* or ulcer* or ulcus)) 267
- S23 ((bladder* or genitourinar* or kidney* or pyelo* or renal* or ureter* or ureth* or urin* or urolog* or urogen*) N7 infect*) 23,184
- S20 (UTI or UTIs) 9,035
- S19 (MH "Cystitis+") 1,739
- S18 (MH "Urinary Tract Infections+") 13,014
- S17 S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 5.549
- S16 (Vagifem or Vagirux or Estring or Imvaggis or Blissel or Ovestin) 2.615
- S15 ((topical* or local*) N3 (estrogen* or oestrogen* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)) 328
- S14 ((topical* or local*) N3 hormon*) 308
- S13 (transvagina* N7 (pessar* or ring* or tablet* or cream* or gel*)) 38
- S12 (intravagina* N7 (pessar* or ring* or tablet* or cream* or gel*)) 128
- S11 (vagina* N7 (pessar* or ring* or tablet* or cream* or gel*)) 1,585
- S10 (transvagina* N7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)) 62
- S9 (intravagina* N7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)) 45
- S8 (vagina* N7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)) 932
- S7 S3 AND S6 606

- S6 S4 OR S5 23,139
- S5 (MH "Hormone Replacement Therapy") 10,741
- S4 (MH "Estrogens+") 15,845
- S3 S1 OR S27,538
- S2 (MH "Administration, Intravaginal") 1,644
- S1 (MH "Vagina") 6,142

Cochrane Central Register of Randomised Controlled Trials

Date run: 28 February 2024

- 1. MeSH descriptor: [Vagina] explode all trees 1858
- 2. MeSH descriptor: [Administration, Intravaginal] explode all trees 1818
- 3. #1 OR #2 3426
- 4. MeSH descriptor: [Estrogens] explode all trees 2365
- 5. MeSH descriptor: [Hormone Replacement Therapy] explode all trees 3792
- 6. #4 or #5 5595
- 7. #3 AND #6 216
- 8. (vagina* NEAR/7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)) 1601
- 9. (intravagina* NEAR/7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol) 374
- 10. (transvagina* NEAR/7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol) 141
- 11. (vagina* NEAR/7 (pessar* or ring* or tablet* or cream* or gel*)) 3786
- 12. (intravagina* NEAR/7 (pessar* or ring* or tablet* or cream* or gel*)) 654
- 13. (transvagina* NEAR/7 (pessar* or ring* or tablet* or cream* or gel*)) 44
- 14. ((topical* or local*) NEAR/3 hormon*) 490
- 15. (topical* or local*) NEAR/3 (estrogen* or oestrogen* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol) 457
- 16. (Vagifem or Vagirux or Estring or Imvaggis or Blissel or Ovestin) 81
- 17. {OR #8-#16} 5844
- 18. #7 OR #17 5876
- 19. MeSH descriptor: [Urinary Tract Infections] explode all trees 3290
- 20. MeSH descriptor: [Cystitis] explode all trees 614
- 21. (UTI OR UTIs) 2774
- 22. Cystitis 2006
- 23. Bacteriuria 1346
- 24. ((bladder* or genitourinar* or kidney* or pyelo* or renal* or ureter* or ureth* or urin* or urolog* or urogen*) NEAR/7 infect*) 16109
- 25. (bladder* NEAR/5 (inflamm* or ulcer* or ulcus)) 107
- 26. ((bacteria* or microb*) NEAR/5 (bladder* or genitourin* or kidney* or renal* or ureter* or ureth* or urin* or urolog* or urogen*)) 1960

- 27. MeSH descriptor: [Urologic Diseases] explode all trees 38097
- 28. proteinuri* 6570
- 29. albuminuri* 3667
- 30. ((protein* or albumin*) NEAR/5 urin*) 8364
- 31. (pyelonephriti* or pyonephrosi* or pyelocystiti* or pyelitis) 1209
- 32. {OR #19-#31} 60710
- 33. #18 AND #32 382

Limited to trials register: 308 trials found.

Database: Web of Science Preprint Citation Index (1990 to current)

Date run: 28 February 2024

TS=(vagina* NEAR/7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or estriol or oestriol)) OR TS=(intravagina* NEAR/7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol) or oestriol)) OR TS=(transvagina* NEAR/7 (oestrogen* or estrogen* or hormon* or dehydroepiandrostenedione or estradiol or oestradiol or oestriol)) OR TS=(vagina* NEAR/7 (pessar* or ring* or tablet* or cream* or gel*)) OR TS=(intravagina* NEAR/7 (pessar* or ring* or tablet* or cream* or gel*)) OR TS=(transvagina* NEAR/7 (pessar* or ring* or tablet* or cream* or gel*)) OR TS=((topical* or local*) NEAR/3 (estrogen* or oestrogen* or dehydroepiandrostenedione or estradiol or oestradiol or estriol or oestriol)) OR TS=(Vagifem or Vagirux or Estring or Imvaggis or Blissel or Ovestin)

And

TS=(UTI or UTIs) OR TS=(cystitis OR bacteriuria) OR TS=((bladder* or genitourinar* or kidney* or pyelo* or renal* or ureter* or ureth* or urin* or urolog* or urogen*) NEAR/7 infect*) OR TS=(bladder* NEAR/5 (inflamm* or ulcer* or ulcus)) OR TS=((bacteria* or microb*) NEAR/5 (bladder* or genitourin* or kidney* or renal* or ureter* or ureth* or urin* or urolog* or urogen*)) OR TS=(proteinuri* OR albuminuri*) OR TS=((protein* or albumin*) NEAR/5 urin*) OR TS=(pyelonephriti* or pyonephrosi* or pyelocystiti* or pyelitis)

4 references found.

WHO International Clinical Trials Registry Platform

Date run: 28 February 2024

(vagina OR intravagina* OR transvaginal*)

And

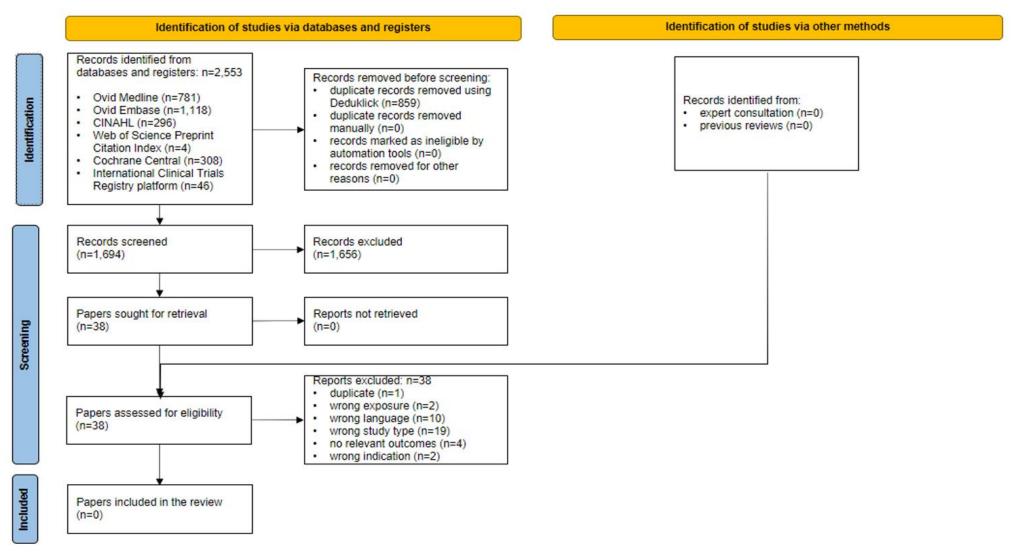
(oestrogen* OR estrogen* OR hormone* OR dehydroepiandrostenedione or estradiol or oestradiol OR estriol OR oestriol OR pessar* OR ring* OR tablet* OR cream* OR gel* OR topical* OR local*)

And

(cystitis OR bacteriuria OR bladder* OR genitourinar* OR kidney* OR pyelo* OR renal* OR ureter* OR ureth* OR urin* OR urolog* OR urogen* OR proteinuri* OR albuminuri* OR pyelonephriti* OR pyonephrosi* OR pyelocystiti* OR pyelitis)

46 references found.

Figure A.1. PRISMA diagram



Text version of Figure A.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this review, ultimately including 0 studies.

From identification of studies via databases and registers, n=2,553 records identified from databases and registers:

- Ovid Medline (n=781)
- Ovid Embase (n=1,118)
- CINAHL (n=296)
- Web of Science preprints (n=4)
- Cochrane CENTRAL (n=308)
- International Clinical Trials Registry platform (n=46)

From these, records removed before screening:

- duplicate records removed using Deduklick (n=859)
- duplicate records removed manually (n=0)
- records marked as ineligible by automation tools (n=0)
- records removed for other reasons (n=0)

n=1,694 records screened, of which n=1,656 were excluded, leaving n=38 papers sought for retrieval, all of which were retrieved.

Of the n=38 papers assessed for eligibility, n=38 reports were excluded:

- duplicate (n=1)
- wrong exposure (n=2)
- wrong language (n=10)
- wrong study type (n=19)
- no relevant outcomes (n=4)
- wrong indication (n=2)

n=0 papers included in the review.

Annexe B. Excluded full texts

Duplicate (n=1)

Bianchi-Ferraro AM and others. 'Analysis of clinical response, sexuality and vaginal health in women with genitourinary syndrome of menopause treated with topical estrogen, microablative fractional CO 2 laser and microablative fractional radiofrequency: randomized controlled trial' Female Pelvic Medicine and Reconstructive Surgery 2022: volume 28, issue 6, pages S21 to S22

No relevant outcomes (n=4)

Bergman J and others. 'Prevention of urinary tract infections in nursing homes: lack of evidence-based prescription?' BMC Geriatrics 2011: volume 11, page 69

Mikkelsen AL and others. 'Clinical effects of preoperative oestradiol treatment before vaginal repair operation. A double-blind, randomized trial' Gynecologic and Obstetric Investigation 1995: volume 40, issue 2, pages 125 to 128

Setty P and others. 'Vaginal estrogen use and effects on quality of life and urogenital morbidity in postmenopausal women after publication of the Women's Health Initiative in New York City' Menopause (New York, NY) 2016: volume 23, issue 1, pages 7 to 10

Tripathi NK. 'The treatment of lower urinary tract symptoms (Luts) in perimenopausal females using alpha-1a blockers (tamsulosin) and estrogens: a comparative study' International Journal of Toxicological and Pharmacological Research 2021: volume 11, issue 2, pages 67 to 71

Wrong exposure (n=2)

Oliveria SA and others. 'Estrogen replacement therapy and urinary tract infections in postmenopausal women aged 45 to 89' Menopause 1998: volume 5, issue 1, pages 4 to 8

Orlander JD and others. 'Urinary tract infections and estrogen use in older women'. Journal of the American Geriatrics Society 1992: volume 40, issue 8, pages 817 to 820

Wrong language (n=10)

Anonymous. 'Postmenopause: Fewer urinary tract infections by means of vaginal estrogen treatment'. Deutsche Apotheker Zeitung 1993: volume 133, issue 49, pages 40 to 41

Anonymous. 'Intravaginal estriol prevents urinary tract infections in the elderly: Comment'. Fortschritte der Medizin 1994: volume 112, issue 5, page 8

Benoit T and others. '[Use of local estrogenotherapy in urology and pelviperineology: A systematic review]' OEstrogenotherapie locale en urologie et pelvi-perineologie. Revue de litterature. 2015: volume 25, issue 11, pages 628 to 635

Brostrom S, Lose G. '[Oestrogen for prevention of recurrent urinary tract infections in postmenopausal women--a survey of a Cochrane review]' Ostrogen til forebyggelse af recidiverende urinvejsinfektioner hos postmenopausale kvinder--gennemgang af et Cochrane-review. 2009: volume 171, issue 36, pages 2,568 to 2,571

Canales JP and others. 'Are vaginal estrogens effective for preventing urinary tract infection in postmenopausal women?' Son los estrogenos vaginales efectivos para prevenir infecciones urinarias en mujeres postmenopausicas? 2017: volume 17, issue 9, page e7093

Riss P. 'Female irritable bladder: Gynecological aspects of female urinary tract infection'. Archives of Gynecology and Obstetrics 1995: volume 257, issue 1, pages 651 to 653

Skerk V and others. 'Urinary tract infections: classification, diagnosis, therapy' Pharmaca 1995: volume 33, issue 3, pages 223 to 233

Sprem M, Milicic D. 'Local estrogen treatment of women with symptoms of urogenital aging' Gynaecologia et Perinatologia 1999: volume 8, issue 1, pages 15 to 20

Terwisscha Van Scheltinga JA and others. 'Adhesion of the labia minora' Tijdschrift voor Kindergeneeskunde 2008: volume 76, issue 5, pages 238 to 241

Wagenlehner FME and others. '[Primary and secondary prevention of urinary tract infections]' Primar- und Sekundarpravention von Harnwegsinfektionen. 2011: volume 50, issue 10, pages 1,248 to 1,246

Wrong study type (n=19)

Anonymous. <u>'Cranberry products or topical estrogen-based therapy for the prevention of urinary tract infections: a review of clinical effectiveness and guidelines</u>' 2016

Barea BM and others. <u>'Nonantibiotic treatments for urinary cystitis: an update'</u> Current opinion in urology 2020: volume 30, issue 6, pages 845 to 852

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