實證醫學研究諮詢-主題討論表

姓名：陳光穎　單位：教研部 GSM/分機：79424 日期：　2025/2/10

Question： *How does estrogen modulate immune function, and what is its role in preventing multiple sclerosis in at-risk populations?*

Participants	Perimenopause (35-65) women with multiple sclerosis or at risk.
Intervention/Exposure/Diagnostic tool	Estrogen or estrogen-based therapies
Comparisons	Non-estrogen therapies or placebo
Outcomes	Immunomodulation, autoimmune disease incidence/prevention
Study design	Studies on humans
key words	
Relevant studies	

Discussion:
Do we have access to Embase and/or Scopus?
What are the conferences where we can present our results? Ex. 台灣婦產科醫學會 115 年度年會暨擴大學術研討會
Do we have any available funding sources or sponsors that we can include in our PROSPERO registration?

Systematic review

*Fields that have an **asterisk (*)** next to them means that they **must be answered. Word limits** are provided for each section. You will be unable to submit the form if the word limits are exceeded for any section. Registrant means the person filling out the form*.

This record cannot be edited because it has been marked as out of scope

1. * Review title.

Give the title of the review in English

Estrogen as an immunomodulator and its role in multiple sclerosis prevention: a systematic review

2. Original language title.

For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

Estrogen as an immunomodulator and its role in multiple sclerosis prevention: a systematic review

3. * Anticipated or actual start date.

Give the date the systematic review started or is expected to start.

10/02/2025

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

31/05/2025

5. * Stage of review at time of this submission.

This field uses answers to initial screening questions. It cannot be edited until after registration.

Tick the boxes to show which review tasks have been started and which have been completed.

Update this field each time any amendments are made to a published record.

The review has not yet started: Yes

Review stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here.

6. * Named contact.

The named contact is the guarantor for the accuracy of the information in the register record. This may be any member of the review team.

Kuang-Ying Chen

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Dr Chen

7. * Named contact email.

Give the electronic email address of the named contact.

s10601053.md06@nycu.edu.tw

8. Named contact address

Give the full institutional/organisational postal address for the named contact.

777 East 25th Street, Suite 203 Hialeah, FL 33013 Hialeah Hospital Medical Plaza Alberto Dominguez-Bali Office

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

+886-965434011

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Florida International University

Organisation web address:

https://www.fiu.edu/

11. * Review team members and their organisational affiliations.

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country now MUST be entered for each person, unless you are amending a published record. PLEASE USE AN INSTITUTIONAL EMAIL ADDRESS IF POSSIBLE.**

Dr Kuang-Ying Chen. Florida International University, Miami, FL; National Chung Cheng University, Chiayi, Taiwan; National Yang Ming Chiao Tung University, Taipei, Taiwan
Dr Praneet Gandhoke. Florida International University, Miami, FL; DR.D.Y.PATIL MEDICAL COLLEGE,PUNE
Dr Nachiket Nijampurkar. Dr. Vaishampayan Memorial Govt. Medical College, Solapur, India; Florida International University, Miami, FL
Dr Hala Nasar. Florida International University, Miami, FL; Jordan University of Science and Technology, Irbid, Jordan
Dr Alberto Dominguez-Bali. Miami Center for Obstetrics/Gynecology and Human Sexuality, Miami, FL

12. * Funding sources/sponsors.

Details of the individuals, organizations, groups, companies or other legal entities who have funded or sponsored the review.

Grant number(s)

State the funder, grant or award number and the date of award

13. * Conflicts of interest.

List actual or perceived conflicts of interest (financial or academic).

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country must be completed for each person, unless you are amending a published record.**

15. * Review question.

State the review question(s) clearly and precisely. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS or similar where relevant.

How does estrogen modulate immune function, and what is its role in preventing autoimmune diseases in at-risk populations?

Population: Individuals with autoimmune diseases or at risk.

Intervention: Estrogen or estrogen-based therapies.

Comparison: Non-estrogen therapies or placebo.

Outcome: Immunomodulation, autoimmune disease incidence/prevention.

16. * Searches.

State the sources that will be searched (e.g. Medline). Give the search dates, and any restrictions (e.g. language or publication date). Do NOT enter the full search strategy (it may be provided as a link or attachment below.)

PubMed

search dates: 2024/12/25

Filters applied: in the last 10 years.

Embase

search dates: 2024/12/25

Cochrane Library

search dates: 2024/12/25

with Cochrane Library publication date from Jan 2015 to present, (Word variations have been searched)

Web of Science

search dates: 2024/12/25

| Timespan: 2015-01-01 to 2024-12-31 (Publication Date)

17. URL to search strategy.

Upload a file with your search strategy, or an example of a search strategy for a specific database, (including the keywords) in pdf or word format. In doing so you are consenting to the file being made publicly accessible. Or provide a URL or link to the strategy. Do NOT provide links to your search **results**.

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied in your systematic review.

Autoimmune replacement therapy

19. * Participants/population.

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

Population: Individuals with autoimmune diseases or at risk.

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the interventions or the exposures to be reviewed. The preferred format includes details of both inclusion and exclusion criteria.

Intervention: Estrogen or estrogen-based therapies.

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the intervention/exposure will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Comparison: Non-estrogen therapies or placebo.

22. * Types of study to be included.

Give details of the study designs (e.g. RCT) that are eligible for inclusion in the review. The preferred format includes both inclusion and exclusion criteria. If there are no restrictions on the types of study, this should be stated.

Studies on humans

23. Context.

Give summary details of the setting or other relevant characteristics, which help define the inclusion or

exclusion criteria.

Studies on humans relevant to estrogen's effects on immune function.

Peer-reviewed journals.

Specific autoimmune diseases: lupus, RA, MS, GPA, psoriasis, Sjögren's syndrome, allergy etc

Timeframe: last 10 years

Exclusion Criteria:

Non-English studies

Irrelevant topics: non-immune functions of estrogen, No mention of estrogen, Studies on animal models

Register the protocol with PROSPERO.

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

Outcome: Immunomodulation, autoimmune disease incidence/prevention.

Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

relative risks, odds ratios, risk difference, and/or 'number needed to treat

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state ‘None’ or ‘Not applicable’ as appropriate to the review

Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Study ID Author, Year, Title, DOI or PubMed ID Smith et al., 2023, "Estrogen and Autoimmunity"

Study Design RCT, cohort, case-control, animal study, etc. Randomized Controlled Trial (RCT)

Population Sample size, age, sex, health status, specific autoimmune disease 120 women, ages 18-45, lupus patients

Intervention Type of estrogen (estradiol, estrone), dose, frequency, route of administration Estradiol 2 mg/day oral

Comparator Placebo, no treatment, or other treatments Placebo group

Outcomes Primary outcomes (immune markers, disease incidence) IL-6, TNF-?, regulatory T cells (Tregs)

Outcome Results Values, effect sizes, mean differences, 95% CI IL-6 reduced by 15% (p 0.05)

Duration Length of follow-up (e.g., 6 weeks, 1 year) 12 weeks

Key Findings Brief summary of important outcomes Estrogen reduced IL-6 and increased Tregs

Risk of Bias Risk of bias assessment (Cochrane RoB2, NOS) Low risk of bias (for RCTs)

Notes Any additional notes, limitations, or special features Small sample size, short follow-up period

27. * Risk of bias (quality) assessment.

State which characteristics of the studies will be assessed and/or any formal risk of bias/quality assessment tools that will be used.

28. * Strategy for data synthesis.

Describe the methods you plan to use to synthesise data. This **must not be generic text** but should be **specific to your review** and describe how the proposed approach will be applied to your data. If meta-analysis is planned, describe the models to be used, methods to explore statistical heterogeneity, and software package to be used.

29. * Analysis of subgroups or subsets.

State any planned investigation of ‘subgroups’. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

Specific autoimmune diseases: lupus, RA, MS, GPA, psoriasis, Sjögren's syndrome, allergy etc

30. * Type and method of review.

Select the type of review, review method and health area from the lists below.

Type of review

Cost effectiveness

No

Diagnostic

No

Epidemiologic

No

Individual patient data (IPD) meta-analysis

No

Intervention

No

Living systematic review

No

Meta-analysis

Yes

Methodology

No

Narrative synthesis

No

Network meta-analysis

No

Pre-clinical

No

Prevention

No

Prognostic

No

Prospective meta-analysis (PMA)

No

Review of reviews

No

Service delivery

No

Synthesis of qualitative studies

No

Systematic review
Yes

Other
No

Health area of the review

Alcohol/substance misuse/abuse
No

Blood and immune system
No

Cancer
No

Cardiovascular
No

Care of the elderly
No

Child health
No

Complementary therapies
Yes

COVID-19
No

Crime and justice
No

Dental
No

Digestive system
No

Ear, nose and throat
No

Education
No

Endocrine and metabolic disorders
No

Eye disorders

No

General interest
No

Genetics
No

Health inequalities/health equity
No

Infections and infestations
No

International development
No

Mental health and behavioural conditions
No

Musculoskeletal
No

Neurological
No

Nursing
No

Obstetrics and gynaecology
Yes

Oral health
No

Palliative care
No

Perioperative care
No

Physiotherapy
No

Pregnancy and childbirth
No

Public health (including social determinants of health)
No

Rehabilitation
No

Respiratory disorders

No

Service delivery

No

Skin disorders

No

Social care

No

Surgery

No

Tropical Medicine

No

Urological

No

Wounds, injuries and accidents

No

Violence and abuse

No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.

English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out. For multi-national collaborations select all the countries involved.

India

Jordan

Taiwan

United States of America

33. Other registration details.

Name any other organisation where the systematic review title or protocol is registered (e.g. Campbell, or The Joanna Briggs Institute) together with any unique identification number assigned by them. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

If the protocol for this review is published provide details (authors, title and journal details, preferably in Vancouver format)

Add web link to the published protocol.

Or, upload your published protocol here in pdf format. Note that the upload will be publicly accessible.

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Do you intend to publish the review on completion?

Yes

Give brief details of plans for communicating review findings.?

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords help PROSPERO users find your review (keywords do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

37. Details of any existing review of the same topic by the same authors.

If you are registering an update of an existing review give details of the earlier versions and include a full bibliographic reference, if available.

38. * Current review status.

Update review status when the review is completed and when it is published.New registrations must be ongoing so this field is not editable for initial submission.

Please provide anticipated publication date

Review_Ongoing

39. Any additional information.

Provide any other information relevant to the registration of this review.

40. Details of final report/publication(s) or preprints if available.

Leave empty until publication details are available OR you have a link to a preprint (NOTE: this field is not editable for initial submission). List authors, title and journal details preferably in Vancouver format.

Give the link to the published review or preprint.

Estrogen as an immunomodulator and its role in multiple sclerosis prevention: a systematic review

Kuang-Ying (Bruce) Chen

Praneet Gandhoke, Nachiket Nijampurkar, Hala Nasar

Alberto Dominguez-Bali, MD

Research Question

How does estrogen modulate immune function, and what is its role in preventing multiple sclerosis in at-risk populations?

- **Population**: Perimenopause (35-65) women with multiple sclerosis or at risk.
- **Intervention**: Estrogen or estrogen-based therapies.
- **Comparison**: Non-estrogen therapies or placebo.
- **Outcome**: Immunomodulation, autoimmune disease incidence/prevention.

Protocol

- **Inclusion Criteria**:
  - Studies on humans relevant to estrogen's effects on immune function.
  - Peer-reviewed journals.
  - Specific autoimmune disease: multiple sclerosis
  - Timeframe: last 10 years
- **Exclusion Criteria**:
  - Non-English studies
  - Irrelevant topics:
    - non-immune functions of estrogen,
    - No mention of estrogen
    - Studies on animal models

Register the protocol with **PROSPERO**.

Comprehensive Literature Search

- **PubMed**: ("Estrogens"[MeSH] OR Estrogen) AND (MS OR “multiple sclerosis”) AND ("Hormone Replacement Therapy"[MeSH] OR “Estrogen Replacement Therapy"[MeSH] OR Prevention)
  - Filters applied: in the last 10 years.
  - 349 results: pubmed-EstrogensM-set (PubMed) (2).nbib

PubMed

1 Cite Share

Nutrition in the **prevention** and treatment of endometriosis: A review.

Barnard ND, Holtz DN, Schmidt N, Kolipaka S, Hata E, Sutton M, Znayenko-Miller T, Hazen ND, Cobb C, Kahleova H.

Front Nutr. 2023 Feb 17;10:1089891. doi: 10.3389/fnut.2023.1089891. eCollection 2023.

PMID: 36875844 **Free PMC article.** Review.

Nutritional interventions may be helpful in the **prevention** and treatment of endometriosis and associated pain. Reducing dietary fat and increasing dietary fiber have been shown to reduce circulating **estrogen** concentrations, suggesting a potential benefit for individ ...

2 Cite Share

Cognitive Problems in Perimenopause: A Review of Recent Evidence.

Metcalf CA, Duffy KA, Page CE, Novick AM.

Curr Psychiatry Rep. 2023 Oct;25(10):501-511. doi: 10.1007/s11920-023-01447-3. Epub 2023 Sep 27.

PMID: 37755656 **Free PMC article.** Review.

Much progress has been made in understanding how perimenopause impacts cognition, and more research is needed to better identify who is at highest risk and how to meaningfully **prevent** and alleviate cognitive problems during this reproductive stage. Larger-scale randomized ...

3 Cite Share

All women with **multiple sclerosis** should start hormone replacement therapy at menopause unless contraindicated: Yes.

Voskuhl R.

Mult Scler. 2024 Aug;30(9):1107-1109. doi: 10.1177/13524585241255002. Epub 2024 Jun 22.

PMID: 38907632 **Free PMC article.** No abstract available.

4 Cite Share

All women with **multiple sclerosis** should start hormone replacement therapy at menopause unless contraindicated: Commentary.

Petheram K, Dobson R.

Mult Scler. 2024 Aug;30(9):1111-1112. doi: 10.1177/13524585241254989. Epub 2024 Jun 22.

PMID: 38907631 **Free PMC article.** No abstract available.

Comprehensive Literature Search

- **Embase**: ('estrogens'/exp OR 'estrogens' OR 'estrogen'/exp OR 'estrogen') AND ('multiple sclerosis' OR 'ms') AND ('hormone therapy'/exp OR 'hormone therapy' OR 'prevention'/exp OR 'prevention') AND [2015-2025]/py
  - ? results: records(Embase).ris

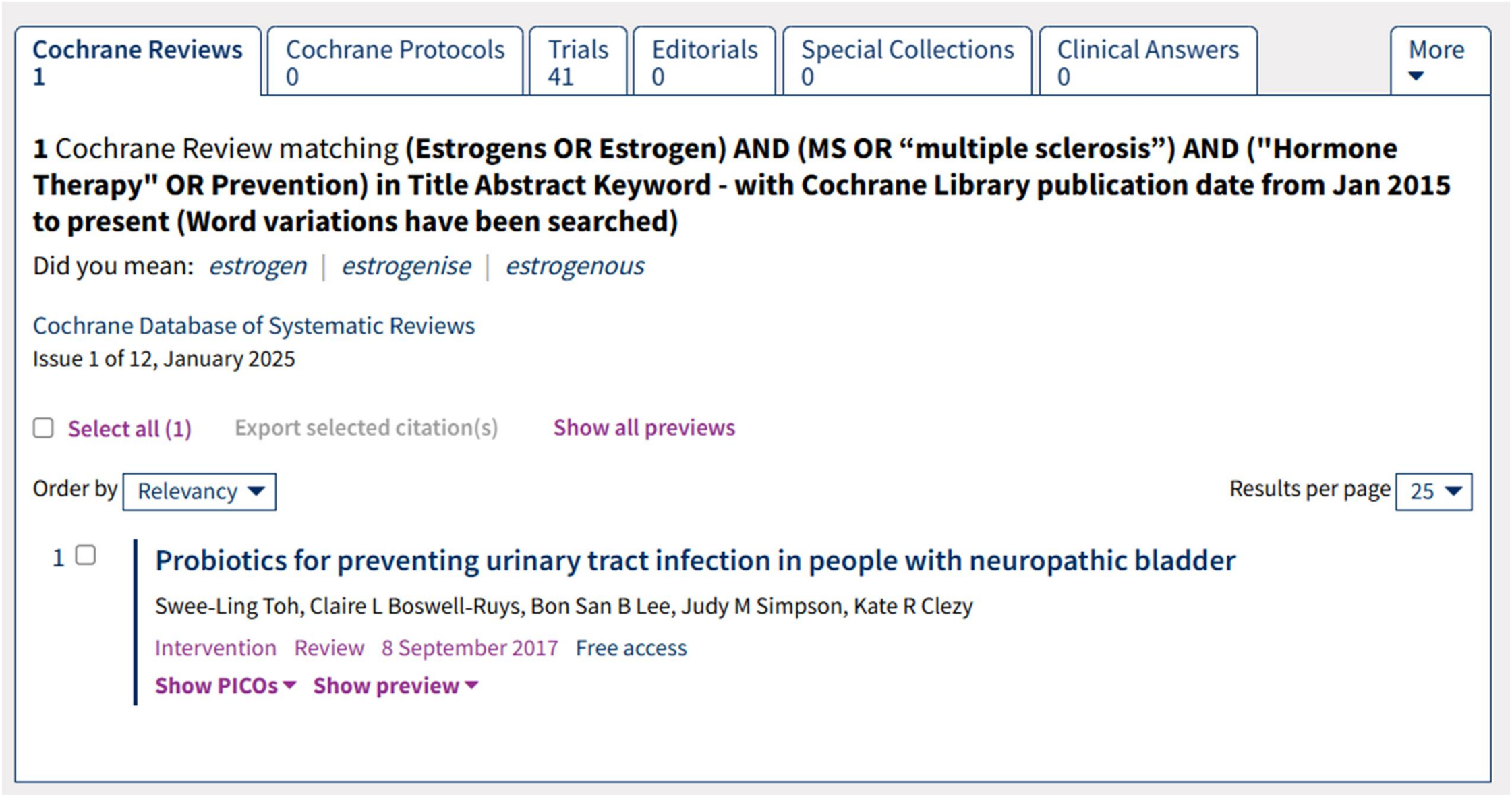
Embase

- ?

Comprehensive Literature Search

- **Cochrane Library**: (Estrogens OR Estrogen) AND (MS OR “multiple sclerosis”) AND ("Hormone Therapy" OR Prevention)
  - with Cochrane Library publication date from Jan 2015 to present, (Word variations have been searched)
  - 1 Cochrane Reviews: citation-export (Cochrane Review) (2).ris
  - 41 Trials: citation-exports (CochraneTrials).ris
- **0** results matching **'Intervention "Estrogens" AND Outcome ("Multiple Sclerosis")'**

Cochrane Reviews



Trials

1 ☐ **Hormonal therapy for menopausal women with MS: a phase II RCT**

A Anderson, W Rowles, G Rush, M Carleton, N Hills, J Cooper, BA Cree, JM Gelfand, J Graves, KM Krysko, T West, S Zamvil, A Green, R Bove

Multiple sclerosis journal, **2020**, 26(1 SUPPL), 45 | added to CENTRAL: 31 January 2021 | 2021 Issue 01

Embase

2 ☐ **Vasomotor hot flashes and cardiac repolarization: a randomized placebo-controlled trial of postmenopausal hormone therapy**

H Lantto, P Haapalahti, M Viitasalo, H Väänänen, ARA Sovijärvi, O Ylikorkala, TS Mikkola

Menopause (New York, N.Y.), **2017**, 24(12), 1386-1391 | added to CENTRAL: 31 August 2018 | 2018 Issue 8

PubMed

3 ☐ **Vasomotor hot flashes and cardiac repolarization: a randomized placebo-controlled trial of postmenopausal hormone therapy**

H Lantto, P Haapalahti, M Viitasalo, H Vaananen, ARA Sovijarvi, O Ylikorkala, TS Mikkola

Menopause (New York, N.Y.), **2017**, 24(12), 1386-1391 | added to CENTRAL: 31 August 2017 | 2017 Issue 8

PubMed | Embase

4 ☐ **A hormonal therapy for menopausal women with MS: a phase Ib/IIa randomized controlled trial**

R Bove, A Anderson, W Rowles, KA Rankin, NK Hills, M Carleton, J Cooper, BAC Cree, JM Gelfand, JS Graves, RG Henry, KM Krysko, G Rush, SS Zamvil, H Joffe, JR Chan, AJ Green

Multiple sclerosis and related disorders, **2022**, 61, 103747 | added to CENTRAL: 30 June 2022 | 2022 Issue 06

PubMed

Comprehensive Literature Search

- **Web of Science**: TS=(Estrogens OR Estrogen) AND TS=(MS OR “multiple sclerosis”) AND TS=("Hormone Therapy" OR Prevention)
  - | Timespan: 2015-01-01 to 2024-12-31 (Publication Date)
  - 164 Documents: savedrecs (Web of Science) (2).ris

Web of Science

1 **Multiple sclerosis at menopause: Potential neuroprotective effects of estrogen**

Christianson, MS; Mensah, VA and Shen, W

Feb 2015 | MATURITAS 80 (2) , pp.133-139

Multiple sclerosis (MS) is an autoimmune demyelinating and neurodegenerative condition of the central nervous system that preferentially afflicts women more than men. Low estrogen states such as menopause and the postpartum period favor exacerbations of multiple sclerosis in women with the disease. Existing and emerging evid ... Show more

Find it @ NYCU Full Text at Publisher •••

2 **Symptoms of multiple sclerosis in women in relation to sex steroid exposure**

Holmqvist, P; Wallberg, M; (...); Brynhildsen, J

May 20 2006 | MATURITAS 54 (2) , pp.149-153

Objective: To investigate if women with multiple sclerosis (MS) experience changes in MS symptoms related to pregnancy, the postpartum period, menopause or use of oral contraception (OC) or postmenopausal hormone therapy (HT). Methods: Women with diagnosed MS were recruited from registers of all MS patients known in t ... Show more

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3 **Hormonal Therapies in Multiple Sclerosis: a Review of Clinical Data**

Hsu, SPN and Bove, R

Jan 2024 | CURRENT NEUROLOGY AND NEUROSCIENCE REPORTS 24 (1) , pp.1-15

Purpose of ReviewGiven the potential for exogenous hormones to influence risk and course of MS, this narrative review aims to summarize current knowledge from observational and interventional studies of exogenous hormones in humans with MS.Recent FindingsLarge randomized clinical trials for combined oral contraceptives and ϵ ... Show more

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Scopus