# Levonorgestrel Intrauterine Systems for Primary Prevention and Treatment of Endometrial Hyperplasia and Endometrial Cancer: A Systematic Review Methodology

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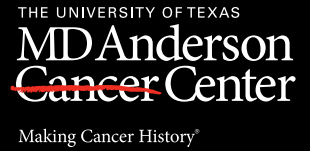
## Introduction

Endometrial cancer (EC), ranking fourth among women's cancers in the US, is showing an alarming increase in incidence among younger individuals. The standard of care for EC is a total hysterectomy, bilateral salpingectomy and/or bilateral oophorectomy.[1]

The levonorgestrel-releasing intrauterine system (LNG-IUS) is a popular and effective contraceptive method that releases controlled amounts of levonorgestrel, a type of progesterone, daily into the uterus. Beyond contraception, researchers are studying its non-contraceptive benefits. Evidence indicates that progesterone plays a role in inhibiting uncontrolled estrogen-driven endometrium growth that can increase the risk of developing endometrial hyperplasia, a precursor to most EC, and EC. There is a growing interest in the use of LNG-IUS for endometrial hyperplasia and EC.[2]

## Aim

To conduct a detailed methodology for a systematic review of existing research on the preventive and/or control effects of LNG-IUS on endometrial hyperplasia and EC, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and PROSPERO guidelines to ensure rigor and transparency.
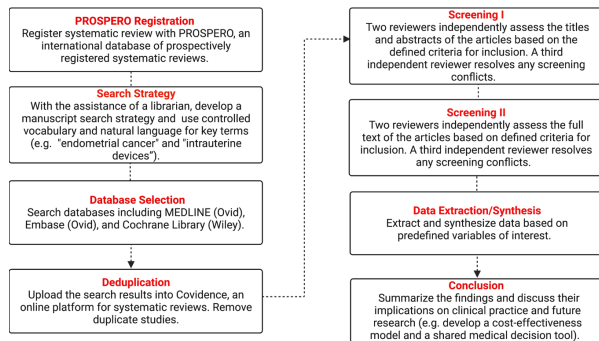
## Methods



Figure 1. Process flowchart for a systematic review on the benefits of LNG-IUS in endometrial hyperplasia and cancer.

Table 1. Inclusion and exclusion criteria for the systematic review.

| Criteria | Inclusion Criteria | Exclusion Criteria |
|---|---|---|
| Population | Populations at risk for EC or who already have EC | Populations with non-EC types |
| Intervention | Hormonal IUS (e.g., LNG-IUS) | Non-hormonal IUSs (e.g., Paragard) |
| Study Types | RCT, Prospective and retrospective cohort studies, Case control studies, Case series, and Case report | In-vitro and animal studies |
| Region | US and non-US countries | N/A |
| Language | English language | Manuscripts in non-English language |

## Results

A total of 1,168 results were retrieved from the three databases including the original set of 2 key articles supplied by the research team (MEDLINE = 314; Embase = 796; Cochrane Library = 58). The results were uploaded to Covidence for deduplication and eligibility screening. After deduplication, 908 unique publications were identified.
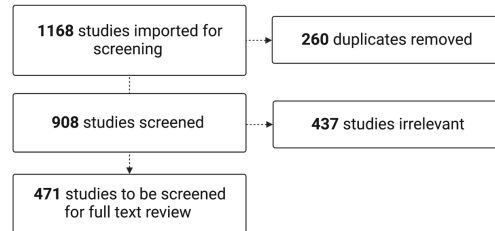


Figure 2. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 flow diagram showing study selection.

## Next Steps

Two independent reviewers will conduct a full-text review and extract relevant data from selected articles. Descriptive statistics will be performed to provide a summary of key characteristics and measures related to the outcomes of interest associated with the prevention and/or control of endometrial hyperplasia and EC by LNG-IUS. Additionally, qualitative interviews will be conducted to assess the feasibility and acceptability of the IUS for our target population.

## Conclusions

A comprehensive systematic review, with the assistance of a medical librarian, can be used to identify evidence analyzing the efficacy of LNG-IUS in inhibiting estrogen-driven endometrial growth associated with endometrial hyperplasia and EC.

The limitations of this systematic review include potential heterogeneity among the included studies, the possibility of publication bias, variations in study quality, challenges in data synthesis due to reporting differences, and potential confounding effects of concomitant interventions.

## Funding Acknowledgment

## References

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- Markowska, A, et al. *Cancers,* 2022; 14(8):1922.[1]
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