Meta-analysis of intrauterine device use and risk of endometrial cancer

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CRD summary
This meta-analysis found a protective association among women who reported ever using an intrauterine device and risk of endometrial cancer. Poor reporting suggested the conclusions may not be reliable, however, an overall protective effect was likely to exist based on the large population-based studies included in this review.

Authors' objectives
To review the association between intrauterine device (IUD) use and the risk of endometrial cancer, and consider potential contributing factors.

Searching
MEDLINE (PubMed) and ProQuest (dissertations and theses) were searched between 1966 and April 2007. Search terms were reported. References were checked for additional eligible studies. Non-English papers were evaluated.

Study selection
Analytic studies that measured IUD use in relation to endometrial cancer were eligible. Outcomes of interest were risk/incidence of endometrial cancer. Included studies were a mixture of population-based and non population-based case control studies reported from a variety of countries including Israel, USA, China, Mexico, Italy and Australia. Where reported, ages of the participants ranged from 20 to 74 years. IUDs used were copper, inert, Lippes Loop, Dalkon Shield, safety coil, Majzlen Spring and stainless steel (not all studies reported this information).

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
The authors discussed adjusting for confounding factors in the analyses, but did not explicitly report carrying out validity assessment.

Data extraction
Information relating to total years of intrauterine device exposure, years since first and last intrauterine device exposure and type of intrauterine device used were extracted, along with the odds ratio and 95% confidence intervals, for the development of endometrial cancer. Where possible, the most adjusted odds ratio controlled for the greatest number of confounders was used. Where no odds ratio was reported, a crude odds ratio and associated 95% confidence interval was calculated from the raw data. One reviewer abstracted the data from included papers.

Methods of synthesis
Fixed- and random-effects models were used to calculate pooled odds ratios and 95% confidence intervals for dichotomous factors (such as ever used versus never used an intrauterine device). Heterogeneity was assessed, but no details were reported. A fixed-effects dose-response method was used to examine multiple ordinal categories of duration, latency and recency for possible linear associations. The appropriateness of using a linear model was checked by a goodness-of-fit test for linear and quadratic models.

Results of the review
Eleven articles reporting on 10 studies were included in this review: six population-based case-control studies and four non population-based case-control studies (total n=4,197 cases and 280,447 controls). Only three studies reported the specific type of intrauterine device used, therefore, this variable was not analysed further. None of the studies consistently adjusted for the four main risk factors for endometrial cancer. Nine studies adjusted for age. Only one study adjusted for the three protective factors. Only two studies adjusted for combined oral contraceptive use, which is a known lifelong protector. No significant heterogeneity was noted in any of the analyses.
There was a significant reduction in the risk of endometrial cancer with intrauterine device use (adjusted odds ratio 0.54, 95% confidence interval: 0.47, 0.63, 10 studies). No heterogeneity was observed. There was a decrease in the number of incidents of endometrial cancer with a five-year increase in both the duration of intrauterine device use (adjusted odds ratio 0.88, 95% confidence interval: 0.84, 0.92, five studies) and the time since first use (adjusted odds ratio 0.89, 95% confidence interval: 0.83, 0.95, four studies). The protective effect of intrauterine device use continued after removal, but reduced over time resulting in an increase in the risk of endometrial cancer with a five-year increase in the time since last use (adjusted odds ratio 0.91, 95% confidence interval: 0.86, 0.95, four studies).

Authors’ conclusions
This meta-analysis found that use of a non-hormonal intrauterine device may be associated with a decreased risk of endometrial cancer.

CRD commentary
This review addressed a clear question with specified inclusion criteria. The search was limited and may have introduced publication bias. Data extraction was conducted by one reviewer, therefore, data extraction errors may have occurred and not been identified. It was unclear whether study selection was conducted in duplicate, therefore, selection bias may have been present. Interpretation of the results was difficult, primarily due to what appeared to be an inaccurate table footnote, typographical errors and discrepancies between the tables and text. The included studies were not assessed for validity. Comments on controlling for confounding factors were included in the discussion, but it was difficult to assess the reliability or validity of the primary data. The meta-analysis may not have been appropriate given the clinical heterogeneity. Although an overall protective effect was likely to exist given the results from several large population-based studies, the methodological shortcomings of this review made the reliability of the conclusions uncertain.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors recommended that future research should explore the three types of intrauterine devices and report data on duration, latency and recency of exposure. Large cohort studies could facilitate controlling for the various confounders.

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