



# Fertility-sparing management of early-stage endometrial cancer in reproductive age women: current treatment outcomes and future directions

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Endometrial cancer is a significant and growing health issue in developed countries across the globe, with an increasing number of women diagnosed each year. The need for fertility-sparing treatment options for endometrial cancer is internationally recognized as an urgent priority to support women who wish to maintain their capability of carrying a pregnancy.<sup>1</sup>

In this December 2021 lead article of the *International Journal of Gynecological Cancer*, Chae-Kim *et al*<sup>2</sup> present an overview of current evidence on outcomes of reproductive age women treated with progestin and metformin for atypical endometrial hyperplasia and early-stage endometrial cancer. Treatment with progestin and metformin was associated with lower rates of disease relapse compared with progestin alone. Disease remission, pregnancy and live birth rates were similar between those two groups.

The authors are to be commended on completion of the first systematic review and meta-analysis to examine outcomes after progestin and metformin therapy. The rising incidence of endometrial cancer is largely attributable to the rising rates of obesity in developed countries.<sup>3</sup> The causes of obesity are complex and influenced by a range of individual factors, such as diet and physical activity, as well as broader social, economic and environmental factors.

In their study,<sup>2</sup> Chae-Kim and colleagues provide a thorough discussion on the limitations of their meta-analysis, including that the results are limited by the small number of studies that met the inclusion criteria. The lack of standardization in the reporting of outcomes, covariates and timepoints of assessment within these studies also represents a challenge. For example, important data such as body mass index (BMI) were missing from several of the included studies, which limits our ability to assess if treatment response varies in patients who are obese or non-obese, or if it can be applied to all patients regardless of their BMI status. These limitations highlight the current study specific approach to reporting of research items, with each

individual study assessing or reporting outcomes in slightly different ways.

The issue of heterogeneity could be reduced through improved international collaboration and standardization of reporting of items in gynecological oncology research, to allow studies to be more easily combined for meta-analysis, and enable statistical comparison between patients based on their clinical characteristics and treatment modality received. Molecular studies on predictive factors are essential to drive better outcomes for affected women. Ultimately, this might contribute to an improved understanding of which treatments work, for whom, and reporting of new research in an efficient and timely manner to support improvements in fertility-sparing treatment options for young women with endometrial cancer. Further work is also required to understand the patient perspective of receiving fertility-sparing or surgical treatment, especially among those women in whom both options are feasible, and to understand their relative adverse events and quality of life impacts. New statistical methods that allow us to compare the relative impact should be applied so that future patients can be better informed about their treatment choices.<sup>4</sup>

While clinical research focusing on treatment is essential to improve health outcomes for women already diagnosed with endometrial cancer,<sup>5</sup> greater emphasis on the causative factors and preventive efforts may be even more critical. Therefore, future research driven by consumers, researchers and clinicians is warranted on the primary prevention of endometrial cancer.

In summary, the analysis by Chae-Kim *et al*<sup>2</sup> challenges the international community to increase efforts to systematically address endometrial cancer prevention and treatment in young women.

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## REFERENCES

- 1 Lucchini SM, Esteban A, Nigra MA, *et al.* Updates on conservative management of endometrial cancer in patients younger than 45 years. *Gynecol Oncol* 2021;161:802–9.
- 2 Chae-Kim JJ, Garg G, Gavrilova-Jordan L. Outcomes of women treated with progestin and metformin for atypical endometrial hyperplasia and early endometrial cancer: a systematic review and meta-analysis. *International Journal of Gynecological Cancer* 2021.
- 3 Raglan O, Kalliala I, Markozannes G, *et al.* Risk factors for endometrial cancer: an umbrella review of the literature. *Int J Cancer* 2019;145:1719–30.
- 4 GebSKI V, Marschner I, Asher R, *et al.* Using recurrent time-to-event models with multinomial outcomes to generate toxicity profiles. *Pharm Stat* 2021;20:840–9.
- 5 Janda M, Robledo KP, GebSKI V, *et al.* Complete pathological response following levonorgestrel intrauterine device in clinically stage 1 endometrial adenocarcinoma: results of a randomized clinical trial. *Gynecol Oncol* 2021;161:143–51.