

## Dysmenorrhea and uterine innervation in adenomyosis and endometriosis

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aberrant reinnervation within the uterosacral insertions rather than the adenomyosis itself, as unilateral uterosacral injuries corresponded to ipsilateral pain presentations.

Do the authors recognize these 2 different patterns of adenomyosis in their large European series? Do the consequences of injuries to uterine nerves account for adverse pregnancy outcomes in painful, asymmetrical adenomyosis?<sup>4</sup>

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The author reports no conflict of interest.

All studies reported in this letter had appropriate institutional review board

#### REFERENCES

- 1. Rees CO, van Vliet H, Siebers A, et al. The ADENO study: ADenomyosis and its Effect on Neonatal and Obstetric outcomes: a retrospective population-based study. Am J Obstet Gynecol 2023;229: 49.e1-12.
- 2. Quinn M. Uterine innervation in adenomyosis. J Obstet Gynaecol 2007;27:287-91.
- 3. Quinn M. The endometrial-myometrial interface. Am J Obstet Gynecol 2003;188:857-8.
- 4. Wu XQ, Cai YY, Xia WT, Quinn MJ. The aetiology of pre-eclampsia, 1945-1953. BJOG 2016;123:2130.
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## Dysmenorrhea and uterine innervation in adenomyosis and endometriosis: the role of the sacrouterine ligament: reply



We thank Quinn et al for sharing their findings with us, as it is an interesting theory concerning how uterine innervation and adenomyosis (symptoms) may be connected. It remains a clinical challenge to separate the effects of endometriosis and adenomyosis from each other, especially concerning which of the 2 conditions plays the primary role in dysmenorrhea. In our study, we were unable to differentiate the groups based on purely uterine characteristics because of the limitation of our anonymized datasets, and thus, we cannot provide a clear answer to your question. Furthermore, we do not have data regarding the state of the sacrouterine ligaments in these patients as these are not looked at in all cases.

However, we believe that the presence of adenomyosis itself will still primarily affect uterine innervation and contractility because of the disruption of myometrial tissue and thereby gap junctions and interstitial Cajal-like cells, leading to symptoms. This theory regarding the effect of adenomyosis on uterine peristalsis has been described in detail in the literature in past years.<sup>1,2</sup>

If the sacrouterine ligaments are additionally affected, this may potentially result in further disruption of uterine innervation, and we know that sacrouterine ligament involvement is associated with more severe dysmenorrhea in endometriosis.3 This would be an interesting area to investigate in prospective studies in the future. However, the question remains whether added pathology comes from the invasion of the sacrouterine ligament or whether the concomitant endometriosis is the added severe disease. Our group is currently in the process of conducting a subanalysis using our existing dataset investigating pregnancy outcomes in women with adenomyosis and concomitant endometriosis vs adenomyosis alone. Potentially, we will be able to answer this query in more detail.

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## REFERENCES

- **1.** Leyendecker G, Kunz G, Wildt L, Beil D, Deininger H. Uterine hyperperistalsis and dysperistalsis as dysfunctions of the mechanism of rapid sperm transport in patients with endometriosis and infertility. Hum Reprod 1996;11:1542–51.
- **2.** Shaked S, Jaffa AJ, Grisaru D, Elad D. Uterine peristalsis-induced stresses within the uterine wall may sprout adenomyosis. Biomech Model Mechanobiol 2015;14:437–44.
- **3.** Gruber TM, Mechsner S. Pathogenesis of endometriosis: the origin of pain and subfertility. Cells 2021;10:1381.

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# Extending use of levonorgestrel 52 mg intrauterine device to 8 years



TO THE EDITORS: We appreciate the journal publishing our reports on the extension of the levonorgestrel 52 mg intrauterine device (IUD) to 8 years for Liletta<sup>1</sup> and Mirena,<sup>2</sup> and also for the corresponding editorial.<sup>3</sup> Unfortunately, the editorial misrepresents the success rates as reported with lifetable analyses. This error is important should a reader choose to simply read the editorial as a synopsis and not review the studies themselves.

The editorial reports 8-year cumulative pregnancy rates of 1.09 (95% confidence interval [CI], 0.56–2.13) for Liletta and 0.68 (95% CI, 0.17–2.71) for Mirena.<sup>1,2</sup> This statement implies that Mirena potentially has a lower pregnancy rate than Liletta. In fact, the life-table pregnancy rate for Liletta reflects an 8-year cumulative rate, whereas the rate for Mirena only reflects the 3-year cumulative failure rate using the Kaplan-Meier method for years 6 to 8. The Liletta study demonstrates a life-table pregnancy rate of approximately 0.46 in years 6 to 8.

Because the Mirena study<sup>2</sup> did not evaluate a single cohort for 8 continuous years, only the data from the Liletta study<sup>1</sup> can be used to report the full 8-year cumulative pregnancy risk with levonorgestrel 52 mg IUD use. However, the consistent results between the 2 studies for years 6 to 8 demonstrate that patients using either device should experience equivalent clinical performance through 8 years of use.

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M.D.C. has received speaking honorarium from Gedeon Richter, Mayne, and Organon, serves on an Advisory Board for Gedeon Richter, GlaxoSmithKline, OLIC, and Organon, and is a consultant for Estetra SRL, Mayne, and Medicines360. The Department of Obstetrics and Gynecology, University of California, Davis, receives contraceptive research funding for M.D.C. from Chemo Research SL, Evofem, Medicines360, Merck, and Sebela.

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### **REFERENCES**

- **1.** Creinin MD, Schreiber CA, Turok DK, Cwiak C, Chen BA, Olariu AI. Levonorgestrel 52 mg intrauterine system efficacy and safety through 8 years of use. Am J Obstet Gynecol 2022;227:871.e1–7.
- **2.** Jensen JT, Lukkari-Lax E, Schulze A, Wahdan Y, Serrani M, Kroll R. Contraceptive efficacy and safety of the 52-mg levonorgestrel intrauterine system for up to 8 years: findings from the Mirena Extension Trial. Am J Obstet Gynecol 2022;227:873.e1–12.
- **3.** Goldberg AB. Extending use of 52-mg levonorgestrel intrauterine systems to 8 years: bridging phases of life. Am J Obstet Gynecol 2022;227:803-4.
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