

**Hormonal treatment of endometriosis:
update searches and screening
for
Universitätsklinikum Schleswig-Holstein/Campus Kiel**



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1. PROJECT OBJECTIVES

A key aim of the research project “Making SDM a reality” is to inform patients as part of shared decision making (SDM).

Kleijnen Systematic Reviews (KSR) Ltd has prepared an evidence report with a synthesis of the evidence of the hormonal treatment of endometriosis.

2. METHODS

LITERATURE SEARCHES

Literature searches were conducted to identify systematic reviews and evidence-based guidelines about endometriosis to update the 2019 evidence report.

The search strategies were developed specifically for each database and the keywords adapted according to the configuration of each database. Searches were limited by date range to update earlier searches: 2019-2021. Searches were not limited by language or publication status.

SEARCH SOURCES

Systematic reviews and guidelines

The following systematic review and health technology assessment specific databases were searched:

- Cochrane Database of Systematic Reviews (CDSR) (Wiley): issue 9 of 12, September 2021
- KSR Evidence (Internet) (<https://ksrevidence.com/>): 2019-2021
- Epistemonikos (Internet) (<https://www.epistemonikos.org/>): 2019-2021
- International HTA Database (INAHTA) (<https://database.inahta.org/>): 2019-2021

The following guidelines resources were searched:

- Guidelines International Network (GIN) (Internet) (<https://www.g-i-n.net/home>): up to 10 September 2021
- NICE Evidence (Internet) (www.evidence.nhs.uk/): 2019-2021
- NICE Guidance (Internet) (<https://www.nice.org.uk/guidance>): 2019-2021
- ECRI Guidelines Trust (Internet) (<https://guidelines.ecri.org/>): 2019-2021
- Trip Database (<https://www.tripdatabase.com/>): 2019-2021
- Canadian Agency for Drugs and Technologies in Health (CADTH) (www.cadth.ca): 2019-2021

Full details of all search strategies are presented in Appendix 1.

Handling of citations

References identified from the searches were downloaded into EndNote bibliographic management software for further assessment and handling.

Supplementary searches

The bibliographies of included studies and review articles were also checked for additional relevant articles.

Prioritisation

During formal screening of titles and abstracts, studies were subject to a prioritisation process whereby the recency e.g., to most up-to-date clinical practice guidelines (CPG), methodological quality e.g., Cochrane systematic review (CSR), quality of the analyses per outcome (e.g., ratio of RCTs to observational studies), the number of included RCTs, the breadth of the timepoints reported etc. were considered to further prioritise which studies would be used to inform analyses. Studies were categorised into the following three categories: '1' = German, American, European or similar CPG; '2' = CSR or similar quality SR; '3' = potentially lower/other quality SR.

3. RESULTS

The original EBSCO searches were conducted in November 18, 2019; and of the 179 references screened, 16 studies were deemed eligible. In the current update, a total of 891 records were retrieved from the electronic literature searches (Table 2). After the removal of duplicate records 468 titles and abstracts were screened by two reviewers. 18 records were found to be potentially eligible and were longlisted after a consensus. Of those, five were short-listed and included in the analyses (Table 1).¹⁻⁵

UPDATE – Concluding Assessment by SHARE TO CARE Evidence Team (30/08/22)

No new information regarding the question of the decision aid (hormonal therapy vs. analgesics) was found in the update searches conducted by KSR Ltd in October 2021. In the studies identified, treatments were predominantly compared to placebo (Table 1). One study (Grammatis, 2021) evaluated pentoxifylline, a drug which is not approved for the treatment of endometriosis in Germany. The updated German guideline (AWMF, 2020) is in line with the information provided in the decision aid.

Conclusion regarding the evidence report: No evidence update required. The present evidence report (October 30, 2019) remains valid until further notice.

Table 1 Evidence sources

Study/year	Evidence type	Primary studies	Number of studies	Intervention	Comparator	Outcome	Date searched
van Hoesel 2021 ¹	SR	RCT	1	Oestrogen receptor modulators	Placebo, no treatment, other medical treatment, or surgery	Relief of pelvic pain, adverse events, QoL	May 2020
Samy 2021 ²	SR/NMA	RTCs	36	Dienogest, combined hormonal contraceptives, and elagolix, gonadotropin-releasing hormone analogues	Placebo, other treatment	Pain severity, non-menstrual pelvic pain	March 2019
Grammatis 2021 ³	SR	RCTs	5	Pentoxifylline	Placebo	Live birth rate and overall pain	December 2020
Chen 2020 ⁴	SR	RCTs	25	Hormonal therapy	Placebo, surgery, no medical therapy	Painful symptoms of endometriosis	November 2019
AWMF 2020 ⁵	CPG	Various	322	Multiple, see chapters 4 and 6 of CPG	Multiple, see chapters 4 and 6 of CPG	Multiple, see chapters 4 and 6 of CPG	August 2020
CPG = clinical practice guideline; NMA = network meta-analysis; RCT = randomised controlled trial; SR = systematic review							

Table 2 Overview of primary studies included in the identified SRs/CPGs

Study/year	Primary study(ies)	Reference (first author & journal)
van Hoesel 2021 ¹	RCT	1. Stratton 2008 Obstetrics & Gynecology 2008;111(1):88-96.
Samy 2021 ²	RTCs	1. Bromham DR. J Obstet Gynaecol 1995;15:188–94. 2. Halbe HW. Br J Obstet Gynaecol 1995;102(Suppl):17–21. 3. Carbonell JL. J Reprod Health Med 2015;2:17–25. 4. Roghaei MA. Int J Fertil Steril 2010;4:67–72. 5. Elstein M. Int J Gynecol Obstet 1992;39: 256–256. 6. Adamson GD. Int J Fertil Menopausal Stud 1994;39:215–7. 7. Hornstein MD. Fertil Steril 1995;63:955–62. 8. Henzl MR. N Engl J Med 1988;318:485–9. 9. Cheng M-H-H. J Chin Med Assoc 2005;68:307–14.

Study/year	Primary study(ies)	Reference (first author & journal)
		10. Rolland R. Am J Obstet Gynecol 1990;162:586–8. 11. Bergqvist A. Gynecol Endocrinol 2000;14:425–32. 12. Shaw RW. Fertil Steril 1992;58:265–72. 13. Rock JA. Obstet Gynecol 1993;82:198–205. 14. Wheeler JM. Am J Obstet Gynecol 1992;167:1367–71. 15. Agarwal SK. J Reprod Med 1997;42:413–23. 16. Dlugi AM. Fertil Steril 1990;54:419–27. 17. Ling FW. Obstet Gynecol 1999;93:51–8. 18. Cirkel U. Eur J Obstet Gynecol Reprod Biol 1995;59:61–9. 19. Bergqvist A. Fertil Steril 1998;69:702–8. 20. Hornstein MD. Obstet Gynecol 1998;91:16–24. 21. Zupi E. Fertil Steril 2004;82:1303–8. 22. Moghissi KS. Fertil Steril 1998;69:1056–62. 23. Carr B. J Endometr 2013;5:105–15. 24. Diamond MP. Reprod Sci 2014;21:363–71. 25. Taylor HS. N Engl J Med 2017;377:28–40. 26. Carr B. Reprod Sci 2014;21:1341–51. 27. Harrison RF. Fertil Steril 2000;74:24–30. 28. Crosignani PG. Hum Reprod 2006;21:248–56. 29. Strowitzki T. Hum Reprod 2010;25:633–41. 30. Harada T. Fertil Steril 2009;91:675–81. 31. Lang J. J Womens Health 2017;27:148–55. 32. Petta CA. Hum Reprod 2005;20:1993–8. 33. Harada T. Fertil Steril 2008;90:1583–8. 34. Schlaff WD. Fertil Steril 2006;85:314–25. 35. Sesti F. Fertil Steril 2007;88:1541–7. 36. Carbonell JL. J Reprod Health Med 2016;2:17–25.
Grammatis 2021³	RCTs	1. Alborzi S. Journal of Minimally Invasive Gynecology 2007;14(1):54-8. 2. Balasch J. Human Reproduction 1997;12(9):2046-50. 3. Creus M. Human Reproduction 2008;23(8):1910-6. 4. Ghahiri A. Iranian Journal of Reproductive Medicine 2012;10(3):219-22.

Study/year	Primary study(ies)	Reference (first author & journal)
		5. Kamencic H. Journal of Minimally Invasive Gynecology 2008;15(1):62-6.
Chen 2020⁴	RCTs	1. Alkatout I. Journal of Minimally Invasive Gynaecology 2013;20(4):473-81. 2. Angioni S. Archives of Gynecology and Obstetrics 2015;291:363-70. 3. Audebert A. Obstetrics and Gynecology 1998;79:145-8. 4. Bianchi S. Human Reproduction 1999;14(5):1335-7. 5. Busacca M. Human Reproduction 2001;16(11):2399-402. 6. Cucinella G. Archives of Gynecology and Obstetrics 2013;288:821-7. 7. Donnez J. Fertility and Sterility 1994;62(1):63-6. 8. Hornstein MD. Fertility and Sterility 1997;68(5):860-4. 9. Huang C. International Journal of Clinical and Experimental Medicine 2018;11:4132-7. 10. Loverro G. Human Reproduction 2001;16 Suppl(1):96. 11. Loverro G. European Journal of Obstetrics, Gynecology, and Reproductive Biology 2008;136(2):194-8. 12. Muzii L. American Journal of Obstetrics and Gynecology 2000;183(3):588-92. 13. Parazzini F. American Journal of Obstetrics and Gynecology 1994;171:1205-7. 14. Rickes D. Fertility and Sterility 2002;78:757-62. 15. Seracchioli R. Fertility and Sterility 2010;93:52-6. 16. Seracchioli R. Fertility and Sterility 2010;94:464-71. 17. Sesti F. Fertility and Sterility 2007;88(6):1541-7. 18. Sesti F. European Journal of Obstetrics and Gynaecology and Reproductive Biology 2009;147:72-7. 19. Shaw R. Gynaecological Endoscopy 2001;10:151-7. 20. Tanmahasamut P. Gynecological Endocrinology 2017;33:534-9. 21. Telimaa S. Gynecological Endocrinology 1987;1(4):363-71. 22. Tsai Y-L. Journal of Reproductive Medicine 2004;49(12):955-9. 23. Vercellini P. British Journal of Obstetrics and Gynaecology 1999;106:672-7. 24. Yang D. Chinese Journal of Integrative Medicine 2006;12(3):218-20. 25. Yang Y. Journal of the College of Physicians and Surgeons Pakistan 2018;29:313-6.
AWMF 2020⁵	Various	Chapter VII presents a total of 365 references cited. Given the potential relevance of a German guideline, each section should be checked for relevant references.
RCT = randomised controlled trial		

REFERENCES

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- [4] Chen I, Veth VB, Choudhry AJ, Murji A, Zakhari A, Black AY, et al. Pre- and postsurgical medical therapy for endometriosis surgery. Cochrane Database of Systematic Reviews 2020, Issue 11. Art. No.: CD003678. DOI: 10.1002/14651858.CD003678.pub3
- [5] AWMF. Diagnostik und Therapie der Endometriose. S2k-LL (DGGG), 2020 Available from: <https://www.awmf.org/leitlinien/detail/II/015-045.html>

APPENDIX 1: SEARCH STRATEGIES

Table 2: Systematic reviews and guideline search results

Database	Dates	Results
CDSR	2019 - Issue 9, September 2021	12
KSR Evidence	2019-2021	216
Epistemonikos	2019-2021	286
INAHTA	2019-2021	1
NICE Evidence	01/01/2019 - 10/09/2021	96
NICE Guidance	2019-2021	1
GIN	2019-2021	1
ECRI	2019-2021	0
Trip	2019-2021	278
CADTH	2019-2021	0
Total		891
Total after de-duplication		468

Search strategies

Cochrane Database of Systematic Reviews (CDSR) (Wiley): Issue 9 of 12, September 2021

Searched: 10.9.21

#1 MeSH descriptor: [Endometriosis] explode all trees 889
#2 endometrio*:ti,ab,kw 3075
#3 #1 or #2 with Cochrane Library publication date Between Jan 2019 and Dec 2021, in Cochrane Reviews, Cochrane Protocols 12

KSR Evidence (Internet): Database last updated 10 September 2021

www.ksrevidence.com

Searched: 10.9.21

1 endometrio* in All text Date published: 2019 - 2021 216 results
Search run Fri Sep 10 2021

Epistemonikos (Internet): up to 10 September 2021

<https://www.epistemonikos.org/en/>

Searched: 10.9.21

(title:(endometriosis OR endometrioma OR endometriomas OR endometrioses) OR
abstract:(endometriosis OR endometrioma OR endometriomas OR endometrioses))
Publication year: Custom year range: From 2019 To 2021
Total: 286

International HTA Database (INAHTA): up to 10 September 2021

<https://database.inahta.org/>

Searched: 10.9.21

("Endometriosis"[mh]) OR (endometrio*) FROM 2019 TO 2021

1 record retrieved

NICE Evidence Search (Internet): up to 10 September 2021

<https://www.evidence.nhs.uk/>

Searched: 10.9.21

Search terms	Results (Guidance; Systematic Reviews): 01/01/2019-10/09/2021
Endometriosis	160
Sifted for relevance	96

National Institute for Health and Care Excellence (NICE): Guidelines

<https://www.nice.org.uk/>

Searched: 10.9.21

NICE Guidance; Conditions and diseases; Gynaecological conditions; Endometriosis and fibroids

Guidance 12 - relevant 0 (2 pre-2019)

NICE advice 1 - relevant 0

Quality standards 0 - relevant 0 (1 pre-2019)

NICE Pathways 1 - relevant 1

Relevant document: 1

Guidelines International Network (GIN). International Guidelines Library (Internet): up to 10 September 2021

<https://g-i-n.net/international-guidelines-library/>

Searched: 10.9.21

endometrio*

2019-2021

1 record retrieved

ECRI Institute Guidelines Trust (Internet): up to 10 September 2021

<https://guidelines.ecri.org/>

Searched: 10.9.21

endometrio*

2019-2021

0 records retrieved

Trip Database: up to 10 September 2021

<https://www.tripdatabase.com/>

Searched: 10.9.21

endometrio* from_date:2019

Systematic Reviews: 191 records retrieved

Guidelines: 87 records retrieved

Total: 278 records retrieved

Canadian Agency for Drugs and Technologies in Health (CADTH): up to 10 September 2021

<https://www.cadth.ca/>

Searched: 10.9.21

endometriosis

0 records retrieved