

Reevaluating response and failure of medical treatment of endometriosis: a systematic review

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Objective: To assess patient response rates to medical therapies used to treat endometriosis-associated pain.

Design: A systematic review with the use of Medline and Embase.

Setting: Not applicable.

Patient(s): Women receiving medical therapy to treat endometriosis.

Interventions(s): None.

Main Outcome Measure(s): The proportions of patients who: experienced no reduction in endometriosis-associated pain symptoms; had pain symptoms remaining at the end of the treatment period; had pain recurrence after treatment cessation; experienced an increase or no change in disease score during the study; were satisfied with treatment; and discontinued therapy owing to adverse events or lack of efficacy. The change in pain symptom severity experienced during and after treatment, as measured on the visual analog scale, was also assessed.

Result(s): In total, 58 articles describing 125 treatment arms met the inclusion criteria. Data for the response of endometriosis-associated pain symptoms to treatment were presented in only 29 articles. The median proportions of women with no reduction in pain were 11%–19%; at the end of treatment, 5%–59% had pain remaining; and after follow-up, 17%–34% had experienced recurrence of pain symptoms after treatment cessation. After median study durations of 2–24 months, the median discontinuation rates due to adverse events or lack of efficacy were 5%–16%.

Conclusion(s): Few studies of medical therapies for endometriosis report outcomes that are relevant to patients, and many women gain only limited or intermittent benefit from treatment. (Fertil Steril® 2017;108:125–36. ©2017 by American Society for Reproductive Medicine.)

Key Words: Endometriosis, pain, medical therapy, systematic review

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Endometriosis is a chronic inflammatory disease that mainly affects women of reproductive

age. Medical therapy can alleviate endometriosis-associated pain, but for many women pain relief is limited in

efficacy and duration, and symptoms often reoccur after treatment cessation (1). Most current medical therapies for endometriosis to treat the disease and its symptoms rely on suppression of local or systemic estrogen levels or direct hormonal effects on endometriosis lesions. To date, all available hormonal therapies appear to have similar efficacy, but their tolerability profiles differ (2). The most widely used long-term therapies are progestins and combined oral contraceptives (COCs), but they are associated with irregular bleeding patterns, breast tenderness, and mood disturbances in some women (3). Other hormonal

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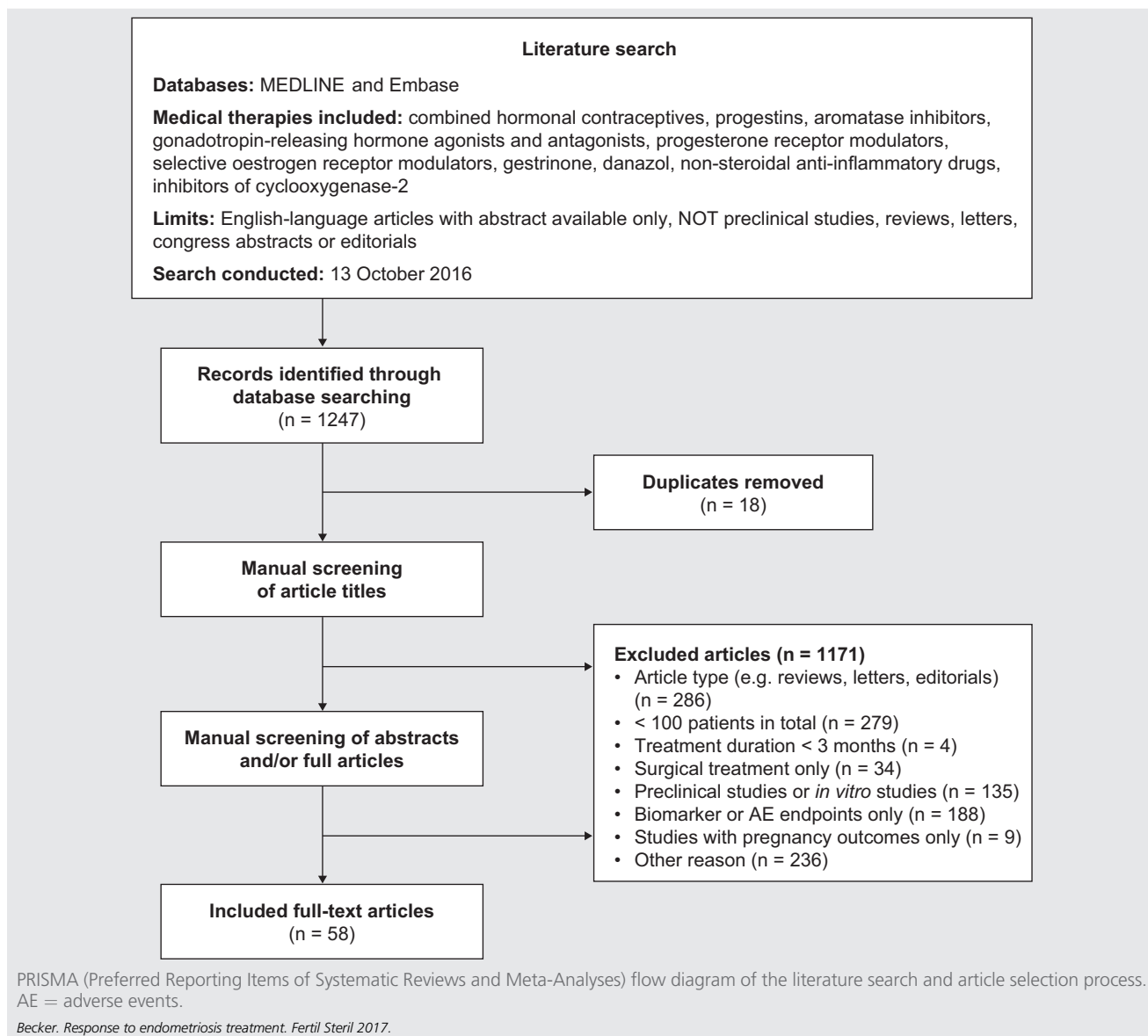
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FIGURE 1



therapies include GnRH agonists, which induce a hypoestrogenic state resulting in menopausal symptoms, such as hot flashes, and are associated with reduced bone mineral density (4). They are therefore normally restricted to short-term use. Combination with add-back therapy may extend the period for which GnRH agonists can be used, although long-term safety data on this treatment regimen are limited (3). Danazol, especially when administered orally, is associated with significant androgenic side effects, which has considerably restricted its routine use. In addition, analgesics, such as nonsteroidal antiinflammatory drugs (NSAIDs), are widely prescribed for pain relief despite limited evidence of their efficacy in endometriosis (1).

It has been suggested that one-fourth to one-third of patients treated with the use of COCs or progestins require

further treatment because of lack of response or poor tolerability (5, 6), but there are limited data to support these figures. A review of randomized controlled trials (RCTs) published in the period 1976–1998 showed that 40%–70% of women receiving surgical treatment or medical therapy had relief from endometriosis-associated pelvic pain for ≥ 6 months (7). In contrast, in a systematic review of the use of progestins published in 1997, $\sim 9\%$ of women had no reduction in pelvic pain and 50% reported pelvic pain at the end of the follow-up period (8).

The main objectives of the present systematic review were to determine response rates to medical therapy, the frequency and extent of remaining endometriosis-associated pain symptoms, and the recurrence of pain symptoms after cessation of therapy. Furthermore, we set out to characterize the

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