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Assessing Research Gaps and Unmet Needs in Endometriosis

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87 **Condensation**

88 A Society for Women's Health Research working group reviews the latest research on
89 endometriosis and identifies areas of need to improve diagnosis, treatment, and access to quality
90 care.

91

92 **Short Title**

93 Assessing Research Gaps and Unmet Needs in Endometriosis

94

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95 **Abstract**

96 Endometriosis, a systemic disease that is often painful and chronic, affects ~10% of
97 reproductive-age women. The disease can negatively impact a patient's physical and emotional
98 well-being, quality of life, and productivity. Endometriosis also places significant economic and
99 social burden on patients, their families, and society as a whole. Despite its high prevalence and
100 cost, endometriosis remains underfunded and under-researched — greatly limiting our
101 understanding of the disease and slowing much-needed innovation in diagnostic and treatment
102 options. Due in part to the societal normalization of women's pain and stigma around menstrual
103 issues, there is also a lack of disease awareness among patients, health care providers, and the
104 public. The Society for Women's Health Research convened an interdisciplinary group of expert
105 researchers, clinicians, and patients for a roundtable meeting to review the current state of the
106 science on endometriosis and identify areas of need to improve a woman's diagnosis, treatment,
107 and access to quality care. Comprehensive and interdisciplinary approaches to disease
108 management and increased education and disease awareness for patients, health care providers,
109 and the public are needed to remove stigma, increase timely and accurate diagnosis and
110 treatment, and allow for new advancements.

111

112 **Key words**

113 chronic pain, endometriosis, infertility, pelvic pain, stigma, women's health

114

115

116 **Introduction**

117 Endometriosis is a painful, chronic, and inflammatory disease that is characterized by the growth
118 of endometrial-like tissue outside of the uterus and affects approximately 10% of reproductive-
119 age women, an estimated 200 million women and teens worldwide.¹⁻³ Common symptoms of this
120 systemic,⁴⁻⁶ debilitating disease include variable experience and severity of dysmenorrhea,
121 dyspareunia, chronic pelvic pain, and infertility,⁷⁻⁹ as well as back pain, and bladder or bowel
122 problems (e.g., painful urination or bowel movements).^{7,8,10-12} Other individuals are
123 asymptomatic.^{7,11,13} Prevalence of endometriosis is highest in women with infertility or chronic
124 pelvic pain, reaching 25-50% and 71–87%, respectively.^{2,3,9} Although data are limited, there is
125 some evidence that approximately 40% of adult cases show spontaneous regression of disease in
126 follow-up studies a few months after initial examination.¹⁴ However, longer-term follow-up
127 studies in baboons, which have spontaneous endometriosis similar to humans, suggest
128 endometriosis is a progressive disease, with periods of regression.¹⁵

129
130 Although the cardinal symptoms of endometriosis are pelvic symptoms, comorbidities are very
131 common in women with endometriosis. Nearly 95% of women with endometriosis reported at
132 least one or more comorbid disorders, such as migraine, depression, anxiety, irritable bowel
133 syndrome (IBS), interstitial cystitis/painful bladder syndrome, chronic fatigue syndrome,
134 fibromyalgia, uterine fibroids, and ovarian cysts.¹⁶⁻²⁰ Endometriosis is also associated with
135 increased risk for several types of cancer (ovarian, breast, cutaneous melanoma), systemic lupus
136 erythematosus, rheumatoid arthritis, and cardiovascular disease.²¹⁻²⁴

137
138 Endometriosis can negatively affect all aspects of a patient's daily life, including sexual
139 relations, appetite, exercise, sleep, emotional well-being, social activities, childcare, and work
140 and household productivity.²⁵⁻²⁸ Total workplace productivity loss averages 6.3 hours per week,
141 with the majority of that loss due to presenteeism, while total household productivity loss
142 averages 4.9 hours per week.²⁹

143
144 Endometriosis is also costly, at an estimated \$69.4 billion per year in excess health expenditures
145 in the United States.^{2,30} Estimated direct costs in the U.S. are \$12,118 per patient per year.³¹
146 Claims data show that average annual health care costs (medical and prescription) are more than
147 three times higher for women with endometriosis compared to patients without endometriosis,
148 even five years pre- and five years post-diagnosis.^{2,18,30} Annual health care costs for women with
149 endometriosis treated in referral centers are similar to costs for other chronic diseases that
150 receive more resources such as diabetes, Crohn's disease, and rheumatoid arthritis.³⁰
151 Endometriosis-associated costs can be greater depending on the severity of disease, presence of
152 pelvic pain, and presence of infertility.³⁰

153
154 Despite the prevalence of endometriosis and its significant burden on women, their families,
155 society, and the health care system, the disease is underfunded and under-researched.³² As such,

156 scientific progress has been slow, and diagnostic and treatment options remain limited. Societal
157 factors such as clinical gender bias and inequities in the treatment of pain based on gender have
158 been well-documented³³⁻³⁶ and may contribute to the under-prioritization of endometriosis
159 research funding. Furthermore, endometriosis symptoms that are associated with menstruation,
160 infertility, and/or bowel issues are often met with societal stigma,³⁷⁻⁴⁰ and thus may further
161 complicate addressing this disease.

162
163 To this end, the Society for Women's Health Research (SWHR), a nearly 30-year-old nonprofit
164 organization, convened an interdisciplinary expert group of researchers, clinicians, and patients
165 for a roundtable meeting to evaluate both diagnostics and treatment in endometriosis. The goals
166 of the meeting were to a) review current practice; b) reflect on the barriers affecting diagnosis
167 and treatment; and c) highlight research priorities for the future of endometriosis care. Below we
168 summarize discussions from the roundtable.

169

170 **Methods**

171 SWHR designed the roundtable to create an interactive dialogue between thought leaders in the
172 field, including researchers, clinicians, patients, and industry and government officials. SWHR
173 selected participants with diverse perspectives with regards to expertise, training, background,
174 gender, and geographic location. Discussions with meeting attendees prior to the roundtable
175 identified topics that experts considered top priorities to address in an interdisciplinary setting.
176 An SWHR facilitator moderated the roundtable, and patients gave personal testimonies, which
177 organically led to discussion among the group. A transcriptionist captured minutes from the
178 meeting, and these minutes were used to identify themes — including barriers to diagnosis and
179 treatment and priorities for the future — that informed the structure of this paper.

180

181 **Diagnostics**

182 **Current Practice**

183 Laparoscopic visualization with or without histologic confirmation is currently the only way to
184 definitively diagnose endometriosis and remains the gold standard for diagnosis in clinical
185 guidelines from many national and international professional societies, including the American
186 College of Obstetricians and Gynecologists (ACOG), the European Society of Human
187 Reproduction and Embryology (ESHRE), the World Endometriosis Society (WES), the National
188 Institute for Health and Care Excellence (NICE), the Society of Obstetricians and
189 Gynaecologists of Canada (SOGC), and the American Society for Reproductive Medicine
190 (ASRM).^{9,41-45} Most of these guidelines have not been updated within the past 5-10 years,
191 although guidelines from the aforementioned groups and many experts in the field state that
192 definitive diagnosis is not always required before initiating medical therapy.^{46,47} Like with most
193 surgeries, laparoscopy is invasive and comes with its own risks, plus economic and geographic
194 barriers may limit patients' access.^{2,47}

195

196 **Barriers to Diagnosis**

197 Diagnostic delays remain a significant barrier to receiving timely and appropriate care for
198 endometriosis. On average, women experience a delay of 7-12 years from the onset of pain
199 symptoms to surgical diagnosis.^{28,48} The delay for patients seeking help due to pelvic pain is
200 longer than the delay for those seeking help due to infertility.^{49,50} Delays in diagnosis can
201 degrade the patient-provider relationship, cause physical and emotional damage, impair quality
202 of life, and add to the significant personal and societal costs associated with the disease.^{28,51,52}

203

204 *Societal barriers and the role of stigma*

205 Stigma around menstrual issues and societal normalization of women's pain play a pivotal role in
206 diagnostic delay. One study found women wait on average 2.3 years from the onset of symptoms
207 before seeking help.⁴⁸ Women may not recognize their pain as a treatable condition, especially if
208 this pain began at menarche.⁵³ Societal normalization of women's pain and the "taboo" around
209 topics like menstruation or painful sex can prevent women from seeking care or discussing
210 symptoms with and receiving support from friends, family, and health care providers (HCPs).³⁸

211

212 *Barriers related to understanding of the disease*

213 The etiology of endometriosis is not fully understood. Retrograde menstruation, coelomic
214 metaplasia, genetics, immune dysfunction, oxidative stress and inflammation, and stem cells are
215 all thought to play a role in the pathogenesis of the disease.^{6,54,55} Some experts argue
216 endometriosis should be considered an amalgamation of disorders due to the diversity of
217 symptoms and symptom severity, as well as differences in lesion types (e.g., superficial
218 peritoneal endometriosis, deep infiltrating endometriosis, ovarian endometriomas, extra-pelvic
219 endometriosis).^{42,56} This lack of clear understanding about the disease's etiology and the
220 spectrum of symptoms, including gynecologic and non-gynecologic issues (described above),
221 can also contribute to diagnostic delay.

222

223 For example, chronic pelvic pain, the most commonly reported symptom of endometriosis, is not
224 specific to endometriosis. Other gynecologic diseases such as pelvic inflammatory disease,
225 uterine fibroids, and adenomyosis, as well as non-gynecologic diseases including IBS, interstitial
226 cystitis/painful bladder syndrome, and fibromyalgia, can have symptoms that overlap with those
227 common in endometriosis.⁴⁴ The process of ruling out these other diseases can contribute to
228 delays in diagnosis and treatment of endometriosis. Further, these conditions are highly
229 comorbid with endometriosis, so delays can occur if HCPs do not recognize that endometriosis
230 can co-exist with other pain conditions, particularly if symptoms persist.

231

232 *Provider-related barriers*

233 On average, women with endometriosis make seven visits to their primary HCP before being
234 referred to specialists,²⁸ and nearly three-quarters of women experience a misdiagnosis.⁴⁸ In
235 addition, the short time allotted for HCP visits may not allow for adequate evaluation.⁵⁷

236

237 One survey of general HCPs found that half could not name three of the main symptoms of
238 endometriosis. Additionally, nearly two-thirds did not feel comfortable in the diagnosis and
239 follow-up of women presenting with endometriosis.⁵⁸ This can have serious implications, as only
240 24% of surveyed practitioners made referrals without delay of additional examinations when
241 endometriosis was suspected.⁵⁸ Another survey of gynecologists found nearly 50% believed that
242 earlier diagnosis of endometriosis cannot prevent the course of the disease since there is no
243 effective treatment.⁵¹ This survey demonstrates that HCPs may not make a referral to a specialist
244 even if endometriosis is suspected, despite the fact that evidence suggests diagnostic delays
245 cause physical, emotional, and social harm for patients.⁵³

246

247 Stigma also plays a role in provider-related delayed diagnosis. HCPs may trivialize symptoms,
248 be quick to dismiss symptoms as “normal,” or feel uncomfortable discussing symptoms with
249 their patients, particularly younger women, who on average have a longer delay in diagnosis.⁴⁹

250

251 There is currently no validated set of screening questions routinely used for HCPs to ask women
252 about their menstrual pain, even though implementing this practice could facilitate earlier
253 diagnosis of endometriosis and other causes of pelvic pain.^{59,60} Standardized screenings, such as
254 those used to identify violence against women during a well-woman visit, could be used as a
255 model in screening for endometriosis. Taken together, inadequate HCP training and societal
256 normalization of menstrual pain create significant barriers for patients in need of referrals to
257 specialists when endometriosis is suspected.

258

259 *Barriers with current diagnostic tools*

260 In addition to the lack of disease awareness and education, the absence of noninvasive or less
261 invasive diagnostic tools (e.g., biomarkers, radiologic imaging) may contribute to diagnostic
262 delay. One survey found that nearly two-thirds of gynecologists agreed there was a significant
263 delay in diagnosing endometriosis, which they partly attributed to the absence of a valid
264 noninvasive diagnostic test.⁵¹ This suggests that the invasiveness of laparoscopic surgery itself
265 may be one reason HCPs delay diagnosis. Lack of access to a specialist with expertise in
266 laparoscopic surgery for endometriosis and/or insurance coverage also remain critical barriers.⁵⁷

267

268 Young women in particular face extended delays from the time they first speak to their HCP
269 about symptoms to receiving a diagnosis of endometriosis. One study found that women under
270 the age of 19 waited on average 12 years.⁴⁹ One possible explanation is that teens, parents, and
271 primary care providers may be hesitant to see/refer to a gynecologist due to feeling uneasy about
272 gynecologic pelvic exams in a non-sexually active young woman. Further, some HCPs and
273 gynecologists are reluctant to recommend or perform an invasive diagnostic procedure, like a
274 laparoscopy, in young girls.^{61,62}

275

276 The current gold-standard guidelines for diagnosing endometriosis only examine whether
277 endometrial lesions are present. The most commonly used disease staging system is also based
278 on the location and amount of lesions within the pelvic cavity.⁶³ However, most evidence has
279 demonstrated there is a marginal relationship among the number of lesions, the severity of
280 disease, its symptoms, and overall impact on quality of life (except for a correlation between
281 deep infiltrating endometriosis sites and some types of pelvic pain).⁶⁴ For example, a woman
282 with revised ASRM stage 4 endometriosis, which is considered “severe,” may experience fewer
283 life-disrupting symptoms than a woman with stage 1 endometriosis, which is classified as
284 “minimal,” suggesting that these adjectives should not be used interchangeably with the numeric
285 stages of disease. Further, current diagnostic and disease staging guidelines provide little
286 predictive value regarding outcomes (e.g., pain relief or fertility) or recurrence risk.⁶⁵⁻⁶⁷ This may
287 be in part because the current approach does not take into account the inflammatory and systemic
288 nature of the disease or the rare but burdensome presence of extra-pelvic endometriosis.

289

290 Requiring a laparoscopy in order to receive a definitive diagnosis can also greatly impede
291 research if women’s participation in research requires a history of disease documented by
292 surgery. This can create a selection bias in clinical research studies, particularly if comparisons
293 are to women who underwent laparoscopies for other indications, for which there may be
294 overlapping etiology. It also greatly precludes population-based studies, which in turn has
295 limited our understanding of the disease and the patient populations it affects.

296

297 **Future of Endometriosis Diagnostics**

298 Due to the invasiveness and costliness of laparoscopy, noninvasive diagnostics for endometriosis
299 in both clinical practice and research are greatly needed. Presently, there are some noninvasive
300 and less invasive tools that may help identify certain types of endometrial lesions. For example,
301 transvaginal ultrasounds or magnetic resonance imaging (MRI) can be used to diagnose ovarian
302 endometriomas and deeply infiltrative endometriosis, such as lesions involving the bladder,
303 rectovaginal septum, and sigmoid colon.⁶⁸ Sensitivity and specificity rates for non-ovarian
304 endometriosis using transvaginal ultrasound are 78-98% and 90-100%, respectively.⁵¹ However,
305 transvaginal ultrasounds are not reliable diagnostic aids for superficial peritoneal disease, which
306 is the most common type of endometriosis. Importantly, diagnostic accuracy is lower if imaging
307 is not performed by individuals with appropriate training, which can limit its usefulness as many
308 sonographers do not receive endometriosis-specific training.^{69,70} However, many studies have
309 shown that competency greatly improves after brief training programs,⁷⁰⁻⁷³ suggesting a new
310 avenue for increasing the number of experts available and thereby increasing women’s access to
311 state-of-the-art imaging for endometriosis.

312

313 In addition, researchers are exploring the use of biomarkers for early diagnosis as a noninvasive
314 approach, but more investment in this area is needed for it to be fruitful. Current blood-based
315 biomarkers under investigation include regulators of gene expression (microRNAs),

316 inflammatory markers, tumor markers, growth factors, and hormonal markers, as well as
317 endometrial and menstrual effluent biomarkers.^{74,75} However, none of these tests have been
318 validated in large heterogeneous samples nor have they been proved to have adequate sensitivity
319 and specificity to be used clinically outside a research setting. Testing of biomarkers on
320 populations that reflect the diversity of those with the disease is needed.

321
322 Given the heterogeneity of endometriosis and multiple pathways that are involved in the etiology
323 of the disease, there may not be one universal biomarker that can accurately diagnose all forms
324 of the disease. A combination of multiple biomarkers may be necessary to diagnose the disease
325 or define different subtypes of endometriosis, which would open up avenues for more
326 personalized treatments. However, discerning this information will require large, diverse, and
327 highly phenotyped patient populations, with detailed prospective data collection on severity and
328 characteristics of pelvic symptoms (e.g., dysmenorrhea, non-menstrual pain, dyspareunia,
329 infertility), associated comorbidities (e.g., other pain conditions, autoimmune disease), and
330 location, appearance, and extent of lesions. Organizations such as the World Endometriosis
331 Research Foundation (WERF) have already begun taking steps to achieve this. The WERF
332 Endometriosis Phenome and Biobanking Harmonisation Project (EPHect) was established to
333 standardize the reporting and pathological processing for endometriosis research and facilitate
334 large-scale international collaborations in order to advance understanding of the disease.⁷⁶⁻⁷⁸

335

336 **Treatment**

337 **Current Practice**

338 There is currently no cure for endometriosis. Since symptoms can appear as early as menarche,
339 management of the disease may span decades, including the optimal years for trying to conceive.
340 Current strategies to manage endometriosis include medical and surgical treatments, as well as
341 complementary approaches designed with the primary goal of managing pain and associated
342 symptoms and possibly restoring fertility.^{8,42}

343

344 Pain and infertility are two of the most common reasons women seek treatment for
345 endometriosis, and the treatment approaches differ for each. Considerations for different
346 treatment types with respect to age, disease severity, and desire to preserve fertility are reviewed
347 elsewhere.^{8,9}

348

349 First-line medical therapies for endometriosis include non-steroidal anti-inflammatory drugs
350 (NSAIDs), combined estrogen-progestin hormonal contraceptives (cyclic or preferably
351 continuous), and progestins (oral, injectable, implants, intrauterine device). Most clinicians
352 consider first-line medical therapies as those that are low-cost, well-tolerated, efficacious, and
353 easily accessible.⁴² Second-line medical treatments have equal efficacy but are more costly
354 and/or have side effects. These include gonadotrophin-releasing hormone agonists and

355 antagonists (with or without add-back hormone replacement therapy) or danazol, an androgenic
356 steroid.

357
358 Laparoscopy with excision or destruction of superficial lesions and excision of deep lesions can
359 be a first-line or second-line surgical approach for treating pain.⁸ Guidelines recommend
360 excision surgeries be performed by surgeons who specialize in this type of surgery.⁴² Surgeries
361 that interrupt nerve pathways (e.g., presacral neurectomy) or hysterectomy (with or without
362 oophorectomy) are third- or fourth-line approaches that are used after other treatment options
363 have failed.⁸ However, even these procedures are not curative and pain can recur, often without
364 evidence of recurrent endometriosis lesions.⁶

365
366 Comorbidities are highly prevalent in women with endometriosis.⁷⁹ Thus, multimodal
367 approaches to the evaluation and treatment of chronic pain and associated symptoms, including
368 non-pharmacologic therapies, are an important part of a comprehensive strategy for managing
369 endometriosis. For example, physical therapists with specialty in treating pelvic floor
370 dysfunction may be beneficial for women with associated myofascial pain.^{80,81} Further, two
371 randomized controlled trials found acupuncture to provide some patients with relief from
372 endometriosis-related pain.^{82,83} A randomized control trial examining the use of yoga found
373 similar effects.⁸⁴ Additionally, mental health professionals can play an important role in
374 addressing issues such as depression and grieving that are associated with the disease, as well as
375 provide cognitive behavioral therapy techniques such as coping and relaxation strategies.^{44,80,81,85}

376 377 **Barriers to Treatment**

378 *Limitations of current therapies*

379 Available medical therapies provide relief from endometriosis-related pain for many women, but
380 not all.⁸⁶ On average, 11-19% of women report no improvement in pain with medical therapy
381 and 5-59% report some degree of persistent pain at the end of the study period.⁸⁶ Discontinuation
382 rates for medical treatments range from 5–16% due to significant side effects — such as bone
383 loss, hot flashes, and weight gain — or limited efficacy, restricting their usefulness or
384 longevity.^{8,41,86} Recurrent pain is common after treatment cessation, with 17-34% of women
385 reporting recurrence of pain after stopping treatment.⁸⁶

386
387 Many medical therapies (e.g., combined hormonal contraceptives, progestins, and gonadotropin-
388 releasing hormone agonists and antagonists) cannot be used when women are trying to get
389 pregnant.^{7,42} This forces many women with endometriosis who wish to become pregnant to
390 choose between minimizing debilitating pain with medication and timing their attempts to
391 conceive while off of their medication.

392

393 After laparoscopy, disease recurrence rates range from 30-50%,⁸ with up to 55% of women
394 undergoing an additional surgery within seven years.⁸⁷ Approximately 20% of women may not
395 show improvement after initial surgery.⁸⁸

396
397 Even hysterectomy is not a cure for all women with endometriosis. In women with endometriosis
398 who underwent a hysterectomy where both ovaries were preserved, 7.3% underwent reoperation
399 within two years due to recurrence of pelvic pain and 21.6% underwent reoperation within seven
400 years.⁸⁷ Reoperation rates for women who underwent hysterectomy and bilateral oophorectomy
401 were 4% by year two and 8.3% by year seven post-hysterectomy. Further, reoperation rates can
402 vary by age at hysterectomy. While bilateral oophorectomy was associated with a lower
403 reoperation rate in women over 40 years old, the incidence of reoperation with bilateral
404 oophorectomy (compared to ovarian preservation) was not lower in women ages 30-39. This
405 suggests that many, but not all, women experience symptom relief following hysterectomy.

406
407 Furthermore, these reoperation rates only capture pain remediation failure among women who
408 return to the same surgeon and undergo reoperation; data are lacking on those who have pain
409 return but discontinue engagement with that HCP and for those who do return to that HCP but
410 are treated without reoperation. Therefore, these pain recurrence rates are likely an
411 underestimate. Incomplete excision of lesions, central sensitization, and under-recognized or
412 under-treated comorbid conditions (e.g., pelvic floor myofascial pain, interstitial cystitis, or IBS)
413 are likely some of the reasons why symptoms can reoccur following a hysterectomy,
414 necessitating the need for additional surgery.^{89,90} In addition, undergoing a hysterectomy has its
415 own health risks that extend beyond those related to reproductive health.^{24,91-93}

416
417 Current medical and surgical options for endometriosis aim at suppressing or eliminating lesions
418 in the pelvic cavity.⁶ However, the relationship between lesions and symptoms (e.g., pain and
419 infertility) is not well established or understood.⁶⁷ Pain can persist or recur after surgery and
420 recurrent symptoms do not necessarily correlate with recurrent lesions. Further, while medical
421 and surgical therapies can be effective in alleviating endometriosis-related pain and fertility
422 issues, they are not always effective and also do not address all the symptoms associated with
423 endometriosis, such as the fatigue, mood disorders, or pain outside of the pelvis.

424
425 *Barriers in accessing care*

426 In addition to the lengthy diagnostic delay discussed above, high costs, insurance issues, stigma,
427 lack of HCP education, and access to specialists can all create barriers to receiving care.

428
429 In one survey of young women with chronic pelvic pain, they cited difficulty with insurance
430 coverage, lack of HCP knowledge or training, and difficulty getting appointments with
431 specialists as the main factors impeding their attempts to receive optimal care.⁹⁴

432

433 Some employers may not be knowledgeable about endometriosis and therefore quick to trivialize
434 or assume women are making up or exaggerating the severity of their symptoms.^{95,96}
435 Unsupportive work environments can make it difficult for women to use sick leave, receive an
436 appropriate amount of sick leave, or take time off for HCP appointments.^{27,95,97} This can greatly
437 affect productivity and overall quality of life at work.

438
439 *Provider-related barriers*

440 As of 2017, there were 35,586 general obstetrician-gynecologists in the U.S.⁵⁷ However,
441 obstetrician-gynecologists are not evenly distributed geographically. Nearly 50% of counties in
442 the U.S., in predominantly rural areas, lack a single obstetrician-gynecologist.⁵⁷ This leaves the
443 approximately 10 million women who reside in these counties without ready access to an
444 obstetrician-gynecologist. Of the general obstetrician-gynecologists, an even smaller percentage
445 specialize in the treatment and management endometriosis, which is imperative for proper care.

446
447 Further, the lack of education about endometriosis and chronic pelvic pain for HCPs may result
448 in unnecessary and invasive procedures. A common misbelief is that a hysterectomy can “cure”
449 endometriosis, which (as discussed in detail above) is not necessarily true. This can cause HCPs
450 to suggest hysterectomy as a first- or second-line treatment option even though guidelines
451 recommend hysterectomies be considered a last-line approach for only severe and refractory
452 cases.

453
454 Endometriosis is the second leading indication for hysterectomy in the U.S. (the first is uterine
455 fibroids and/or abnormal bleeding). Endometriosis accounts for 17.7% of all hysterectomies and
456 is the leading cause of hysterectomy among women 30-34 years old.⁹⁸ Black women are
457 disproportionately more likely than white women to undergo hysterectomy for benign
458 gynecological conditions and are more likely to have complications from surgery.⁹⁹

459
460 **Future of Endometriosis Treatments**

461 Current medical and surgical treatment options focus on suppressing lesion proliferation in hopes
462 of eliminating pain and/or infertility, even though the relationship between lesions and these
463 symptoms is not well understood. Future treatments and care should shift toward a patient-
464 centric, multidisciplinary approach that focuses on the patient as a whole, rather than one
465 symptom at a time.

466
467 Centers of expertise — specialized programs that provide capability and resources related to a
468 particular medical area — offer one type of patient-centric model for treating and managing
469 endometriosis. Centers of expertise in endometriosis take an interdisciplinary approach to patient
470 care with a team that includes experts in laparoscopy, medical management, pain education,
471 physical therapy, and psychology.¹⁰⁰ A recent prospective study from a center of expertise for
472 chronic pelvic pain in Canada found that its interdisciplinary approaches were successful in

473 lessening pain, reducing emergency room and physician visits, decreasing the prevalence of
474 comorbid conditions, and improving functional quality of life.¹⁰⁰ The implementation of
475 comprehensive treatment strategies — like those in centers of expertise — that address all the
476 needs of the patient, including quality-of-life issues, is imperative.

477
478 In addition, current care for women with endometriosis is sometimes based on low-value care
479 tests and procedures, meaning they have defined harm, uncertain benefits, or effectiveness that is
480 no better than less expensive alternatives.¹⁰¹ Given the economic burden of endometriosis,
481 moving toward care that is based on the best available data and funding studies that increase this
482 knowledge base remains a priority.

483
484 More research is also needed to better understand the underlying biology of endometriosis and
485 possible endometriosis subtypes, which could lead to new therapeutic avenues and more
486 individualized treatment plans. Of particular interest are alternatives to hormonal therapy, for
487 those patients who are intolerant to current hormonal regimens due to side effects as well as
488 patients who are trying to conceive. Non-hormonal options, such as those modulating
489 angiogenesis or neuroinflammation, are urgently needed.¹⁰² Moreover, future treatments should
490 aim to address the issues most important to patients and future clinical trials should utilize
491 patient-reported outcomes and include current first-line medications as a comparator when
492 possible.¹⁰¹

493
494 Increased funding is necessary to accomplish these goals. Despite the high prevalence and
495 impact of endometriosis, the National Institutes of Health (NIH) funding for the disease in 2018
496 was \$7 million, near the bottom of NIH's 285 funded disease/research areas.³² Insufficient
497 funding means fewer researchers have the opportunity to study endometriosis, further impeding
498 the advancements that are needed in the field.

500 **Conclusion**

501 Endometriosis places a significant burden on teens and adult women, their families, and society
502 as a whole, yet the stigma surrounding the disease and societal normalization of women's pain
503 continue to preclude fast and accurate diagnosis, effective treatment, and innovation in the field.

504
505 The gold standard diagnostic is invasive and costly, although research into noninvasive
506 diagnostics is underway.⁴⁷ Currently, medical and surgical therapies focus on treating lesions,
507 but often do not address the negative impact endometriosis has on a woman's quality of life.
508 Comprehensive and interdisciplinary approaches that take patients' holistic needs into account
509 are needed, along with more research that can give insights into the underlying biology of the
510 disease, enable new therapies, and create high-quality evidence to help improve care.

511

512 Evidence-based public health campaigns could also improve disease knowledge among patients,
 513 HCPs, and the public. Such campaigns, as well as more training for providers, could also address
 514 the stigma associated with endometriosis and improve social support for those experiencing the
 515 disease.³⁸ The Society for Women's Health Research is committed to improving education and
 516 awareness around endometriosis and other conditions that disproportionately, differently, or
 517 exclusively affect women in order to improve diagnosis, treatment, and access to quality care.

518

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