



PUTTING THE FOCUS ON ENDOMETRIOSIS

UNDERSTANDING THE IMPACT OF
COMPLEX CHRONIC DISEASES BEYOND
DIABETES AND HYPERTENSION

WHAT IS ENDOMETRIOSIS?

ENDOMETRIOSIS IS A CHRONIC, DEBILITATING DISEASE IN WOMEN¹

Endometriosis happens when tissue lining the uterus grows elsewhere in the body and continues to grow and bleed as it normally does during the menstrual cycle.

Scar tissue and inflammation can result, causing pain and other complications, including fertility problems.



SYMPTOMS OF ENDOMETRIOSIS MAY INCLUDE*:

- **Chronic and intense pelvic pain** during and outside of menstruation¹
- Painful sex¹
- Heavy menstrual bleeding¹

*This list is not all-inclusive.

In one cross-sectional study of 638 participants **who reported overall symptom severity at diagnosis**^{2†}:

- **54.5%** of women reported **severe symptoms**
- **37.2%** reported **moderate** symptoms
- **8.3%** reported **mild** symptoms

[†]Results from an online, cross-sectional survey conducted from August 6, 2012 through September 14, 2012. Respondents aged 18 to 54 years who reported a physician's diagnosis/suspicion of endometriosis within the previous 10 years were included.

WHO GETS ENDOMETRIOSIS?

ENDOMETRIOSIS AFFECTS WOMEN DURING THEIR REPRODUCTIVE YEARS³

6%-10% of women of reproductive age are affected by endometriosis.³

- In addition to employees who have endometriosis, some employees may have covered family members, including **wives or daughters**, with the disease

An estimated **4.1 million women age 18-49 years** in the United States are diagnosed with endometriosis.^{4*}

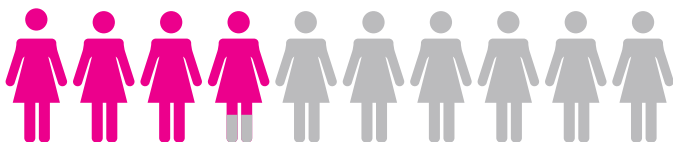
- Most often diagnosed in women in their 30s and 40s¹
- Average time to endometriosis diagnosis is up to 6-10 years^{5,6}

Studies suggest there is a **family component** to endometriosis.^{7,8}

- A member who has a first-degree relative with endometriosis may be **~7-10x more likely** to develop endometriosis

*Number derived from an online, cross-sectional survey that used 3 panels in which 48,020 women aged 18 to 49 years responded between August 6, 2012 through September 14, 2012, of whom 6.1% reported a diagnosis of endometriosis. The authors used sampling weights from US population statistics to estimate that 4.1 million had diagnosed endometriosis.

ENDOMETRIOSIS AND INFERTILITY

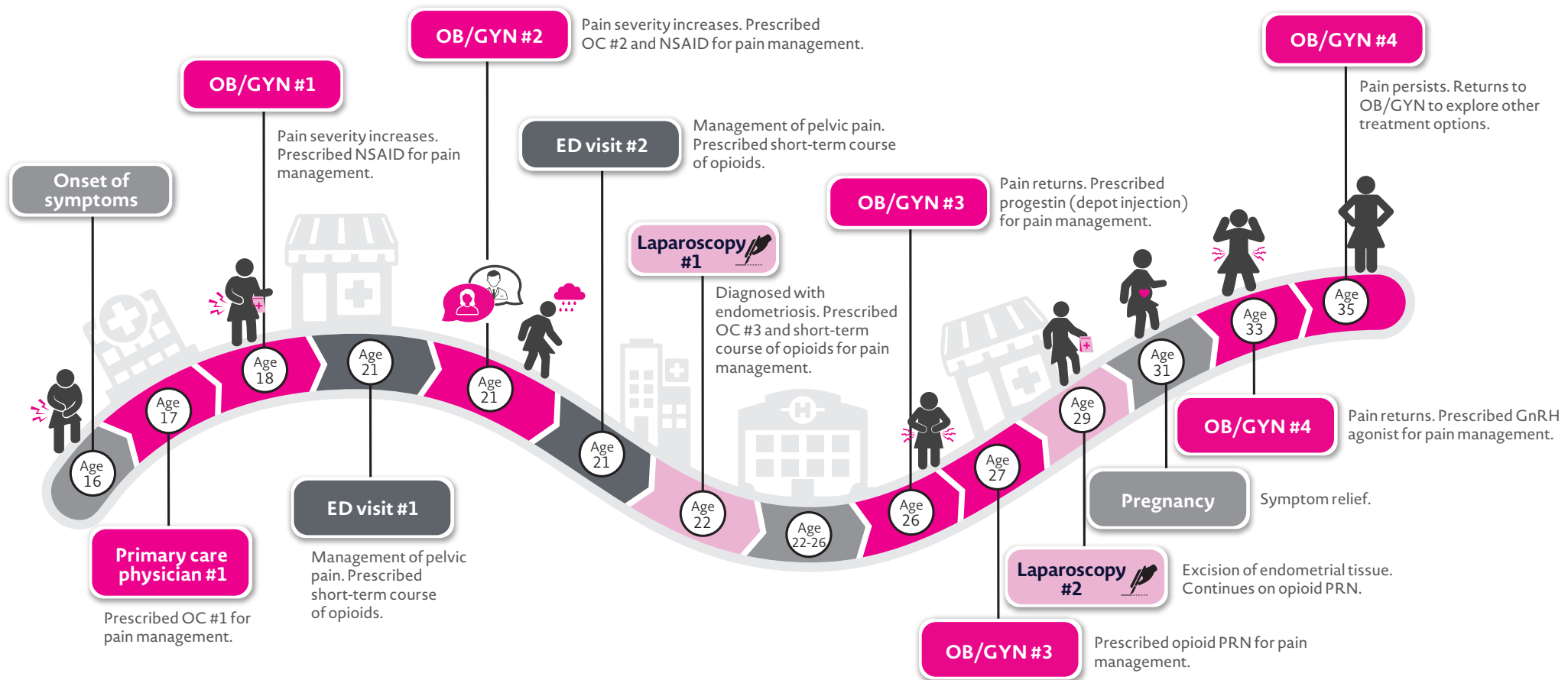


38% of women with infertility
have endometriosis³

**HOW MANY OF YOUR EMPLOYEES
AND THEIR FAMILY MEMBERS
DOES ENDOMETRIOSIS AFFECT?**

ENDOMETRIOSIS CAN BE A LONG, PAIN-FILLED JOURNEY FOR MANY WOMEN

THIS DIAGRAM IS FOR ILLUSTRATIVE PURPOSES ONLY AND MAY NOT REPRESENT A TYPICAL PATIENT'S JOURNEY OR EVERY PATIENT'S EXPERIENCE



ED=emergency department; GnRH=gonadotropin-releasing hormone;
NSAID=nonsteroidal anti-inflammatory drug; OB/GYN=obstetrician/gynecologist;
OC=oral contraceptive; PRN=pro re nata, or as needed.

HOW IS ENDOMETRIOSIS TREATED?

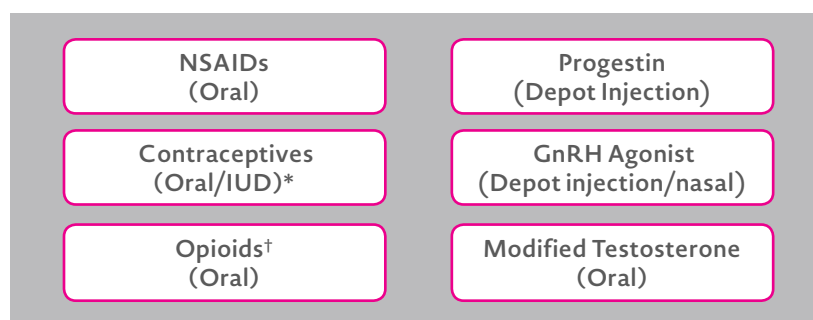
THERE ARE A VARIETY OF PHARMACOLOGICAL AND SURGICAL OPTIONS TO MANAGE ENDOMETRIOSIS

Physicians use their clinical expertise to determine the appropriate course of treatment for patients with endometriosis.⁹

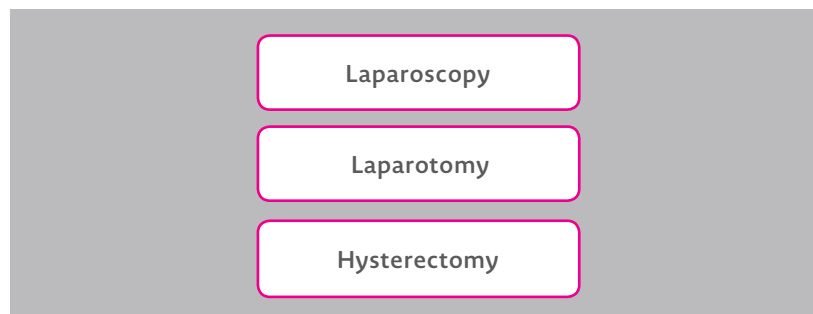
Opioids may be prescribed to some patients to help them manage their pain.¹⁰

Endometriosis treatment options include:

PHARMACOLOGICAL^{9,10}



SURGICAL^{9,10}



*Oral contraceptives are more frequently used, but the use of IUDs can be employed anywhere along the treatment path.

[†]Although less common, opioids are sometimes used for pain management.

WHAT IS THE IMPACT OF ENDOMETRIOSIS ON YOUR MEMBERS?

WOMEN OFTEN SEEK MULTIPLE MEDICAL AND SURGICAL TREATMENTS IN SEARCH OF PAIN RELIEF¹¹

According to a survey of 1160 women with surgically diagnosed endometriosis:



- **45.5%** reported **3 or more medical treatments** during their lifetime
 - The number of treatments received ranged from 1 to 11
 - Medications used most often and for the longest duration were **analgesics** and **oral contraceptives**



- **41.5%** reported 3 or more surgical procedures during their lifetime
 - The number of surgical procedures performed ranged from 1 to 17
 - 75.4% received a **laparoscopy**, which is used to confirm endometriosis

OVER 70% OF PATIENTS WITH ENDOMETRIOSIS ARE UNABLE TO RELIEVE THEIR PAIN DESPITE ATTEMPTS TO MANAGE IT^{12*}

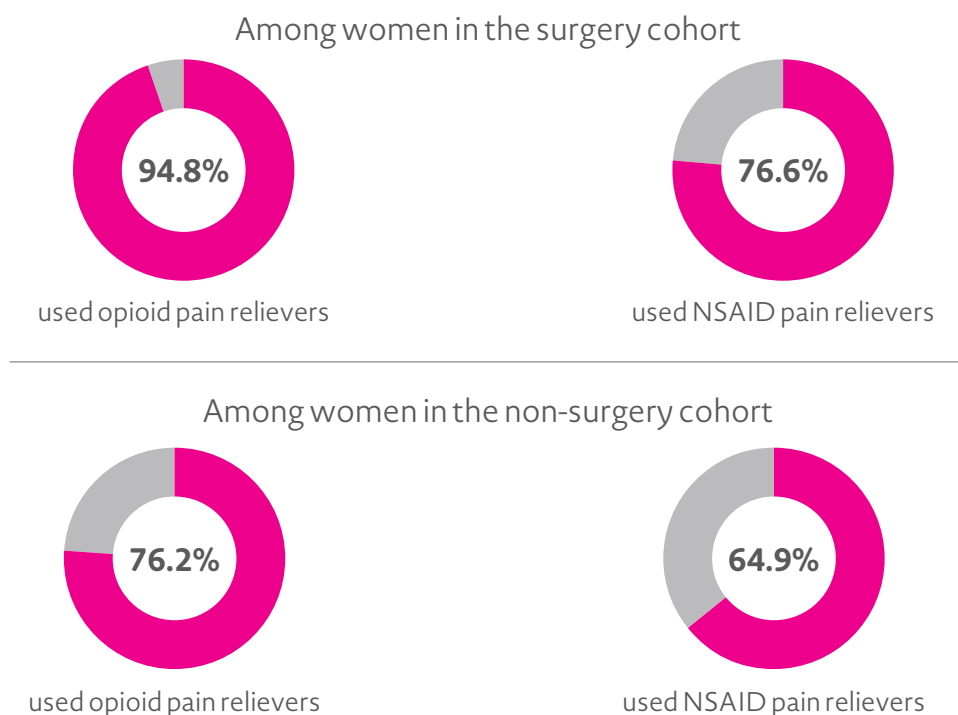
*According to an international multicenter survey of patients treated in tertiary care centers.

WHAT IS THE IMPACT OF ENDOMETRIOSIS ON YOUR MEMBERS? (CONT'D)

PAIN RELIEVERS—BOTH OPIOIDS AND NSAIDS—ARE COMMONLY USED BY WOMEN WITH ENDOMETRIOSIS^{13*}

A retrospective claims analysis[†] examined the incremental direct and indirect healthcare costs of women with endometriosis who underwent endometriosis-related surgical procedures (n=124,530) compared with those who did not get surgery (n=37,106).

Baseline characteristics showed that pain medication was commonly used by women at some point during the year prior to surgery.



*Patients reported use of pain medication at any time during the year prior to endometriosis-related surgery.

[†]Data were extracted from the Truven Health MarketScan Commercial Claims and Encounters and the Health Productivity Management databases for women aged 18 to 49 years with a claim for endometriosis between January 2006 and June 2014.

ENDOMETRIOSIS IMPACTS ALL ASPECTS OF A WOMAN'S LIFE¹²

In an international, multicenter, cross-sectional study of 931 women with endometriosis treated in tertiary care centers who completed an HRQoL questionnaire:

- 51%** reported their **work** being affected
- 50%** reported their **relationship** being affected
- 16%** reported their **education** being affected

HRQoL=health-related quality of life; NSAID=nonsteroidal anti-inflammatory drug.

WHAT ARE THE HEALTH RISKS IN MEMBERS WITH ENDOMETRIOSIS?

ENDOMETRIOSIS IS ASSOCIATED WITH MULTIPLE COMORBIDITIES⁴

One study showed that women with endometriosis self-reported more comorbidities than those without endometriosis ^{4*}

ODDS RATIO OF SELECT COMORBIDITIES (95% CI)

Immune system diseases

- 4.9X** Ulcerative colitis (3.6-6.6)
- 4.1X** Crohn's disease (3.0-5.6)
- 3.4X** Celiac disease (2.5-4.5)
- 3.3X** Multiple sclerosis (2.3-4.8)
- 1.9X** Psoriasis (1.6-2.4)

Cancers

- 4.1X** Ovarian cancer (2.8-6.1)
- 2.8X** Breast cancer (1.9-4.1)

Heart conditions

- 2.8X** High triglycerides (2.4-3.3)
- 2.2X** High cholesterol (1.9-2.5)
- 1.9X** Hypertension (1.6-2.1)

Mental health conditions

- 2.0X** Depression (1.8-2.2)

$P < 0.001$

Additionally, women 40 years of age and younger with endometriosis may have 3X greater risk of coronary heart disease.^{14†}

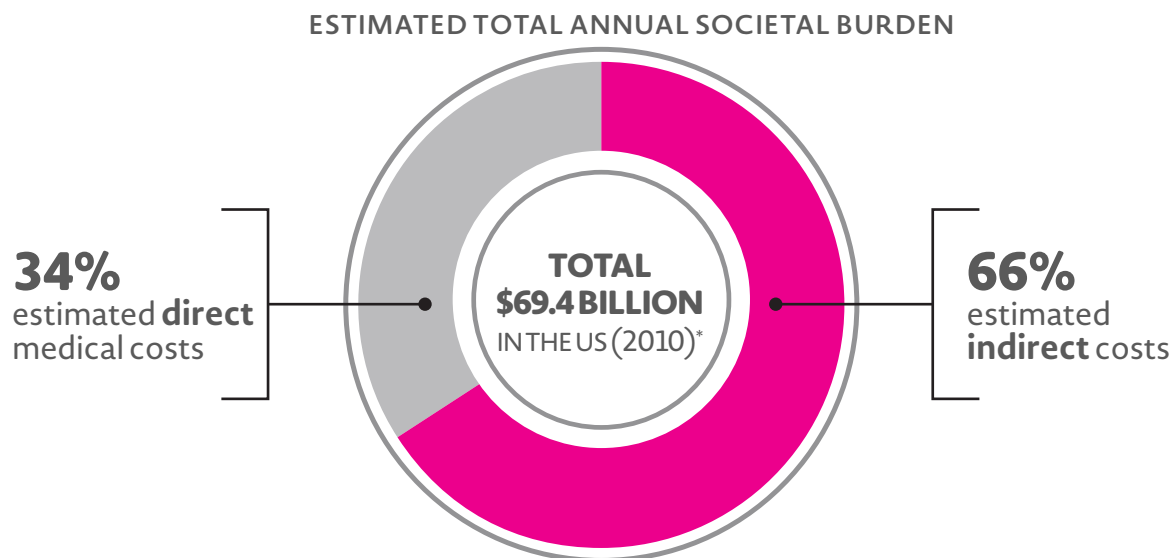
*An online, cross-sectional study of 48,020 women aged 18 to 49 years examined the prevalence and symptoms of endometriosis in which 2922 reported being diagnosed with endometriosis. Women completed an online survey that, in addition to having questions pertaining to endometriosis-related symptoms, asked respondents to select all comorbidities that applied to them from a list of 23. Data were collected between August 2012 and September 2012.

†RR 3.08; 95% CI, 2.02-4.70. The Nurses' Health Study II prospectively examined the association between endometriosis and coronary heart disease over a 20-year period (1989-2009) in 116,430 female patients in the United States. When compared to women without endometriosis, women with endometriosis had a higher risk of myocardial infarction (MI), angina, and coronary artery bypass graft (CABG)/angioplasty/stent.

WHAT ARE THE COSTS ASSOCIATED WITH ENDOMETRIOSIS?

ENDOMETRIOSIS IS A COSTLY BURDEN¹⁵

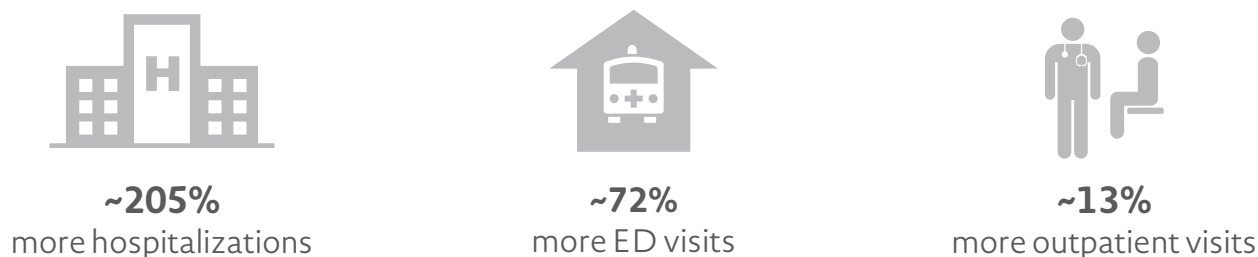
Based on a prospective, questionnaire-based survey of 909 women with endometriosis across 12 tertiary care centers in 10 countries who had at least one tertiary-care-center-specific contact related to endometriosis-associated symptoms in 2008.



*Extrapolation of tertiary care center-specific costs to national cost estimates was performed via a theoretical model and calculated as follows: annual average (in) direct costs per woman multiplied by the national number of women of reproductive age (ie, 15 to 49 years of age) multiplied by the estimated prevalence of endometriosis among women of reproductive age. In this model, a prevalence of 7% was used. Price year was 2009, but is expressed in 2010 USD based on the conversion rate 1 euro = \$1.40 US on October 25, 2010.

ENDOMETRIOSIS IS ASSOCIATED WITH HIGHER HEALTHCARE UTILIZATION^{16†}

A retrospective claims analysis found that compared to women without endometriosis, women with endometriosis in the year immediately before and after diagnosis had, on average:

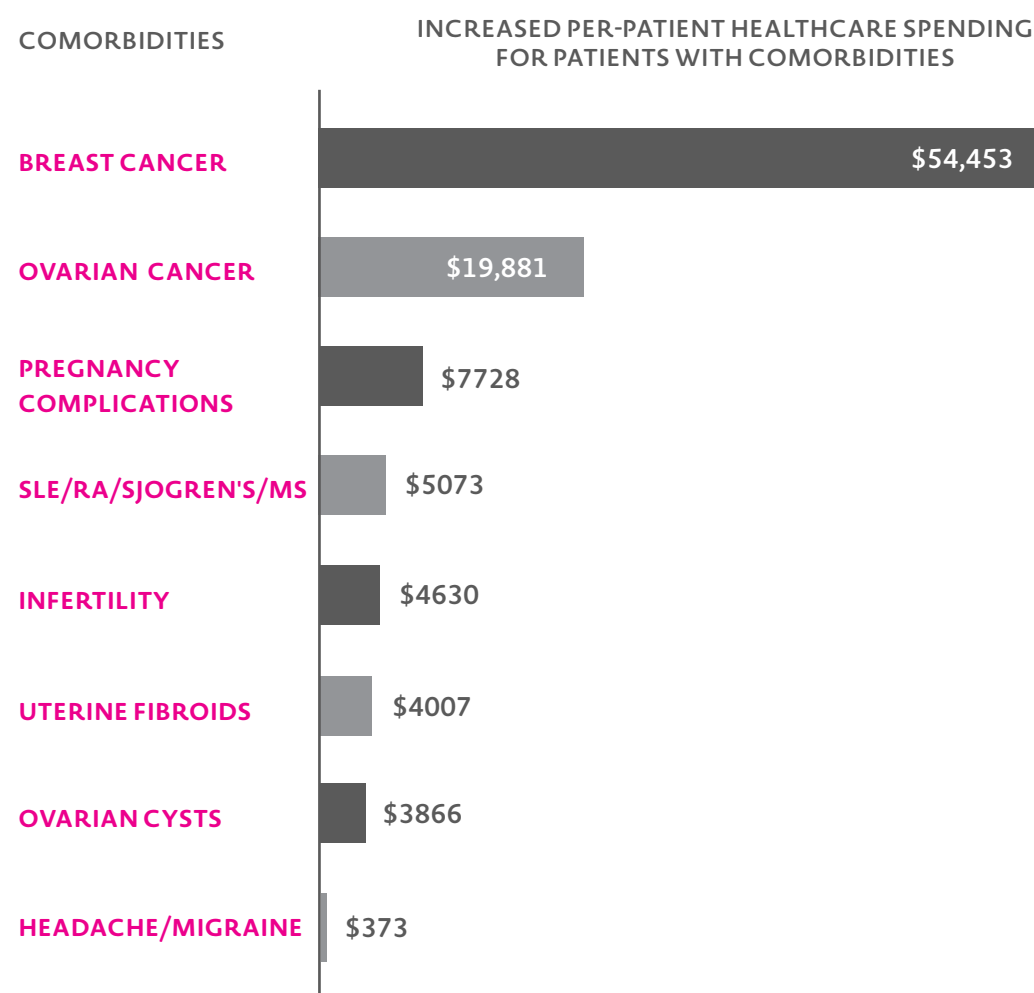


†Data source: Truven Health MarketScan claims database (2000-2010). Data from a 10-year retrospective claims analysis of healthcare utilization and costs of women with endometriosis compared with those without (N=75,140) showed that women with endometriosis had: 205% more hospitalizations in the years immediately before and after diagnosis (3229 vs 3077 one year prediagnosis and 14,902 vs 2877 one year post diagnosis [$P<0.05$]); 72% more ED visits in the years immediately before and after diagnosis (9901 vs 5695 one year prediagnosis and 9651 vs 5652 one year post diagnosis [$P<0.05$]); and, 13% more outpatient visits in the years immediately before and after diagnosis (36,800 vs 32,583 one year prediagnosis and 36,902 vs 32,704 one year post diagnosis [$P<0.05$]).

WHAT ARE THE COSTS ASSOCIATED WITH ENDOMETRIOSIS? (CONT'D)

CERTAIN COMORBIDITIES SIGNIFICANTLY INCREASED HEALTHCARE COSTS^{17*†}

Based on a retrospective, matched cohort study of 54,070 women aged 18 to 49 years with endometriosis that examined the impact of certain comorbidities on healthcare spending 12 months before and after an index date.



MS=multiple sclerosis; RA=rheumatoid arthritis; SLE=systemic lupus erythematosus.

*Total spending amounts in 2015 USD.

†Data source: Clinformatics™ DataMart (Optum Insight) de-identified commercial insurance claims database. Claims and enrollment records drawn from January 1, 2006 through December 31, 2015.

HAVE YOU MEASURED THE DIRECT HEALTHCARE COSTS OF ENDOMETRIOSIS IN YOUR ORGANIZATION?

HOW DOES ENDOMETRIOSIS AFFECT ABSENCE AND PERFORMANCE?

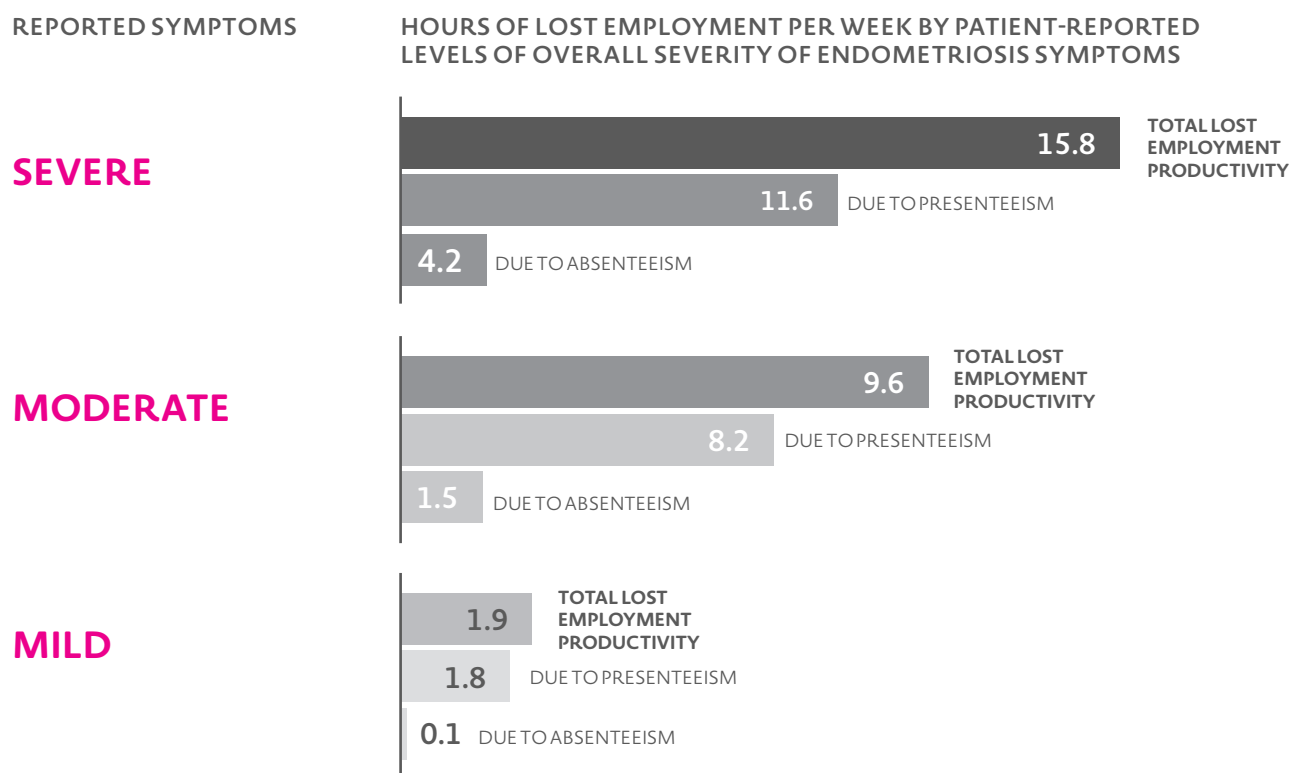
ENDOMETRIOSIS RESULTS IN SUBSTANTIAL HOURS OF LOST PRODUCTIVITY PER WEEK

48% of women had to reduce the number of hours they worked per week due to endometriosis, based on a multinational, international, questionnaire-based, cross-sectional study of 931 women with endometriosis who completed an HRQoL questionnaire.¹²

Women reported an average of **6.4 to 10.8 hours of work lost** (both absenteeism and presenteeism) per week due to endometriosis.⁶

WOMEN WITH HIGHER LEVELS OF PATIENT-REPORTED SEVERITY OF ENDOMETRIOSIS SYMPTOMS LOST EVEN MORE HOURS IN EMPLOYMENT PRODUCTIVITY¹⁸

Based on a cross-sectional, web-based survey of 5879 women with endometriosis, of which 810 were employed, reported a significant association between symptoms and the hours of lost employment



WHAT DO MEMBERS WITH ENDOMETRIOSIS NEED TO DO?



TAKE ACTION—RECOGNIZE SYMPTOMS AND SEEK APPROPRIATE CARE FROM A GYNECOLOGIST

Women with endometriosis often spend years in the healthcare system searching for relief due to the challenges of diagnosing the disease. Early intervention can get these women on the path to treatment sooner.

Average time to endometriosis diagnosis is up to 6-10 years, and it can be longer for younger women.^{5,6}

- In 2 cross-sectional, self-reported surveys of women with endometriosis, **younger patients often experience a longer delay in diagnosis** than older patients^{2,19}



Most women saw **up to 4 physicians before diagnosis**^{19*}

Seeing a gynecologist first resulted in visiting fewer physicians overall compared with those who saw a generalist or another specialist first^{19*}



63% of women surveyed said **1 or more physicians told them nothing was wrong**^{19*}

*Results from a 1998 cross-sectional, self-reported survey of 4334 women with surgically diagnosed endometriosis, which examined the time from onset of symptoms to diagnosis. Women completed a 10-page survey developed by the Endometriosis Association, which included questions on pain, infertility, bleeding, and nongynecological symptoms.

MEMBERS NEED EDUCATION AND ACCESS
TO CARE FROM GYNECOLOGISTS WHO CAN HELP
THEM GET **PROPERLY DIAGNOSED AND
MANAGE THEIR DISEASE**

WHAT SHOULD AN EMPLOYER DO?

BE SURE YOUR MEMBERS AFFECTED BY ENDOMETRIOSIS HAVE ACCESS TO THE SUPPORT, EDUCATION, AND CARE THEY NEED

STEP 1: Talk to your benefits partners about the **right plan design** for your members to ensure access to appropriate care



- **Promote preventive care benefits** for women, including annual gynecological exams



- **Ensure access** to healthcare providers and services for endometriosis diagnosis
 - For example, physical exams, ultrasounds, and laparoscopies



- **Medication**, especially for pain management, may be needed **to help manage endometriosis**



- Some members will require **medical procedures**, such as laparoscopies and hysterectomies, to treat endometriosis¹¹



- **Additional support and education** may be needed, such as guidance from infertility specialists and other healthcare professionals

STEP 2: Provide your members with **appropriate educational resources**



- Raise awareness of endometriosis symptoms among undiagnosed women
- Help those with endometriosis better manage their condition

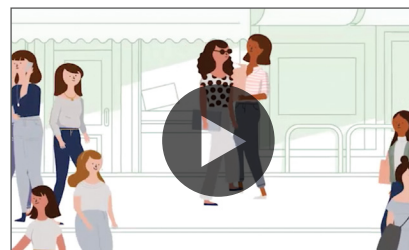
WHAT RESOURCES CAN YOU PROVIDE TO YOUR EMPLOYEES?

DISTRIBUTE EDUCATIONAL RESOURCES THAT SUPPORT AND EMPOWER WOMEN WITH ENDOMETRIOSIS

Brochures and videos you can provide to your employees.



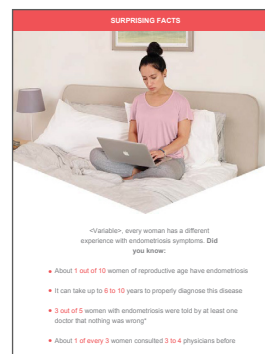
Endometriosis Awareness Advertisement



Mechanism of Disease Video

A form titled "SPEAKEENDO WITH YOUR GYNECOLOGIST". It contains sections for "Rate your pain symptoms on a scale of 0-10", "Painful periods", "Pain in between periods", "Pain with sex", and "Other symptoms". It also includes a section for "How you experience any of the following" with checkboxes for various symptoms like heavy bleeding, pelvic pain, and bloating. At the bottom, there is a section for "What you want to discuss" with checkboxes for "Pain", "Fertility", "Diagnosis", "Treatment", and "Other".

"Speak Endo" With Your Gynecologist



Surprising Endometriosis Statistics



Endometriosis Patient Testimonial Videos

A fact sheet titled "WHAT IS ENDOMETRIOSIS?". It defines endometriosis as a chronic and painful disease that affects about 1 in 10 women of reproductive age. It lists symptoms: "Painful periods", "Pain with sex", and "Pain in between periods". It also lists signs: "My pain has gotten worse over time", "My pain has affected school or work", "My pain has affected plans with family or friends", and "Other". It includes a section for "HOW WOULD YOU DESCRIBE YOUR PAIN?" with checkboxes for "My pain has gotten worse over time", "My pain has affected school or work", "My pain has affected plans with family or friends", and "Other". It ends with a note: "If you've checked off any of the above, discuss these and any other symptoms, impact to your day-to-day activities, and any concerns with your gynecologist."

Are You Ready to Speak Endometriosis Fact Sheet

ENDOMETRIOSIS IS A CHRONIC, DEBILITATING DISEASE THAT MAY BE AFFECTING EMPLOYEE PERFORMANCE IN YOUR ORGANIZATION

References

1. The American College of Obstetricians and Gynecologists. Frequently asked questions gynecologic problems. <https://www.acog.org/Patients/FAQs/Endometriosis#symptoms>. Accessed January 4, 2018.
2. Soliman AM, Fuldeore M, Snabes MC. Factors associated with time to endometriosis diagnosis in the United States [published online ahead of print April 25, 2017]. *J Womens Health*. doi:10.1089/jwh.2016.6003.
3. American College of Obstetricians and Gynecologists Practice Bulletin. Management of endometriosis. *Obstet Gynecol*. 2010;116:223-236.
4. Fuldeore MJ, Soliman AM. Prevalence and symptomatic burden of diagnosed endometriosis in the United States: national estimates from a cross-sectional survey of 59,411 women. *Gynecol Obstet Invest*. 2016;82(5):453-461. doi:10.1159/000452660.
5. Giudice LC. Endometriosis. *N Engl J Med*. 2010;362(25):2389-2398.
6. Nnoaham KE, Hummelshoj L, Webster P, et al. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. *Fertil Steril*. 2011;96(2):366-373.
7. Malinak LR, Buttram VC Jr, Flias S, Simpson JL. Heriuge aspects of endometriosis. II. Clinical characteristics of familial endometriosis. *Am J Obstet Gynecol*. 1980;137:332-337.
8. Matalliotakis IM, Arici A, Cakmak H, Goumenou AG, Koumantakis G, Mahutte NG. Familial aggregation of endometriosis in the Yale Series. *Arch Gynecol Obstet*. 2008;278:507-11.
9. The Practice Committee of the American Society for Reproductive Medicine. *Fertil Steril*. 2014;101(4):927-935.
10. Soliman AM, Fuldeore M, Yang H, Du EX, Wu EQ, Winkel C. Treatment patterns among US women diagnosed with endometriosis: a retrospective claims analyses pre- and post-diagnosis. Poster presented at: American Society for Reproductive Medicine 70th Annual Meeting; October 18-22, 2014; Honolulu, Hawaii. Poster 460.
11. Sinaii N, Cleary SD, Younes N, Ballweg ML, Stratton P. Treatment utilization for endometriosis symptoms: a cross-sectional survey study of lifetime experience. *Fertil Steril*. 2007;87(6):1277-1286.
12. De Graaff AA, D'Hooghe TM, Dunselman GAJ, Dirksen CD, Hummelshoj L; WERF EndoCost Consortium, Simoens S. The significant effect of endometriosis on physical, mental and social wellbeing: results from an international cross-sectional survey. *Hum Reprod*. 2013;28(10):2677-2685.
13. Soliman AM, Taylor H, Bonafede M, Nelson JK, Castelli-Haley J. Incremental direct and indirect cost burden attributed to endometriosis surgeries in the United States. *Fertil Steril*. 2017;107(5):1181-1190.
14. Mu F, Rich-Edwards J, Rimm EB, Spiegelman D, Missmer SA. Endometriosis and risk of coronary heart disease. *Circ Cardiovasc Qual Outcomes*. 2016;9(3):257-264.
15. Simoens S, Dunselman G, Dirksen C, et al. The burden of endometriosis: costs and quality of life of women with endometriosis and treated in referral centres. *Hum Reprod*. 2012;27(5):1292-1299.
16. Fuldeore MJ, Yang H, Du EX, Soliman AM, Wu EQ, Winkel C. Healthcare utilization and costs in women diagnosed with endometriosis before and after diagnosis: a longitudinal analysis of claims databases. *Fertil Steril*. 2015;103:163-171.
17. Epstein, AJ, Surrey ES, Soliman AM, Davis M, Johnson SJ, Castelli-Haley J, Snabes, MC. Changes in Healthcare Spending After Diagnosis of Comorbidities Among Endometriosis Patients. Poster presented at; ISPOR's 22nd Annual International Meeting; May 20-24, 2017; Boston, Massachusetts.
18. Soliman AH, Coyne KS, Gries KS, Catell-Haley J, Snabes MC, Surrey ES. The effect of endometriosis symptoms on absenteeism and presenteeism in the workplace and at home. *J Manage Care Spec Pharm*. 2017;23(7):745-754.
19. Greene R, Stratton P, Cleary SD, Ballweg ML, Sinaii N. Diagnostic experience among 4,334 women reporting surgically diagnosed endometriosis. *Fertil Steril*. 2009;91(1):32-39.