Greetings ENDO Study Participant,

A decade has passed since we enrolled the first participant in the Endometriosis, Natural History, Diagnosis, and Outcomes (ENDO) study. We so greatly appreciated your participation in the ENDO study and commitment to the rigorous study protocol. The study was a great success, enrolling a total of 626 women, 527 from Utah and 99 from California. To date, 25 papers have been published. Turn the page to find a summary of the study discoveries to date. For those wishing more details, we include the list of publications with the retrieval link. Since this was an NIH funded study, all publications can be downloaded for free via Pubmed Central (PMC).
Environmental Chemicals and Risk of Endometriosis

The many notable discoveries focusing on endocrine disrupting chemicals are summarized in the table below. Of the 99 chemicals assessed in relation to odds of an incident diagnosis of endometriosis, 19 were observed to be significantly associated with disease. Key results highlighted below.

<table>
<thead>
<tr>
<th>Chemical Class and ENDO-associated Paper</th>
<th>Risk Factor</th>
<th>Protective Factor</th>
<th>No Association</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nonpersistent Chemicals</strong></td>
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<tr>
<td>Benzophenone (BP)-type UV filters, widely used in sunscreens (Kunisue et al. 2012)</td>
<td>✅ 1 out of 5 BP-type filters</td>
<td>✅</td>
<td>✅ 4 out of 5 BP-type filters</td>
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<tr>
<td>Phthalates: group of chemicals used to make plastics more flexible and harder to break. Used in hundreds of products including vinyl flooring, adhesives, detergents, lubricating oils, automotive plastics, plastic clothes (raincoats), and personal-care products (soaps, shampoos, hair sprays, and nail polishes) (Buck Louis et al. 2013)</td>
<td>✅ 6 out 14 phthalates</td>
<td>✅</td>
<td>✅ 8 out 14 phthalates</td>
</tr>
<tr>
<td>Bisphenol A: used in manufacture of polycarbonate plastics including beverage containers, plastic dinnerware, automobile parts, toys, resins used in food can linings (Buck Louis et al. 2013)</td>
<td>✅</td>
<td></td>
<td></td>
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<tr>
<td><strong>Persistent Chemicals</strong></td>
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<td>Metals &amp; trace elements include arsenic, cadmium, chromium, copper, lead, mercury, nickel, tin, and zinc. Formed from fuel combustion, incineration, and industrial processes and found in the environment (water, soil, or air) (Pollack et al. 2013)</td>
<td>✅ 2 out of 20 (Chromium and Copper)</td>
<td>✅ 1 out of 20 (Cadmium)</td>
<td>✅ 17 out of 20 metals/trace elements</td>
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<tr>
<td>Organochlorine pesticides: group of chlorinated compounds widely used as pesticides. These chemicals belong to the class of persistent organic pollutants (POPs) with high persistence in the environment (examples include DDT and hexachlorocyclohexane) (Buck Louis et al. 2012)</td>
<td>✅ 2 POPs from the same chemical class, γ-HCH and β-HCH</td>
<td></td>
<td></td>
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<tr>
<td>Perfluoralkyl and polyfluoroalkyl substances (PFAAs): group of chemicals that persist in the environment and human body. Used in many commercial household products such as polishes, waxes, paints, non-stick products (Teflon) (Buck Louis et al. 2012)</td>
<td>✅ 2 of nine PFAAs (PFOA, PFNA)</td>
<td></td>
<td>✅ 7 of nine PFAAs</td>
</tr>
<tr>
<td>Polychlorinated biphenyl ethers (PBDE): used as a flame retardant and while being phased out, persistent in the environment including casing of older electronics and wire insulation (Buck Louis et al. 2012)</td>
<td>✅ 1 out of 2 (PBDE-47)</td>
<td></td>
<td>✅ 1 out of 2 (PBDE-183)</td>
</tr>
<tr>
<td>Polychlorinated biphenyls: once used in industrial and commercial applications, banned in 1979 but can be released into the environment from poorly maintained hazardous waste sites. (Buck Louis et al. 2012)</td>
<td>✅ 2 out of 5 (74, 156)</td>
<td></td>
<td>✅ 3 out of 5 but trended as risk factors</td>
</tr>
</tbody>
</table>
Incidence of Endometriosis

ENDO Study investigators, fellows and collaborators have found a number of notable discoveries, and these findings have relevancy for designing research and synthesizing findings. First, the incidence of surgically visualized endometriosis for the operative sample was 41% and varied depending upon the diagnostic method (0.7% for histology only and 7% for MRI only), whereas the incidence was 11% in the population sample (Buck Louis et al. 2011). This latter finding underscores how much asymptomatic or undiagnosed disease may be at the population level because diagnosis in the population was by MRI which only accurately detects moderate or severe endometriosis.

Endometriosis, Infertility, and Pelvic Pain

When doing a comprehensive assessment of purported risk factors for endometriosis across study samples, infertility was consistently associated with diagnosis. Roughly 1/3 of women report having sought out treatment for infertility among both the women who were and were not seeking out gynecologic care (Peterson et al. 2013). Recent research presented at October’s American Society of Reproductive Medicine conference indicates that among women with versus without endometriosis who do achieve pregnancy, they are 1.5 times more likely to report having had a miscarriage or 6.2 times more likely to report having had an ectopic pregnancy. Overall, approximately 30% of reproductive age women reported pelvic or cyclic pain and often without seeking care (Schliep et al. 2015). Approximately 44% of women diagnosed with endometriosis reported pain, especially in the perineal region.

Adiposity and Endometriosis

A thorough assessment of multiple anthropometric measures clearly showed that lean body composition (including weight, skinfold thickness, waist and hip circumferences, body mass index (BMI), and upper arm area) is associated with risk for endometriosis (Backonja et al. 2017).

Other Risk Factors and Endometriosis

In-utero exposures and Endometriosis: This novel study assessed whether women with versus without endometriosis may have been exposed to various early exposures, including those arising from parents’ lifestyles, as a developing fetus. Findings indicated that in utero exposures were not statistically significantly associated with the odds of an endometriosis diagnosis in either the population or operative cohorts (Wolff et al. 2013).

Sexual and physical abuse and Endometriosis: Prevalence of reported abuse was high with 43% and 39% of women reported having experienced sexual and physical abuse, respectively. No association was observed between either a history of sexual or physical abuse and risk of endometriosis; however, a history of physical abuse was associated with a higher likelihood of adhesions after taking into account important confounding factors (Schliep et al. 2016).

Lifestyle factors and Endometriosis: Our recently published study indicated that while there were no associations between alcohol and caffeine consumption, smoking, or weekly occurrences of physical activity and endometriosis, a modest trend was found for total time spent sitting and increased risk for endometriosis (Hemmert et al. 2018).
Environmental Chemicals and Risk of Endometriosis and Fibroids


Incidence of Endometriosis and Endometriosis Diagnosis


**Endometriosis, Infertility, and Pelvic Pain**


**Adiposity and Endometriosis**


**Other Risk Factors and Endometriosis**


We could not have done this research without your incredible commitment to the study protocol. We are so very appreciative of your participation! For more information, visit endostudy.utah.edu or karen.schliep@utah.edu.