HHS Public Access

Author manuscript

J Expo Sci Environ Epidemiol. Author manuscript; available in PMC 2016 May 01.

Published in final edited form as:

J Expo Sci Environ Epidemiol. 2015 May ; 25(3): 278–285. doi:10.1038/jes.2014.31.

Persistent organic pollutants (POPs) and fibroids: results from the ENDO Study

Britton Trabert, PhD[1], **Zhen Chen, PhD**[2], **Kurunthachalam Kannan, PhD**[3], **C. Matthew Peterson, MD**[4], **Anna Z. Pollack, PhD**[5], **Liping Sun, MD**[2], and **Germaine M. Buck Louis, PhD**[2]

[1]Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland, USA

[2]Division of Intramural Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Department of Health and Human Services, Rockville, Maryland, USA

[3]Division of Environmental Health Sciences, Wadsworth Center, New York State Department of Health and the Department of Environmental Health Sciences, University at Albany, State University of New York, Albany, New York, USA

[4]Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Utah, Salt Lake City, Utah, USA

[5]Department of Global and Community Health, College of Health and Human Services, George Mason University, Fairfax, Virginia, USA

Abstract

To evaluate the association between persistent organic pollutants (POPs) and uterine fibroids we used previously collected data from a cohort of women 18–44 years of age undergoing laparoscopy or laparotomy at 14 participating hospital surgical centers (n=473). POP concentrations were measured in omental fat and serum. Presence of fibroids was defined based on a postoperative diagnosis (n=99). Odds ratios (OR) and 95% confidence interval (CI) for each POP by biologic medium was estimated using unconditional logistic regression adjusted for identified covariates. Concentrations were higher in omental fat than in serum for all POPs. Serum *p*,*p*′-dichlorodiphenyldichloroethylene (*p*,*p*′-DDE) was the only POP associated with fibroids [per 1-SD increase in log-transformed *p*,*p*′-DDE OR (95% CI): 1.37 (1.05–1.80)]. In analyses excluding women diagnosed with endometriosis, a number of polychlorinated biphenyls (PCBs) measured in omental fat were associated with fibroids [PCB 99: 1.64 (1.08, 2.49); PCB 138: 1.64 (1.03, 2.59); PCB 146: 1.54 (1.01, 2.37); PCB 153: 1.88 (1.12, 3.13); PCB 196: 1.60 (1.02, 2.51); PCB 206: 1.52 (1.01, 2.29)]. Although exploratory, our study suggests that PCBs may be associated with fibroids in the absence of other gynecologic disorders such as endometriosis, but the associations varied by biologic media with more POPs emerging when quantified in fat.

Corresponding author: Britton Trabert, 9609 Medical Center Drive, Bethesda, MD 20892-9774, Phone: 240-276-7331, Fax: 240-276-7838, britton.trabert@nih.gov.

The authors declare they have no actual or potential competing financial interests.

Keywords

epidemiology; uterine fibroids; persistent organic pollutants; omental fat; serum

Background

Uterine leiomyomas, or fibroids as they are commonly called, are benign tumors that develop from the smooth muscular tissue of the uterus of premenopausal women. Although they are often asymptomatic, fibroids can cause heavy menstrual bleeding, prolonged menses, pelvic pain or pressure, and may reduce fertility.[1] Because of their considerable morbidity, fibroids are the leading indication for hysterectomy in the United States and health care costs related to diagnosis and treatment exceed 6 billion dollars annually.[2,3] There are few known risk factors for uterine fibroids other than family history and race, with black women having higher incidence, earlier onset, and more severe symptoms than white women.[4–6] Fibroids are hormone dependent tumors that typically appear after menarche and regress along with steroid hormone levels around menopause.

A growing body of literature suggests that environmental agents that alter endocrine function, either by altering hormone function or synthesis or by binding to estrogen or androgen receptors, may influence risk of hormonally-dependent disease. Many persistent organic pollutants (POPs) are hypothesized endocrine disrupting agents, including synthetic chemicals used as industrial solvents or lubricants and their byproducts [polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), dioxins] and pesticides [methoxychlor, chlorpyrifos, dichlorodiphenyltrichloroethane (DDT].[7]

The role of human exposure to POPs in the development of hormone-related disease has been addressed in numerous epidemiologic studies since the early 1990s. However, few studies have evaluated the role of POPs in the development of fibroids.[8–10] High serum levels of dioxin after the 1976 chemical explosion in Seveso, Italy, were associated with a reduced risk of fibroids.[8] This could be due to the primarily anti-estrogenic effects of dioxin, or dioxin's ability to reduce extracellular matrix production via TGF-beta pathways.[11] Fibroids have been positively associated with consumption of sport fish, a known source of exposure to *p*,*p*′-diphenyldichloroethene (DDE) and polychlorinated biphenyls (PCBs).[9] In the same study, fibroids were positively associated with serum total PCB concentration.[9] Mean concentrations of a number of POPs measured in subcutaneous fat (HCB, HCH (β-HCH+γ-HCH), *p*,*p*′-DDE, *p*,*p*′-DDD, *p*,*p*′-DDT, PCBs 123, 126, 180, and PBDEs 85, 99, 100, 119) were higher among women with fibroids compared to the women without fibroids.[10] Given the paucity of data on the topic, we investigated associations of POPs as potential contributors to odds of a fibroid diagnosis in a cohort of women scheduled for laparascopy or laparotomy.

Materials and Methods

Data for this study were collected as part of a previously described matched cohort study of endometriosis, the Endometriosis: Natural History, Diagnosis and Outcomes (ENDO) Study[12,13], conducted in Salt Lake City, Utah and San Francisco, California between 2007

and 2009. The current study utilizes data from the operative cohort of the ENDO study. Briefly, the operative cohort comprised menstruating women 18–44 years of age scheduled for a laparascopy or laparotomy irrespective of indication at one of 14 participating hospital surgical centers. Women were eligible to participate if they had no history of surgically visualized endometriosis (to reduce the likelihood of prevalent disease for the primary outcome), no injectable hormone treatment within the past 2 years, ceased breast-feeding at least 6 months prior to enrollment and no history of cancer other than non-melanoma skin cancer.

Demographic and reproductive factors were ascertained via an in-person interview approximately 2 months before surgery and were followed by anthropometric assessment using electronic scales and standardized portable stadiometers. Surgeons completed standardized data collection instruments for the classification of operative findings and diagnoses. Omental fat (1–5 grams) was obtained from women by surgeons depending upon both availability and clinical judgment. Omental fat samples were collected via Harmonic ACE 36P shears and scalpel blades at the Utah study site and by bipolar electrocautery and scissors at the California site; following excision, samples were placed into acetone and hexane washed Wheaton brown glass bottles. Epiploica apendiceal fat was obtained in lieu of omental fat for four women, two from each study site. Nonfasting blood (~24 mL) specimens were obtained for all women using collection kits determined to be free of POPs. Institutional review board approval was obtained from all participating study sites. The women provided full consent before any data were collected and all were remunerated for their time and travel.

Measurement of persistent environment chemical concentrations in omental fat and serum was completed for the operative cohort (n=473). Presence of uterine fibroids was defined based on a postoperative diagnosis, 99 women were diagnosed with fibroids, of which 75 were listed as primary and 24 as secondary diagnosis. Physicians were not instructed to change their postoperative designations for study purposes; therefore we included both primary and secondary diagnoses in our analyses. Body mass index (BMI in kg/m^2) was estimated using measured weight and height and categorized into obese (≥ 30 kg/m^2) versus not obese (<30 kg/m^2) for analysis. Breast-feeding history was derived as a conditional variable based upon parity (nulliparous/parous) and categorized as no prior birth, prior birth but no breast-feeding, and prior birth with breast-feeding.

Laboratory analysis

All samples were processed and quantified in the same laboratory. Fat and serum samples were analyzed using gas chromatography (GC)/mass spectrometry (MS) techniques[14–16] for the major chemical classes of persistent pollutants: 1) organochlorine pesticides including hexachlorobenzene (HCB), hexachlorocyclohexane (HCH) isomers, gamma-HCH and beta-HCH, *p,p′*-dichlorodiphenyltrichloroethane (*p,p′*-DDT) and its metabolites *o,p′*-dichlorodiphenyldichloroethylene (*o,p′*-DDE) and *p,p′*-DDE, and chlordanes, *trans*- and *cis*-chlordane, *trans*- and *cis*-nonachlor, and oxychlordane; 2) polybrominated diphenyl ether (PBDE) congeners 47, 99, 100, 153, 154, 183, and 209; 3) polychlorinated biphenyl (PCB) congeners 18, 28, 44, 49, 52, 66, 74, 87, 99, 101, 118, 128, 138, 146, 149, 151, 153, 156,

157, 167, 170, 172, 177, 178, 180, 183, 187, 189, 194, 196, 201, 206, and 209; and 4) in serum only perfluorochemicals (PFCs), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluorohexane sulfonic acid (PFHxS), perfluoroheptanoic acid (PFHpA), perfluoroundecanoic acid (PFUNDA), perfluorododecanoic acid (PFDoDA), and perfluorooctanesulfonamide (PFOSA). Briefly, fat samples were extracted by the Soxhlet extraction procedure, and further details of the methods are given elsewhere.[15,16] Serum samples were fortified with isotopically labeled internal standards along with the addition of formic acid (80%) and water for denaturation and dilution of samples using a Gilson 215 liquid hander (Gilson Inc., Middleton, WI). The samples were extracted by solid-phase extraction (SPE) using a Rapid Trace Caliper Life Science, Hopkinton, MA) modular SPE system. Removal of co-extracted lipids was performed on a silica: silica/sulfuric acid column using Rapid Trace equipment for automation. Final analytical determination of the target analytes was performed by GC/isotope-dilution MS employing a Thermo Finnigan MAT95XP (Thermo Fisher Scientific, Bremen, Germany). External calibration standards were analyzed with every set of samples, and recoveries of internal standards were checked against external calibration standards. Three blanks were included in every batch comprising 30 samples. All concentrations are reported in nanograms per gram of fat or serum after subtracting background. All machine-observed concentrations were used without any substitution of concentrations below the limits of detection (LODs) to avoid introducing biases.[17–19] Serum lipids were quantified using published enzymatic methods.[20] Total serum lipids (TL) were estimated as [TL = (2.27 ×TC) + TG + 62.3 mg/dL], where TC denotes total cholesterol and TG denotes triglycerides, and were reported in milligrams per deciliter. Serum cotinine was quantified using high-performance liquid chromatography/tandem MS using an isotope dilution method and external standard calibration plots.[21] Serum cotinine was further categorized to help identify passive (<10 ng/mL) and active (≥10 ng/mL) smoking exposure using established cut-points.[22] PFCs were analyzed by high performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) as described elsewhere.[23]

Statistical analyses

Information on number of samples with POP measurements above the limit of detection is provided in Table 2. The distributions of all chemicals were summarized by geometric means with corresponding 95% confidence intervals. Comparisons of select variables by fibroid status were made to assess *a priori* defined variables (e.g. age, BMI, serum cotinine and lipids) for analysis. All chemical concentrations were log (X+1)-transformed to achieve normality and then rescaled by their standard deviation such that the odds ratios (OR) could be interpreted per 1-standard deviation change in the log-transformed chemical concentration. All analyses used wet-weight concentrations. The OR and corresponding 95% confidence interval (CI) for each chemical by biologic medium was estimated using unconditional logistic regression. Omental lipids were included in the logistic regression model evaluating the association between POPs and fibroids in omental fat. Serum lipids were entered into serum POPs models to minimize potential biases associated with automatic lipid adjustment. In addition to adjustment for total lipids, all models were also adjusted for *a priori* selected potential confounding factors: age, race, study site, BMI, and

serum cotinine[24]; variables were categorized as described above. Sensitivity analyses were conducted excluding women with an operative diagnosis of endometriosis to assess POPs and shared gynecologic pathology.

Results

The prevalence of surgically visualized fibroids resulting in a postoperative diagnosis was 20.9% in the operative cohort. The average age at fibroids diagnosis was 37.8 years (standard deviation = 4.9). As expected, the percentage of surgically visualized fibroids was higher among black women (87.5%) than women of other race/ethnicities (19.8%). The proportion of women diagnosed with fibroids was higher at the San Francisco site (55.7%) compared with the Utah study site (15.8%) (Table 1).

Lipid-adjusted geometric mean concentrations were higher in omental fat than in serum for all POPs (Table 2). For selected POPs there was a pattern of higher lipid-adjusted geometric mean concentrations for women with than without fibroids. Mean differences were significantly higher for women with than without fibroids for *p,p′*-DDT, *p,p′*-DDE, four chlordanes (*cis*-chlordane, *cis*-nonachlor, *trans*-nonachlor, and oxychlordane), and the majority of PCB congeners (27 of 35) measured in omental fat. In serum, geometric means remained significantly higher for women with fibroids than for women without fibroids for *p,p′*-DDE and the majority of PCB congeners measured (23 of 35). Geometric means were also significantly higher for women with than without fibroids for three PBDEs (PBDE 153, PBDE 154, and PBDE 209), which showed no difference in omental fat, and three PFCs (PFOS, PFHXS, and PFHPA), which were only measured in serum. Geometric mean concentrations of fat lipid content, serum total cholesterol and serum triglycerides were not different by fibroid status.

The odds of a fibroids diagnosis was increased per one standard deviation increase in *p,p′*-DDE concentration [adjusted odds ratio (aOR): 1.37 (95% confidence interval (CI): 1.05–1.80)] measured in serum (Table 3). The other POPs measured in omental fat or in serum were not significantly associated with increased or decreased odds of a fibroids diagnosis. In sensitivity analyses, excluding women diagnosed with endometriosis from the analysis (n=190), PCB 99, 138, 146, 153, 196, and 206 [aOR (95% CI) = PCB 99: 1.64 (1.08, 2.49); PCB 138: 1.64 (1.03, 2.59); PCB 146: 1.54 (1.01, 2.37); PCB 153: 1.88 (1.12, 3.13); PCB 196: 1.60 (1.02, 2.51); PCB 206: 1.52 (1.01, 2.29)] measured in omental fat were significantly associated with increased odds of a fibroids diagnosis. The other POPs measured in omental fat or in serum were not significantly associated with a fibroids diagnosis in sensitivity analyses (results not shown).

Discussion

We observed a significant positive association between *p,p′*-DDE, measured in serum, and the odds of a fibroid diagnosis. Intriguingly, a significant positive association emerged between six PCB congeners—PCB 99, 138, 146, 153, 196, and 206—measured in omental fat and the odds of a fibroids diagnosis in a sensitivity analysis excluding women with a postoperative diagnosis of endometriosis. However, a diagnosis of fibroids was not

associated with these same PCBs measured in serum, likely the result of the lower concentrations in serum consistent with their lipophilicity[15,25,26], demonstrating the importance of biologic medium when measuring POPs. Notably absent were significant ORs less than 1.0. Our findings are based on exploratory analyses and need to be corroborated in additional studies that can account for the prevalence of other gynecologic conditions.

To our knowledge, two prior studies have evaluated the association between PCBs and fibroids in women.[9,10] In a study of Chinese women living in Hong Kong, POP concentrations measured in both subcutaneous and visceral (omental) fat from 24 women with fibroids were compared with POP concentrations measured in subcutaneous fat only from 20 women without fibroids.[10] The authors report significantly higher mean concentrations of the majority of POPs measured in subcutaneous fat (HCB, HCH (β-HCH +γ-HCH), *p,p′*-DDE, *p,p′*-DDD, *p,p′*-DDT, PCBs 123, 126, 180, and PBDEs 85, 99, 100, 119) among the women with fibroids compared to the women without, and moderate-to-high correlation between POPs measured in visceral and subcutaneous fat in women with fibroids ($r^2>0.5$). However, they did not present results adjusted for potential confounders. Based on POPs quantified in omental fat for the entire operative cohort, we observed higher geometric mean concentrations of HCB, β-HCH, *p,p′*-DDE, *p,p′*-DDT, and PCB 180 from women with fibroids compared to women without fibroids which were consistent with the study of Qin et al. We did not corroborate the findings for PBDE 99 and PBDE 100. *p,p′*-DDD, PCBs 123 and 126, and PBDEs 85 and 119 were not measured in our study. However, in our adjusted analyses, none of the associations remained statistically significant. The Great Lakes Fish Consumption Study evaluated dietary sport fish consumption, and reported increased odds of self-reported fibroids for each 10-year increment in fish consumption.[9] Among a subset of their study population (n=197 out of 579 women studied) they measured DDE and PCB concentrations in serum and reported no association with serum DDE concentration, but reported an increased odds of self-reported fibroids with increasing quartile of log-adjusted total PCB concentration.[9] We report an increased odds of fibroid(s) associated with PCB concentration measured in omental fat in a sensitivity analysis; however, we did not observe a consistent association between PCBs and fibroids in our serum analyses. It should be noted, that the geometric mean serum concentration of the PCBs measured in the current operative cohort were much lower than the concentration among the cohort of women who consume large amounts of sport fish. Therefore the lack of association in our serum analyses may be the result of low exposure levels which likely contributes to reduced variability of the exposure at low levels, further supporting the need to measure PCBs in omental fat. We also report an increased odds of fibroid diagnosis with *p,p′*-DDE measured in serum, however, this association was not corroborated in analyses using omental fat. An association with DDT and its metabolites, however, is biologically plausible, given that total DDT and its metabolites were higher in fibroid tissue compared to normal uterine tissue[27] and uterine fibroids were induced in nonhuman primates after long-term dietary supplementation.[28]

Although the exact mechanism by which POPs may influence the development of fibroids remains unknown, hormones play a significant role in the etiology of fibroids and as such fibroids may be sensitive to influences of the potential endocrine disrupting properties of

certain POPs.[29] Further, a number of POPs and their metabolites have been detected in the endometrium of premenopausal women undergoing hysterectomies for fibroids.[30]

A strength of this investigation is the quantification of lipophilic POPs in both omental fat and serum. Given that our study population was based on an operative cohort and all women underwent surgical evaluation, our investigation has limited etiological interpretation. Women with uterine fibroids in the current study were identified as a result of surgical evaluation; therefore small intramural or submucosal fibroids are likely not diagnosed unless they protrude externally or into the uterine cavity, respectively. This limitation likely results in the misclassification of women with true, but not surgically detected, fibroids as having none. This same detection error applies to those diagnosed as having no fibroids. Thus, our results are applicable to visually recognized fibroids. Future studies using ultrasound diagnosed fibroids may provide additional information. There is no evidence that this type of misclassification, if present, is associated with POP exposure in those diagnosed either with or without fibroids in this study. Our comparison population, women with no fibroids, may be a biased sample in that they are more likely to have characteristics associated with a willingness to undergo surgical evaluation. Further, we cannot rule out that POPs associated with other gynecologic conditions that may be related to a woman's need for and/or willingness to undergo surgical evaluation are not masking an underlying association. Endometriosis is a common gynecologic condition that has been shown to be associated with POPs in a number of studies.[12,31,32] Further, in the operative cohort from this study, endometriosis was positively associated with gamma-HCH and inversely associated with PBDE 47, PCB 74 and PCB 156 measured in omental fat. We attempted to address the concern that the presence of other gynecologic conditions may be masking an underlying association between POPs and fibroids with our sensitivity analysis that excluded women with a postoperative diagnosis of endometriosis. In this analysis, we report a significant positive association with six PCBs measured in omental fat as summarized above. The short interval between quantification of chemical exposures and diagnosis is another limitation of our study. We are not aware of any data regarding the interval between exposure and fibroids onset in humans, nor are we aware of sufficient data from relevant animal models (Eker rats or domestic hens).[33,34] Given the long half-life of the POPs evaluated, it is likely that the measured concentrations are reasonable approximations of exposure during the relevant period of exposure. Finally, our results would not retain statistical significance after adjusting for multiple comparisons; however, the exploratory nature of our analysis supports the need for additional studies to evaluate associations between POPs and fibroids.

Our study provides the first evidence that POPs may be associated with fibroids in the absence of other gynecologic disorders such as endometriosis, but the specific chemicals associated with an increased odds of diagnosis varied by biologic media with more POP-fibroids associations emerging when quantified in fat.

Acknowledgments

This work was funded in part by the Intramural Research Program, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), National Institutes of Health (contracts NO1-DK-6-3428, NO1-DK-6-3427, 10001406-02, and 10001406-02). Ethicon Endo-Surgery, LLC, donated the HARMONIC® ACE 36P shears and scalpel blades through a signed materials transfer agreement with the University of Utah and NICHD.

References

1. Pritts EA, Parker WH, Olive DL. Fibroids and infertility: an updated systematic review of the evidence. Fertil Steril. 2009; 91:1215–23. [PubMed: 18339376]
2. Farquhar CM, Steiner CA. Hysterectomy rates in the United States 1990–1997. Obstet Gynecol. 2002; 99:229–34. [PubMed: 11814502]
3. Cardozo ER, Clark AD, Banks NK, Henne MB, Stegmann BJ, Segars JH. The estimated annual cost of uterine leiomyomata in the United States. Am J Obstet Gynecol. 2012; 206:211–9. [PubMed: 22244472]
4. Kjerulff KH, Langenberg P, Seidman JD, Stolley PD, Guzinski GM. Uterine leiomyomas. Racial differences in severity, symptoms and age at diagnosis. J Reprod Med. 1996; 41:483–90. [PubMed: 8829060]
5. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol. 2003; 188:100–7. [PubMed: 12548202]
6. Laughlin SK, Baird DD, Savitz DA, Herring AH, Hartmann KE. Prevalence of uterine leiomyomas in the first trimester of pregnancy: an ultrasound-screening study. Obstet Gynecol. 2009; 113:630–5. [PubMed: 19300327]
7. Diamanti-Kandarakis E, Bourguignon JP, Giudice LC, Hauser R, Prins GS, Soto AM, Zoeller RT, Gore AC. Endocrine-disrupting chemicals: an Endocrine Society scientific statement. Endocr Rev. 2009; 30:293–342. [PubMed: 19502515]
8. Eskenazi B, Warner M, Samuels S, Young J, Gerthoux PM, Needham L, Patterson D, Olive D, Gavoni N, Vercellini P, Mocarelli P. Serum dioxin concentrations and risk of uterine leiomyoma in the Seveso Women's Health Study. Am J Epidemiol. 2007; 166:79–87. [PubMed: 17443023]
9. Lambertino A, Turyk M, Anderson H, Freels S, Persky V. Uterine leiomyomata in a cohort of Great Lakes sport fish consumers. Environ Res. 2011; 111:565–72. [PubMed: 21310402]
10. Qin YY, Leung CKM, Leung AOW, Wu SC, Zheng JS, Wong MH. Persistent organic pollutants and heavy metals in adipose tissues of patients with uterine leiomyomas and the association of these pollutants with seafood diet, BMI, and age. J Environmental Science and Pollution Research. 2010; 17:229–40.
11. Gomez-Duran A, Carvajal-Gonzalez JM, Mulero-Navarro S, Santiago-Josefat B, Puga A, Fernandez-Salguero PM. Fitting a xenobiotic receptor into cell homeostasis: how the dioxin receptor interacts with TGFbeta signaling. Biochem Pharmacol. 2009; 77:700–12. [PubMed: 18812170]
12. Buck Louis GM, Chen Z, Peterson CM, Hediger ML, Croughan MS, Sundaram R, Stanford JB, Varner MW, Fujimoto VY, Giudice LC, Trumble A, Parsons PJ, et al. Persistent lipophilic environmental chemicals and endometriosis: the ENDO Study. Environ Health Perspect. 2012; 120:811–6. [PubMed: 22417635]
13. Buck Louis GM, Hediger ML, Peterson CM, Croughan M, Sundaram R, Stanford J, Chen Z, Fujimoto VY, Varner MW, Trumble A, Giudice LC. Incidence of endometriosis by study population and diagnostic method: the ENDO study. Fertil Steril. 2011; 96:360–5. [PubMed: 21719000]
14. Sjodin A, Jones RS, Lapeza CR, Focant JF, McGahee EE III, Patterson DG Jr. Semiautomated high-throughput extraction and cleanup method for the measurement of polybrominated diphenyl ethers, polybrominated biphenyls, and polychlorinated biphenyls in human serum. Anal Chem. 2004; 76:1921–7. [PubMed: 15053652]
15. Johnson-Restrepo B, Kannan K, Rapaport DP, Rodan BD. Polybrominated diphenyl ethers and polychlorinated biphenyls in human adipose tissue from New York. Environ Sci Technol. 2005; 39:5177–82. [PubMed: 16082945]
16. Johnson-Restrepo B, Addink R, Wong C, Arcaro K, Kannan K. Polybrominated diphenyl ethers and organochlorine pesticides in human breast milk from Massachusetts, USA. J Environ Monit. 2007; 9:1205–12. [PubMed: 17968447]
17. Richardson DB, Ciampi A. Effects of exposure measurement error when an exposure variable is constrained by a lower limit. Am J Epidemiol. 2003; 157:355–63. [PubMed: 12578806]

18. Schisterman EF, Vexler A, Whitcomb BW, Liu A. The limitations due to exposure detection limits for regression models. Am J Epidemiol. 2006; 163:374–83. [PubMed: 16394206]
19. Guo Y, Harel O, Little RJ. How well quantified is the limit of quantification? Epidemiology. 2010; 21(Suppl 4):S10–S16. [PubMed: 20526201]
20. Akins JR, Waldrep K, Bernert JT Jr. The estimation of total serum lipids by a completely enzymatic 'summation' method. Clin Chim Acta. 1989; 184:219–26. [PubMed: 2611996]
21. Bernert JT, Jacob P III, Holiday DB, Benowitz NL, Sosnoff CS, Doig MV, Feyerabend C, Aldous KM, Sharifi M, Kellogg MD, Langman LJ. Interlaboratory comparability of serum cotinine measurements at smoker and nonsmoker concentration levels: a round-robin study. Nicotine Tob Res. 2009; 11:1458–66. [PubMed: 19933777]
22. Wall MA, Johnson J, Jacob P, Benowitz NL. Cotinine in the serum, saliva, and urine of nonsmokers, passive smokers, and active smokers. Am J Public Health. 1988; 78:699–701. [PubMed: 3369604]
23. Kannan K, Corsolini S, Falandysz J, Fillmann G, Kumar KS, Loganathan BG, Mohd MA, Olivero J, Van WN, Yang JH, Aldoust KM. Perfluorooctanesulfonate and related fluorochemicals in human blood from several countries. Environ Sci Technol. 2004; 38:4489–95. [PubMed: 15461154]
24. Wise, LA.; Laughlin-Tommaso, SK. Uterine Leiomyomata. In: Goldman, MB.; Troisi, R.; Rexrode, KM., editors. Women and Health. 2. San Diego, CA: Academic Press; 2013. p. 285-305.
25. Allam MF, Lucena RA. Breast cancer and PCBs: true or false association? Eur J Cancer Prev. 2001; 10:539–40. [PubMed: 11916354]
26. Whitcomb BW, Schisterman EF, Buck GM, Weiner JM, Greizerstein H, Kostyniak PJ. Relative concentrations of organochlorines in adipose tissue and serum among reproductive age women. Environ Toxicol Pharmacol. 2005; 19:203–13. [PubMed: 21783478]
27. Saxena SP, Khare C, Farooq A, Murugesan K, Buckshee K, Chandra J. DDT and its metabolites in leiomyomatous and normal human uterine tissue. Arch Toxicol. 1987; 59:453–5. [PubMed: 3606393]
28. Takayama S, Sieber SM, Dalgard DW, Thorgeirsson UP, Adamson RH. Effects of long-term oral administration of DDT on nonhuman primates. J Cancer Res Clin Oncol. 1999; 125:219–25. [PubMed: 10235477]
29. Crain DA, Janssen SJ, Edwards TM, Heindel J, Ho SM, Hunt P, Iguchi T, Juul A, McLachlan JA, Schwartz J, Skakkebaek N, Soto AM, et al. Female reproductive disorders: the roles of endocrine-disrupting compounds and developmental timing. Fertil Steril. 2008; 90:911–40. [PubMed: 18929049]
30. Schaefer WR, Hermann T, Meinhold-Heerlein I, Deppert WR, Zahradnik HP. Exposure of human endometrium to environmental estrogens, antiandrogens, and organochlorine compounds. Fertil Steril. 2000; 74:558–63. [PubMed: 10973655]
31. Louis GM, Peterson CM, Chen Z, Hediger ML, Croughan MS, Sundaram R, Stanford JB, Fujimoto VY, Varner MW, Giudice LC, Kennedy A, Sun L, et al. Perfluorochemicals and endometriosis: the ENDO study. Epidemiology. 2012; 23:799–805. [PubMed: 22992575]
32. Upson K, De Roos AJ, Thompson ML, Sathyanarayana S, Scholes D, Barr DB, Holt VL. Organochlorine Pesticides and Risk of Endometriosis: Findings from a Population-Based Case-Control Study. Environ Health Perspect. 2013; 121:1319–24. [PubMed: 24192044]
33. Machado SA, Bahr JM, Hales DB, Braundmeier AG, Quade BJ, Nowak RA. Validation of the aging hen (Gallus gallus domesticus) as an animal model for uterine leiomyomas. Biol Reprod. 2012; 87:86. [PubMed: 22811571]
34. Everitt JI, Wolf DC, Howe SR, Goldsworthy TL, Walker C. Rodent model of reproductive tract leiomyomata. Clinical and pathological features. Am J Pathol. 1995; 146:1556–67. [PubMed: 7778693]

Table 1

Comparison of operative cohort by select sociodemographic and health characteristics and fibroid status, ENDO Study, 2007–2009

	Fibroids (n=99)	None (n=374)
Characteristic	**mean (SD)**	**mean (SD)**
Age (years)*	37.8 (4.9)	31.7 (6.9)
Race*	n (%)	n (%)
Black	7 (87.5)	1 (12.5)
Other	92 (19.8)	373 (80.2)
Obese body mass index (kg/m^2)		
<30	67 (21.5)	245 (78.5)
≥30	32 (20.5)	124 (79.5)
Smoking based on serum cotinine (ng/mL)*		
Non-smoker (0–9.99)	91 (22.6)	311 (77.4)
Current smoker (10+)	8 (11.3)	63 (88.7)
Study site*		
Utah	65 (15.8)	347 (84.2)
UCSF	34 (55.7)	27 (44.3)
Breast feeding history conditional on parity		
Nulliparous	50 (24.5)	154 (75.5)
Parous/no breastfeed	9 (15.8)	48 (84.2)
Parous/breastfed	39 (18.7)	170 (81.3)
Primary reason for surgery*		
Fibroids	49 (100.0)	0 (0.0)
Tubal ligation	2 (4.2)	46 (95.8)
Pelvic pain	22 (10.7)	184 (89.3)
Pelvic mass	15 (20.3)	59 (79.7)
Infertility	1 (2.9)	34 (97.1)
Menstrual irregularities	9 (15.0)	51 (85.0)

SD indicates standard deviation

N (%) except where indicated

* p-value < 0.05 for Chi-square or Student's t-test comparing fibroids status within cohort.

Table 2

Geometric mean comparison of persistent organic pollutant by fibroid status, the ENDO Study operative cohort, 2005–2009 (n=473).

	Omental Fat				Serum			
	% > LOD*	Geometric mean (95% CI)** Fibroids (n=99)	Geometric mean (95% CI)** None (n=374)	p-value	% > LOD*	Geometric mean (95% CI)** Fibroids (n=99)	Geometric mean (95% CI)** None (n=374)	p-value
HCB (ng/g)	100	7.72 (6.44, 9.26)	6.90 (6.26, 7.62)	0.11	68	1.86 (1.35, 2.57)	2.96 (2.61, 3.36)	0.12
γ-HCH (ng/g)	88	0.23 (0.19, 0.28)	0.20 (0.18, 0.22)	0.07	33	1.24 (0.93, 1.65)	0.94 (0.83, 1.07)	0.07
β-HCH (ng/g)	88	0.27 (0.20, 0.36)	0.20 (0.18, 0.23)	0.05	36	1.33 (1.00, 1.79)	1.00 (0.88, 1.14)	0.08
p,p′-DDT (ng/g)	93	1.61 (1.07, 2.42)	0.68 (0.55, 0.84)	<0.01	12	1.20 (0.89, 1.62)	1.22 (1.04, 1.43)	0.92
o,p′-DDE (ng/g)	93	0.20 (0.15, 0.27)	0.15 (0.13, 0.17)	0.09	21	0.61 (0.47, 0.80)	0.69 (0.59, 0.79)	0.90
p,p′-DDE (ng/g)	100	187.43 (146.62, 239.61)	98.91 (88.11, 111.04)	<0.01	99	36.95 (29.09, 46.94)	16.90 (15.31, 18.66)	<0.01
Chlordanes (ng/g)								
trans-chlordane	67	0.12 (0.09, 0.15)	0.13 (0.11, 0.14)	0.49	27	0.49 (0.36, 0.67)	0.74 (0.62, 0.89)	0.26
cis-chlordane	88	0.32 (0.26, 0.40)	0.21 (0.19, 0.24)	<0.01	14	0.39 (0.28, 0.57)	0.67 (0.55, 0.82)	0.38
cis-nonachlor	93	0.47 (0.35, 0.64)	0.32 (0.28, 0.36)	0.01	1	0.49 (0.38, 0.64)	0.51 (0.44, 0.59)	0.78
trans-nonachlor	99	9.63 (7.89, 11.75)	5.15 (4.57, 5.80)	<0.01	17	0.58 (0.43, 0.79)	0.52 (0.44, 0.63)	0.78
oxychlordane	100	8.28 (7.04, 9.74)	4.50 (4.02, 5.05)	<0.01	5	0.64 (0.47, 0.88)	0.69 (0.57, 0.83)	0.52
PBDEs (ng/g)								
PBDE 47	100	23.14 (17.75, 30.15)	24.40 (21.46, 27.76)	0.27	93	6.03 (4.67, 7.78)	6.86 (6.16, 7.62)	0.51
PBDE 99	76	0.80 (0.36, 1.78)	0.97 (0.65, 1.45)	0.65	91	3.36 (2.73, 4.12)	3.51 (3.17, 3.88)	0.85
PBDE 100	83	1.21 (0.57, 2.55)	1.77 (1.23, 2.54)	0.57	79	1.77 (1.50, 2.08)	1.91 (1.75, 2.08)	0.83
PBDE 153	91	6.13 (3.81, 9.86)	4.86 (3.52, 6.71)	0.56	94	2.66 (2.18, 3.23)	3.62 (3.32, 3.94)	0.01
PBDE 154	41	0.13 (0.06, 0.28)	0.11 (0.07, 0.15)	0.21	63	0.90 (0.72, 1.13)	1.17 (1.05, 1.30)	0.02
PBDE 183	32	0.14 (0.06, 0.33)	0.09 (0.06, 0.14)	0.08	7	0.52 (0.50, 0.54)	0.53 (0.52, 0.54)	0.65
PBDE 209	92	2.19 (1.53, 3.15)	2.55 (2.16, 3.01)	0.41	94	15.12 (10.31, 22.18)	8.75 (7.32, 10.46)	0.01
PCBs (ng/g)								
PCB 18	53	0.13 (0.09, 0.18)	0.13 (0.10, 0.15)	0.62	41	5.97 (3.73, 9.56)	3.43 (2.61, 4.51)	0.04
PCB 28	63	0.28 (0.18, 0.43)	0.20 (0.16, 0.24)	0.18	57	4.17 (2.90, 5.99)	2.89 (2.32, 3.61)	0.05
PCB 44	67	0.18 (0.13, 0.27)	0.07 (0.06, 0.09)	<0.01	55	4.27 (3.01, 6.06)	2.37 (1.93, 2.90)	0.01
PCB 49	63	0.07 (0.05, 0.08)	0.06 (0.05, 0.07)	0.25	55	2.61 (1.91, 3.57)	1.52 (1.26, 1.83)	<0.01

	Omental Fat				Serum			
	% > LOD*	Geometric mean (95% CI)** Fibroids (n=99)	Geometric mean (95% CI)** None (n=374)	p-value	% > LOD*	Geometric mean (95% CI)** Fibroids (n=99)	Geometric mean (95% CI)** None (n=374)	p-value
PCB 52	63	0.06 (0.05, 0.08)	0.06 (0.05, 0.07)	0.24	56	6.15 (4.26, 8.89)	5.14 (4.15, 6.38)	0.01
PCB 66	71	0.08 (0.07, 0.10)	0.07 (0.06, 0.08)	0.05	55	7.70 (5.18, 11.45)	3.96 (3.09, 5.09)	<0.01
PCB 74	93	2.18 (1.54, 3.08)	1.01 (0.81, 1.26)	<0.01	47	2.36 (1.64, 3.39)	1.68 (1.35, 2.08)	0.02
PCB 87	68	0.07 (0.06, 0.09)	0.06 (0.05, 0.07)	0.37	48	1.82 (1.29, 2.57)	1.51 (1.21, 1.88)	<0.01
PCB 99	99	2.33 (1.93, 2.80)	1.13 (1.01, 1.26)	<0.01	53	2.03 (1.45, 2.84)	1.39 (1.14, 1.68)	<0.01
PCB 101	91	0.26 (0.19, 0.34)	0.19 (0.17, 0.22)	0.03	54	5.48 (3.72, 8.07)	4.27 (3.38, 5.40)	0.02
PCB 118	99	2.69 (2.08, 3.47)	1.59 (1.39, 1.82)	<0.01	50	4.46 (3.17, 6.27)	3.46 (2.71, 4.43)	<0.01
PCB 128	74	0.12 (0.10, 0.15)	0.09 (0.08, 0.10)	<0.01	27	0.61 (0.41, 0.89)	0.52 (0.41, 0.65)	0.01
PCB 138	100	9.07 (7.65, 10.75)	4.53 (4.08, 5.03)	<0.01	75	5.31 (4.24, 6.64)	3.55 (3.04, 4.13)	<0.01
PCB 146	96	1.24 (0.99, 1.56)	0.46 (0.39, 0.53)	<0.01	39	0.79 (0.63, 1.01)	0.64 (0.54, 0.76)	0.10
PCB 149	73	0.09 (0.07, 0.11)	0.06 (0.06, 0.07)	<0.01	44	2.17 (1.42, 3.32)	1.91 (1.52, 2.40)	0.06
PCB 151	70	0.08 (0.07, 0.10)	0.06 (0.05, 0.07)	<0.01	38	1.24 (0.94, 1.65)	0.97 (0.81, 1.16)	<0.01
PCB 153	100	12.74 (10.73, 15.11)	5.98 (5.38, 6.65)	<0.01	69	4.07 (3.19, 5.20)	2.86 (2.42, 3.39)	<0.01
PCB 156	80	1.03 (0.69, 1.52)	0.32 (0.25, 0.41)	<0.01	0	0.25 (0.23, 0.28)	0.27 (0.26, 0.28)	<0.01
PCB 157	77	0.11 (0.09, 0.13)	0.08 (0.07, 0.09)	<0.01	0	0.25 (0.23, 0.28)	0.27 (0.26, 0.28)	<0.01
PCB 167	72	0.17 (0.13, 0.22)	0.09 (0.07, 0.10)	<0.01	1	0.28 (0.24, 0.34)	0.28 (0.27, 0.30)	0.01
PCB 170	99	3.23 (2.65, 3.92)	1.51 (1.30, 1.75)	<0.01	49	1.03 (0.82, 1.30)	0.80 (0.70, 0.92)	<0.01
PCB 172	96	0.42 (0.33, 0.54)	0.22 (0.19, 0.25)	<0.01	50	1.37 (1.06, 1.76)	0.98 (0.86, 1.12)	0.05
PCB 177	94	0.50 (0.40, 0.63)	0.23 (0.20, 0.26)	<0.01	16	0.46 (0.36, 0.60)	0.42 (0.38, 0.47)	0.17
PCB 178	95	0.66 (0.52, 0.83)	0.28 (0.24, 0.33)	<0.01	10	0.38 (0.33, 0.44)	0.33 (0.31, 0.36)	0.67
PCB 180	100	7.85 (6.43, 9.58)	4.08 (3.59, 4.64)	<0.01	49	2.20 (1.62, 2.99)	2.08 (1.78, 2.43)	0.17
PCB 183	98	1.10 (0.88, 1.36)	0.48 (0.41, 0.56)	<0.01	23	0.61 (0.50, 0.73)	0.46 (0.41, 0.51)	<0.01
PCB 187	100	2.87 (2.41, 3.41)	1.43 (1.26, 1.62)	<0.01	54	1.44 (1.15, 1.80)	1.10 (0.96, 1.26)	0.01
PCB 189	85	0.12 (0.10, 0.14)	0.09 (0.08, 0.10)	<0.01	1	0.26 (0.22, 0.31)	0.27 (0.26, 0.29)	<0.01
PCB 194	90	0.95 (0.66, 1.35)	0.36 (0.29, 0.44)	<0.01	3	0.31 (0.22, 0.44)	0.37 (0.31, 0.43)	<0.01
PCB 195	90	0.28 (0.22, 0.36)	0.17 (0.15, 0.20)	<0.01	17	0.63 (0.44, 0.91)	0.40 (0.34, 0.48)	0.34
PCB 196	98	1.59 (1.30, 1.95)	0.68 (0.59, 0.79)	<0.01	19	0.54 (0.43, 0.66)	0.39 (0.35, 0.44)	0.74
PCB 201	84	0.11 (0.09, 0.15)	0.11 (0.09, 0.12)	0.46	9	0.44 (0.26, 0.74)	0.71 (0.54, 0.92)	0.01

	Omental Fat				Serum			
	% > LOD*	Geometric mean (95% CI)** Fibroids (n=99)	Geometric mean (95% CI)** None (n=374)	p-value	% > LOD*	Geometric mean (95% CI)** Fibroids (n=99)	Geometric mean (95% CI)** None (n=374)	p-value
PCB 206	89	0.91 (0.70, 1.18)	0.36 (0.31, 0.43)	<0.01	33	0.40 (0.30, 0.53)	0.48 (0.42, 0.56)	0.06
PCB 209	83	0.39 (0.31, 0.50)	0.22 (0.19, 0.26)	<0.01	21	0.46 (0.35, 0.61)	0.39 (0.32, 0.46)	0.81
PFCs (ng/g)								
PFOS	--	--	--	--	100	5.90 (5.16, 6.74)	6.71 (6.22, 7.23)	0.04
PFOA	--	--	--	--	99	2.24 (1.99, 2.52)	2.37 (2.19, 2.55)	0.11
PFNA	--	--	--	--	97	0.60 (0.53, 0.69)	0.63 (0.58, 0.68)	0.18
PFDA	--	--	--	--	84	0.19 (0.16, 0.21)	0.18 (0.17, 0.20)	0.79
PFHxS	--	--	--	--	97	0.37 (0.32, 0.43)	0.47 (0.43, 0.51)	0.01
PFHpA	--	--	--	--	34	0.05 (0.03, 0.06)	0.06 (0.05, 0.06)	0.21
PFUNDA	--	--	--	--	39	0.09 (0.07, 0.11)	0.05 (0.05, 0.06)	<0.01
PFDoDA	--	--	--	--	3	0.02 (0.02, 0.03)	0.02 (0.02, 0.02)	0.67
PFOSA	--	--	--	--	0	0.02 (0.02, 0.03)	0.02 (0.02, 0.02)	0.05
Fat lipid content (ng/g)	100	77.70 (74.53, 81.00)	80.87 (79.36, 82.40)	0.10				
Serum total cholesterol (ng/g)					100	179.66 (174.24, 185.25)	177.46 (173.95, 181.05)	0.58
Serum triglycerides (ng/g)					100	123.77 (110.85, 138.18)	126.588 (120.73, 132.73)	0.54

*For PFCs percent above LOQ reported

**Geometric means and corresponding 95% confidence intervals were adjusted for lipid (total fat lipid or serum lipids#).

#Serum lipid = (serum total cholesterol × 2.27) + serum triglycerides + 62.3.

Table 3

Persistent organic pollutants (POPs) measured in omental fat and serum and odds of a fibroids diagnosis, the ENDO Study operative cohort, 2005–2009 (n=473).

Analyte	Omental fat Adjusted OR (95% CI)*	Serum Adjusted OR (95% CI)*
HCB	1.18 (0.86, 1.61)	0.83 (0.64, 1.09)
γ-HCH	0.89 (0.63, 1.25)	1.04 (0.81, 1.35)
β-HCH	0.95 (0.71, 1.28)	1.07 (0.83, 1.37)
p,p′-DDT	0.95 (0.68, 1.33)	1.05 (0.81, 1.35)
o,p′-DDE	0.82 (0.60, 1.13)	0.98 (0.76, 1.27)
p,p′-DDE	1.22 (0.88, 1.71)	**1.37 (1.05, 1.80)**
Chlordanes		
trans-chlordane	1.08 (0.82, 1.44)	0.92 (0.72, 1.17)
cis-chlordane	1.16 (0.88, 1.53)	0.94 (0.75, 1.18)
cis-nonachlor	0.81 (0.56, 1.17)	0.90 (0.67, 1.20)
trans-nonachlor	1.27 (0.89, 1.82)	0.94 (0.70, 1.28)
oxychlordane	1.39 (0.95, 2.02)	0.81 (0.50, 1.29)
PBDEs		
PBDE 47	0.93 (0.69, 1.26)	1.05 (0.80, 1.37)
PBDE 99	0.99 (0.73, 1.34)	1.05 (0.84, 1.32)
PBDE 100	0.94 (0.69, 1.27)	0.95 (0.70, 1.29)
PBDE 153	1.07 (0.79, 1.44)	0.92 (0.68, 1.25)
PBDE 154	1.13 (0.87, 1.45)	1.05 (0.80, 1.39)
PBDE 183	0.97 (0.66, 1.41)	0.99 (0.75, 1.30)
PBDE 209	0.84 (0.61, 1.15)	1.23 (0.96, 1.57)
PCBs		
PCB 18	1.07 (0.80, 1.44)	0.88 (0.68, 1.13)
PCB 28	1.04 (0.75, 1.44)	1.07 (0.79, 1.45)
PCB 44	1.22 (0.79, 1.87)	0.82 (0.58, 1.16)
PCB 49	1.15 (0.87, 1.51)	0.98 (0.69, 1.39)
PCB 52	1.02 (0.75, 1.40)	0.89 (0.66, 1.21)
PCB 66	1.07 (0.83, 1.36)	0.77 (0.56, 1.06)
PCB 74	1.10 (0.81, 1.51)	0.81 (0.56, 1.16)
PCB 87	0.99 (0.73, 1.33)	0.85 (0.64, 1.13)
PCB 99	1.28 (0.94, 1.75)	0.90 (0.65, 1.26)
PCB 101	0.78 (0.56, 1.08)	0.88 (0.66, 1.17)
PCB 118	1.00 (0.73, 1.37)	0.93 (0.67, 1.28)
PCB 128	0.79 (0.53, 1.19)	1.09 (0.88, 1.36)
PCB 138	1.22 (0.87, 1.70)	0.79 (0.58, 1.07)
PCB 146	1.20 (0.88, 1.64)	0.84 (0.61, 1.17)
PCB 149	0.98 (0.71, 1.37)	0.93 (0.70, 1.24)
PCB 151	0.87 (0.63, 1.20)	0.97 (0.75, 1.27)

Analyte	Omental fat Adjusted OR (95% CI)*	Serum Adjusted OR (95% CI)*
PCB 153	1.28 (0.90, 1.82)	0.82 (0.60, 1.12)
PCB 156	1.11 (0.83, 1.47)	1.00 (0.75, 1.34)
PCB 157	0.89 (0.62, 1.28)	1.00 (0.75, 1.34)
PCB 167	1.12 (0.83, 1.51)	1.16 (0.89, 1.51)
PCB 170	0.98 (0.70, 1.39)	0.92 (0.71, 1.19)
PCB 172	1.02 (0.76, 1.37)	1.10 (0.87, 1.39)
PCB 177	1.02 (0.75, 1.38)	0.79 (0.59, 1.06)
PCB 178	0.95 (0.69, 1.30)	0.84 (0.64, 1.12)
PCB 180	0.99 (0.69, 1.42)	0.84 (0.64, 1.10)
PCB 183	1.07 (0.78, 1.46)	1.00 (0.78, 1.29)
PCB 187	1.01 (0.71, 1.43)	0.92 (0.71, 1.20)
PCB 189	0.89 (0.62, 1.28)	0.95 (0.73, 1.24)
PCB 194	1.06 (0.78, 1.44)	0.87 (0.56, 1.38)
PCB 195	0.94 (0.68, 1.29)	1.01 (0.81, 1.26)
PCB 196	1.20 (0.86, 1.67)	0.76 (0.42, 1.39)
PCB 201	0.89 (0.65, 1.21)	0.62 (0.33, 1.16)
PCB 206	1.15 (0.85, 1.56)	1.27 (0.95, 1.70)
PCB 209	0.90 (0.63, 1.27)	0.96 (0.63, 1.48)
PFCs		
PFOS	--	0.83 (0.64, 1.07)
PFOA	--	0.83 (0.64, 1.08)
PFNA	--	0.83 (0.64, 1.09)
PFDA	--	0.81 (0.60, 1.08)
PFHxS	--	0.89 (0.67, 1.19)
PFHpA	--	0.86 (0.62, 1.20)
PFUNDA	--	0.92 (0.71, 1.20)
PFDoDA	--	0.93 (0.69, 1.26)
PFOSA	--	1.21 (0.93, 1.59)

All chemical concentrations were log(x+1) transformed then rescaled by the standard deviation (SD) for analysis; results are odds of a fibroids diagnosis per one SD change in POP concentration.

* Odds ratios (OR) adjusted for age (continuous), race (black vs. others), BMI (categorical at <29.9 vs. >=30.0), smoking status (based on cotinine cutoffs of current vs. non-smoker), site, and lipid (total fat lipid or serum lipids**).

** Serum lipid = (serum total cholesterol × 2.27) + serum triglycerides + 62.3.

Table 4

Persistent organic pollutants (POPs) and odds of fibroid diagnosis in sensitivity analysis excluding women with postoperative diagnosis of endometriosis, ENDO Study, 2005–2009 (n=283).

	Fibroids only (n=63) vs. no fibroids no endo (n=220)	
	Omental fat Adjusted OR (95% CI)*	Serum Adjusted OR (95% CI)*
Analyte		
HCB	0.86 (0.51, 1.44)	0.74 (0.51, 1.07)
γ-HCH	0.55 (0.27, 1.09)	0.98 (0.70, 1.38)
β-HCH	0.79 (0.51, 1.20)	1.01 (0.74, 1.39)
p,p′-DDT	1.11 (0.72, 1.71)	1.13 (0.79, 1.61)
o,p′-DDE	0.67 (0.42, 1.07)	1.01 (0.66, 1.55)
p,p′-DDE	1.19 (0.74, 1.91)	1.24 (0.87, 1.77)
CHLORDANES		
trans-chlordane	0.86 (0.52, 1.42)	0.78 (0.41, 1.47)
cis-chlordane	1.08 (0.73, 1.60)	0.75 (0.40, 1.41)
cis-nonachlor	0.95 (0.56, 1.61)	1.08 (0.74, 1.55)
trans-nonachlor	1.53 (0.91, 2.58)	1.06 (0.73, 1.53)
oxychlordane	1.61 (0.91, 2.84)	1.01 (0.59, 1.73)
PBDEs		
PBDE 47	1.08 (0.73, 1.61)	1.18 (0.82, 1.70)
PBDE 99	1.09 (0.74, 1.60)	1.30 (0.85, 1.99)
PBDE 100	1.07 (0.70, 1.62)	0.97 (0.64, 1.46)
PBDE 153	1.06 (0.71, 1.58)	0.87 (0.56, 1.35)
PBDE 154	1.11 (0.83, 1.47)	1.32 (0.88, 1.96)
PBDE 183	0.58 (0.27, 1.23)	0.81 (0.54, 1.22)
PBDE 209	0.93 (0.62, 1.40)	1.17 (0.84, 1.63)
PCBs		
PCB 18	1.30 (0.90, 1.88)	0.90 (0.61, 1.33)
PCB 28	0.80 (0.45, 1.43)	1.00 (0.67, 1.51)
PCB 44	0.93 (0.41, 2.12)	0.63 (0.35, 1.11)
PCB 49	0.74 (0.37, 1.51)	0.67 (0.34, 1.35)
PCB 52	0.78 (0.42, 1.45)	0.66 (0.40, 1.09)
PCB 66	1.08 (0.82, 1.41)	0.62 (0.38, 1.01)
PCB 74	1.33 (0.87, 2.06)	0.59 (0.33, 1.06)
PCB 87	0.97 (0.65, 1.45)	0.73 (0.46, 1.15)
PCB 99	**1.64 (1.08, 2.49)**	0.62 (0.32, 1.19)
PCB 101	1.00 (0.56, 1.76)	0.75 (0.48, 1.17)
PCB 118	1.27 (0.86, 1.88)	0.71 (0.39, 1.29)
PCB 128	0.72 (0.41, 1.26)	0.84 (0.41, 1.72)
PCB 138	**1.64 (1.03, 2.59)**	0.76 (0.47, 1.22)
PCB 146	**1.54 (1.01, 2.37)**	0.83 (0.49, 1.41)

	Fibroids only (n=63) vs. no fibroids no endo (n=220)	
	Omental fat Adjusted OR (95% CI)*	Serum Adjusted OR (95% CI)*
PCB 149	0.89 (0.52, 1.52)	0.83 (0.53, 1.31)
PCB 151	0.90 (0.50, 1.61)	0.84 (0.56, 1.28)
PCB 153	**1.88 (1.12, 3.13)**	0.76 (0.48, 1.21)
PCB 156	1.37 (0.96, 1.96)	0.85 (0.56, 1.28)
PCB 157	0.80 (0.47, 1.36)	0.85 (0.56, 1.28)
PCB 167	1.12 (0.76, 1.66)	1.05 (0.73, 1.51)
PCB 170	1.34 (0.86, 2.11)	0.94 (0.67, 1.31)
PCB 172	1.06 (0.72, 1.57)	1.05 (0.78, 1.40)
PCB 177	1.32 (0.87, 1.98)	0.65 (0.41, 1.05)
PCB 178	1.25 (0.84, 1.86)	0.89 (0.60, 1.31)
PCB 180	1.46 (0.90, 2.39)	0.79 (0.54, 1.16)
PCB 183	1.40 (0.91, 2.16)	0.95 (0.67, 1.35)
PCB 187	1.31 (0.82, 2.10)	0.84 (0.58, 1.21)
PCB 189	0.72 (0.42, 1.23)	0.94 (0.67, 1.32)
PCB 194	1.32 (0.84, 2.09)	0.28 (0.02, 3.62)
PCB 195	1.01 (0.66, 1.55)	1.71 (0.64, 4.54)
PCB 196	**1.60 (1.02, 2.51)**	0.66 (0.27, 1.60)
PCB 201	1.02 (0.68, 1.52)	0.61 (0.25, 1.49)
PCB 206	**1.52 (1.01, 2.29)**	1.32 (0.92, 1.90)
PCB 209	1.17 (0.75, 1.81)	0.94 (0.50, 1.77)
PFCs		
PFOS		0.88 (0.62, 1.24)
PFOA		0.72 (0.50, 1.03)
PFNA		0.74 (0.50, 1.08)
PFDA		0.62 (0.39, 0.99)
PFHxS		0.96 (0.65, 1.44)
PFHpA		0.93 (0.64, 1.35)
PFUNDA		1.28 (0.89, 1.84)
PFDoDA		0.96 (0.62, 1.49)
PFOSA		1.29 (0.90, 1.85)

All chemical concentrations were log(x+1) transformed then rescaled by the standard deviation (SD) for analysis; results are odds of a fibroids diagnosis per one SD change in POP concentration.

* Odds ratios (OR) adjusted for age (continuous), race (black vs. others), BMI (categorical at <29.9 vs. >=30.0), smoking status (based on cotinine cutoffs of current vs. non-smoker), site, and lipid (total fat lipid or serum lipids**).

** Serum lipid = (serum total cholesterol × 2.27) + serum triglycerides + 62.3.