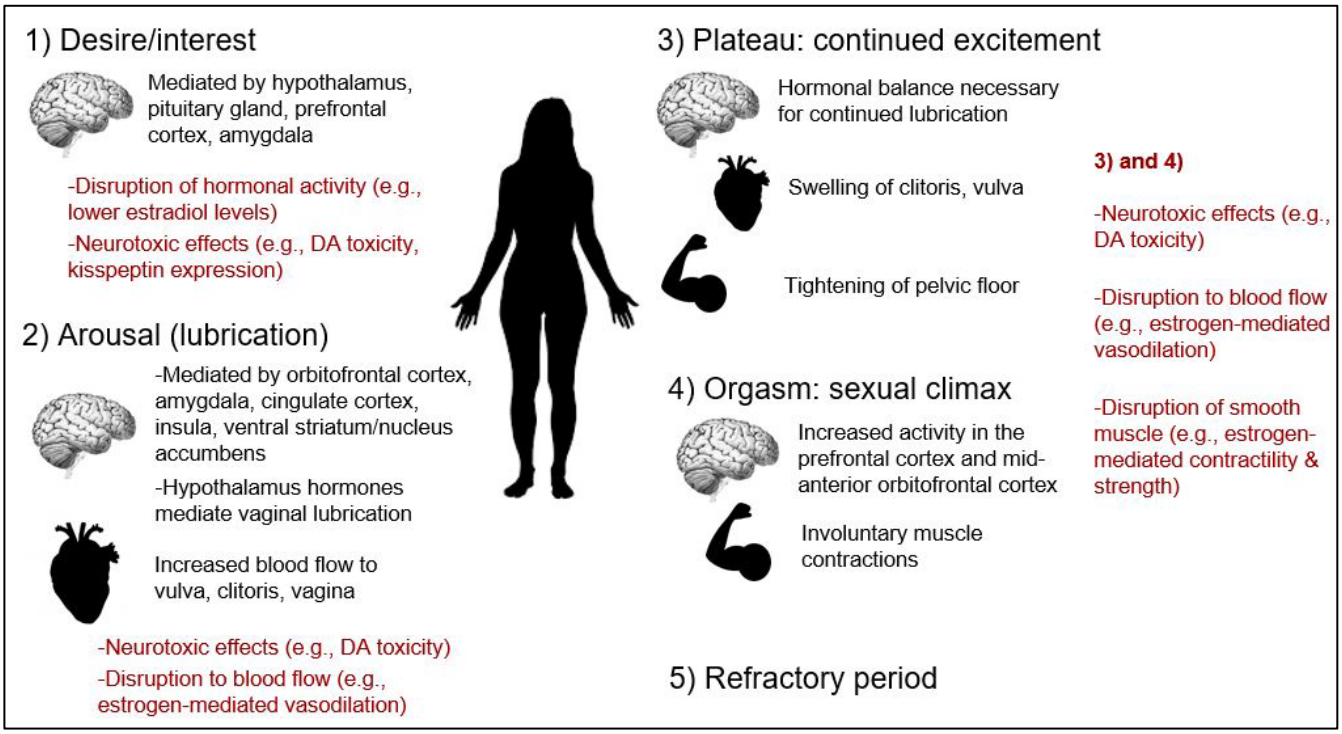
Per- and polyfluoroalkyl substances (PFAS) are a class of endocrine disrupting chemicals (EDCs) characterized by their environmental persistence and ability to interfere with hormonal systems. Notably, PFAS interfere with the production, metabolism, and secretion of reproductive hormones (estrogen, progesterone, luteinizing hormone) and induce dopaminergic toxicity. Given these toxic mechanisms, PFAS may play a role in the etiology of female sexual dysfunction (FSD), defined as the inability to partake in or enjoy sexual activity. FSD affects up to 43% of females, but its etiology is not fully understood. Where sexual function is strongly tied to the emotional well-being and quality of life among women, understanding the role of PFAS in the development of FSD is an important public health and clinical objective. This proposal aims to 1) characterize associations between biomarker (serum) concentrations of PFAS and female sexual function, and 2) investigate the impact of PFAS on specific domains of female sexual function (e.g., arousal, lubrication) to better understand the biological mechanisms underlying PFAS toxicity. To address these aims, we will use data from the Pregnancy Study Online (PRESTO), an ongoing prospective cohort of pregnancy planners in North America. In this application, we show compelling preliminary data on sexual health (measured using items from the Female Sexual Function Index FSFI) and serum levels of PFAS for 82 PRESTO participants indicating that higher serum PFAS levels are associated with lower sexual function scores. In support of our aims, we propose to use this award to 1) add further measures of female sexual function, including the Orgasm Rating Scale, Orgasmometer, and additional items from the FSFI, and 2) provide incentives to PRESTO participants to complete the sexual health questionnaires. These activities will provide richer sexual function data and help to improve the current sample size. PFAS exposure is widespread and FSD is also highly prevalent, but treatment options are limited. The research in this proposal will help to elucidate the impact of a pervasive and highly toxic class of chemicals on female sexual function, informing the current etiological understanding of FSD and public health interventions.

Female sexual dysfunction (FSD), a heterogenous group of conditions that adversely affect the ability to partake in or enjoy sexual activity, affects up to 43% of women.[1–3] FSD may manifest as decreased desire, low arousal, reduced lubrication, orgasmic difficulty, or pain during sex.[1–5] The etiology of FSD is multifactorial and includes physiological, relational, and psychosocial factors,[1,2,5] but remains incompletely characterized. Treatment options are limited.[6] Elucidating causes of FSD is therefore an important public health objective.

PFAS are a class of endocrine disrupting chemicals (EDCs) that are used extensively in industry and consumer products.[7] Because of their chemical structures, PFAS are highly persistent and mobile in the environment,[7] and human exposure is ubiquitous: the U.S. Centers for Disease Control and Prevention (CDC) estimates that 98% of Americans have measurable PFAS levels in their blood.[8] PFAS interfere with the production, metabolism, and secretion of reproductive hormones, and have neurotoxic properties.[9–13] Given their pervasive physiological impact on hormonal systems,[7] PFAS may play a role in the etiology of FSD. **Figure 1** illustrates the hypothesized mechanisms of action of PFAS (**in red**) at distinct phases of the female sexual response cycle, as originally defined by Masters and Johnson and updated by Kaplan and Basson.[14–16] Notably, PFAS may have deleterious effects on 1) desire/interest by disrupting estrogen, progesterone, and luteinizing hormone metabolism,[17–22] reducing kisspeptin levels,[13] and inducing dopaminergic (DA) toxicity, especially in the amygdala and hypothalamus;[13,17,23,24] 2) arousal and lubrication by interfering with catecholamine and serotonin metabolism (i.e., in the amygdala, nucleus accumbens)[13,17,23,24] and disrupting estrogen-mediated vasodilation;[1,2,17,25] and 3) plateau and orgasm by dysregulating estrogen-mediated smooth muscle strength and contractility,[21,22,26–28] disrupting estrogen-mediated vasodilation,[1,2,17,25] and inducing DA toxicity.[13,23,24,29]

Figure 1. Hypothesized mechanisms of action of PFAS on domains of female sexual function.



Despite the plausible biologic relationship between PFAS and multiple domains of sexual function, and the high prevalence of both PFAS exposure and FSD in the general population, no study has researched the connection between PFAS and FSD. Elucidating a potential role of PFAS in the etiology of FSD has significant public health and policy relevance.

Specific Aims

The objective of this proposal is to examine associations between biomarker (serum) concentrations of PFAS and self-reported sexual function in Pregnancy Study Online (PRESTO), a prospective cohort study of pregnancy planners in North America. We will further examine associations of serum PFAS with specific sexual function domains (desire, arousal, orgasm), to elucidate potential biological mechanisms underlying observed relationships.

- Aim 1: Evaluate associations of PFAS with overall sexual function.
  Hypothesis: Greater serum PFAS concentrations will be associated with worse self-reported scores for sexual function.
- Aim 2: Investigate associations of PFAS with individual domains of sexual function.
  Hypothesis: Higher serum PFAS levels will be associated with poorer self-reported ratings of arousal, lubrication, and orgasm, reflecting specific toxic mechanisms of PFAS (DA toxicity, dysregulation of estrogen; **Figure 1**).

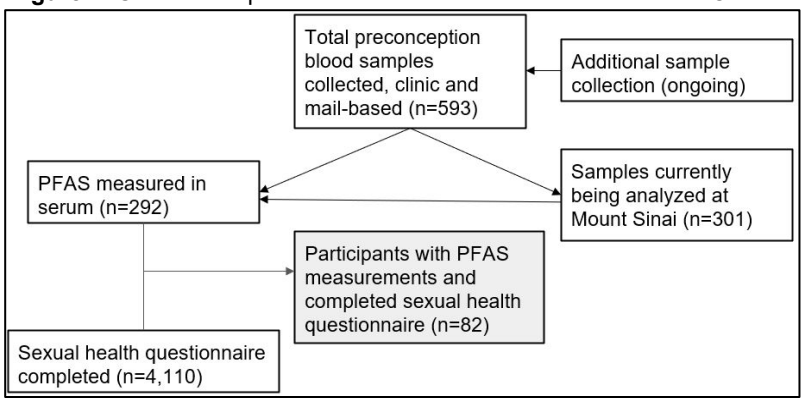
Approach: Study Design and Preliminary Findings

Study Overview: This proposal will leverage data from PRESTO to investigate associations between serum PFAS and 1) self-reported overall sexual function (**Aim 1**) and 2) domains of sexual function (desire, arousal, orgasm; **Aim 2**). We specifically request funding to add additional measures to the sexual health questionnaire in PRESTO (described below), and to provide incentives for completing the sexual health questionnaire to improve the current sample size to achieve the specific aims of the grant.

Study Population: PRESTO is an ongoing prospective cohort of pregnancy planners in the U.S. and Canada (n>17,700).[30] Participants were eligible for participation in PRESTO if they identified as female, were living in North America, were 21-45 years of age, and were trying to conceive without the use of fertility treatments. In 2019, we obtained NIH funding to collect biospecimen (blood, urine) data from a subset of participants. To date, we have collected ~600 blood samples. Information on all potential covariates, including demographic, socioeconomic, and behavioral factors, were collected via structured questionnaires or in-clinic visits.[30]

Measurement of PFAS: Participants provided preconception non-fasting blood samples at clinic visits or blood spot samples via a mail-based protocol.[31] We stored samples at -80°C and then shipped them to the CDC (clinic blood samples) or the Icahn School of Medicine at Mount Sinai (blood spots) on dry ice for quantification of 6 PFAS using isotope dilution tandem mass spectrometry. PFAS measured in serum include perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorohexanesulfonic acid (PFHxS), perfluorodecanoic acid (PFDA), and perfluoroundecanoic acid (PFUA). To date, we have analyzed serum PFAS concentrations from 292 participants; an additional 301 samples are currently being analyzed (to be completed in 2024; **Figure 2**). Blood sample collection is ongoing via the mail-based protocol.[31]

Figure 2. Current sample sizes for PFAS and FSD data in PRESTO.



Assessment of sexual function: In 2021, we added a supplemental Sexual Health and Wellbeing Questionnaire (SHWQ) to the PRESTO protocol. Over 4,000 participants have completed the SHWQ and these data have been used to report on the prevalence of FSD in a

preconception sample.[32] The SHWQ includes questions from the Female Sexual Distress Scale (FSDS)[33] and Female Sexual Function Index (FSFI) 6-Item (FSFI-6),[34] which has demonstrated excellent validity in identifying clinically relevant sexual dysfunction. We assessed sexual function as a continuous measure by summing scores across a modified version of the FSFI-6 in which the original question about lubrication (concerning frequency) was replaced with a question from the full FSFI scale (FSFI-19) related to lubrication difficulty to increase the specificity of the measure for true dysfunction. This grant proposal will support the addition of additional items, which will enable us to capture more detailed information about specific domains (see below).

Collection of Additional Sexual Health Data: We propose to use funding from this award to expand the sexual health questionnaire in PRESTO. We will add one question on arousal frequency from the FSFI-19,[35] four questions from the female Orgasm Rating Scale (ORS),[36] and the Orgasmometer.[37] These additional measures will improve our ability to examine effects of PFAS on specific facets of sexual function in detail, specifically evaluating both frequency and intensity of measured sexual health constructs. Finally, we propose to increase our sample size by providing incentives to participants who complete the SHWQ.

Statistical Approach and Preliminary Findings: We will use all available serum and sexual health data to investigate associations between PFAS and sexual function (current n=82, **Figure 2**). We will explore associations for eight primary outcomes of interest across four domains of sexual function (**Table 1**). There is very little missing data in PRESTO (<4%); we will employ fully conditional specification (FCS) methods to generate twenty multiply imputed datasets and findings from regression modeling (described below) will be pooled using Rubin's rule.[38] Prior to statistical modeling, we will explore distributions of all variables and compute summary statistics (medians, 25th—75th percentiles, percents [%], Spearman correlation coefficients). PFAS with detectable concentrations in >60% of participants will be included in analyses; concentrations below the limits of detection (LOD) will be imputed as the $LOD/\sqrt{2}$.[39] **Table 2** provides median serum PFAS concentrations (>60% detection) from the current sample (n=82) and stratified by parity status. We will first use Generalized Additive Models (GAMs) to investigate potential non-linear dose responses between PFAS and sexual function scores. Our primary approach will use multivariable linear regression to estimate mean differences (β) in sexual function scores per interquartile range increase (IQR) in PFAS concentrations (after checking for linearity) and 95% confidence intervals (CIs), adjusting for confounders selected using directed acyclic graphs (DAGs).[40] Because placental transfer, menstruation, and breastfeeding are known routes of elimination for PFAS,[41–44] we will also fit linear regression models stratified by parity. Preliminary findings for overall FSD scores (**Table 1**) are shown in **Figure 3** (lower scores indicate worse function; possible scores: 0-30); notably, in the full cohort (n=82) an IQR increase in PFHxS was associated with a 1.4 point decrease (95% CI: -2.1, -0.6) in summed sexual function scores, after adjustment for age, income,

Table 1. Primary sexual function outcomes considered under this proposal.

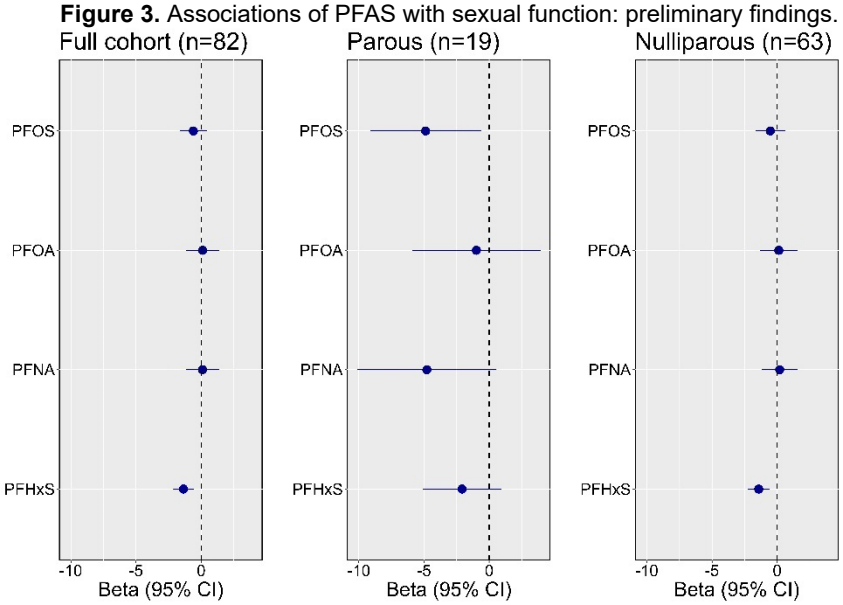
Outcome	Description of measure (target construct)
Overall function (**Aim 1**)	(a) Summed scores from items from FSFI (b) Summed scores from 12 items from FSDS
Desire (**Aim 2**)	Scores for desire question (intensity) on FSFI
Arousal (**Aim 2**)	Summed scores from two arousal questions (frequency and intensity) from FSFI
Lubrication (**Aim 2**)	(a) Summed scores for two lubrication questions from FSFI (frequency and difficulty)
Orgasm (**Aim 2**)	(a) Scores for orgasm question (frequency) on FSFI (b) Summed scores, 4 questions (satisfaction) from the ORS (c) Orgasmometer rating (intensity)

Table 2. Median (25th-75th %) concentrations for PFAS in PRESTO.

PFAS, ng/mL	Full cohort (n=82)	Parous (n=19)	Nulliparous (n=63)
PFOS	1.3 (0.9—2.1)	1.0 (0.9—1.6)	1.5 (0.9—2.1)
PFOA	1.1 (0.8—1.7)	0.5 (0.4—0.8)	1.4 (0.9—1.7)
PFNA	0.3 (0.2—0.4)	0.2 (0.2—0.3)	0.3 (0.2—0.5)
PFHxS	0.7 (0.4—1.2)	0.4 (0.3—0.6)	0.8 (0.5—1.3)

education, parity, and body mass index. Effect estimates were markedly stronger among parous participants.

Figure 3. Associations of PFAS with sexual function: preliminary findings.



Strengths & Limitations: The main limitation of this proposal is the use of cross-sectional data, where PFAS and sexual function were measured concurrently. Our sample size is currently limited but will be expanded with additional PFAS measurements (**Figure 2**) and sexual health data, supported by the incentives proposed in this application. The primary strength of this proposal is its novelty: we are the first to examine associations between PFAS and female sexual function. In addition, we will leverage data from an ongoing cohort of pregnancy planners with extensive covariate data, allowing for adjustment of important confounders.

Significance

As the first study to investigate the impact of environmental chemicals on female sexual function, this work will add significantly to the current understanding of the etiology of FSD and reproductive toxicity of PFAS. These data will serve to inform future research devoted to understanding the impact of environmental chemicals on sexual function. The findings generated in this proposal may have broad clinical and policy implications. Notably, identifying adverse impacts of PFAS on FSD will help to inform clinical practice by providing actionable steps (i.e., exposure reduction strategies) to improve female sexual function, as well as potentially provide insights into the etiology of FSD that could inform targets for future treatment development. Finally, this research will provide additional basis and justification for policies aimed at reducing environmental PFAS exposure (e.g., via greater regulation of PFAS in consumer products).

Study Timeline

A proposed 12-month timeline (starting in July 2024) for this award is shown below. In the first two months of the award, we will add questions from the FSFI, ORS, and Orgasmometer to the sexual health questionnaire, and launch the incentive program. Data collection for the expanded sexual health questionnaire will occur for the duration of the award; analyses using these data will be carried out in the last 6-months of the award. We will present findings at the ISSWSH (March 2025) and Society for Epidemiologic Research (June 2025) annual meetings. Primary findings (**Aim 1**) will be submitted for publication in the last month of the award. Findings for **Aim 2** will be submitted after the completion of this award.

Activity	1	2	3	4	5	6	7	8	9	10	11	12
Sexual health data collection												
Add FSFI, ORS & Orgasmometer to questionnaire	■	■										
Launch incentives for SHWQ questionnaire	■	■										
Ongoing sexual health data collection			■	■	■	■	■	■	■	■	■	■
Data analysis and presentation of findings												
Analysis with expanded sexual health data							■	■	■	■	■	■
Presentation of preliminary findings at conferences									■			■
Submission of initial findings for publication												■

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(43) Upson, K.; Shearston, J. A.; Kioumourtzoglou, M. A. An Epidemiologic Review of Menstrual Blood Loss as an Excretion Route for Per- and Polyfluoroalkyl Substances. *Curr Environ Health Rep* **2022**, *9* (1), 29–37. https://doi.org/10.1007/S40572-022-00332-0.

(44) Mondal, D.; Weldon, R. H.; Armstrong, B. G.; Gibson, L. J.; Lopez-Espinosa, M. J.; Shin, H. M.; Fletcher, T. Breastfeeding: A Potential Excretion Route for Mothers and Implications for Infant Exposure to Perfluoroalkyl Acids. *Environ Health Perspect* **2014**, *122* (2), 187–192. https://doi.org/10.1289/EHP.1306613.

The goal of this proposal is to investigate associations between per- and polyfluoroalkyl substances (PFAS) and female sexual function (**Aim 1**), including individual domains (i.e., desire, arousal, orgasm; **Aim 2**) of sexual function in the Pregnancy Study Online (PRESTO). We currently measure female sexual health using a Sexual Health and Wellbeing Questionnaire (SHWQ) that includes the Female Sexual Distress Scale (FSDS), 6-item Female Sexual Function Index (FSFI-6), and two additional items from the 19-item FSFI (FSFI-19) querying difficulty in achieving lubrication and intensity of sexual pain. We will use the requested funds to support these aims by adding 1) one item from the FSFI-19, four items from the female Orgasm Rating Scale (ORS), and the Orgasmometer to the SHWQ; and 2) incentives for participants that complete the SHWQ (see **Table 1**). The addition of items to the SHWQ and incentives will allow us to conduct **Aims 1** and **2** by providing more detailed sexual health data in a larger sample.

Table 1. Overview of activities that will be funded under this award.

Staff time	Fund staffing time to add FSFI-19, ORS, and Orgasmometer items to the SHWQ	$2,730
Incentives	Provide incentives to newly enrolled PRESTO participants to complete the SHWQ	$3,540
Staff time	Fund staffing time to monitor completion of SHWQ and disseminate incentives	$1,230
	Total	$7,500

1) Staff time for SHWQ: We propose adding items from the FSFI-19, ORS, and Orgasmometer to the SHWQ in PRESTO, allowing us to characterize potential biological mechanisms underlying adverse associations between PFAS and female sexual health observed in our preliminary findings. We will utilize $2,730 to fund staffing time for PRESTO's computer programmer to add these items to the SHWQ. Our computer programmer has a base salary of $90,000 and spends 40% effort in PRESTO. We estimate that adding these items to the SHSQ will require two weeks of his time, for a total direct cost of $1,385 ($90,000/52 weeks * 40% time * 2 weeks); fringe benefits (32%) and indirect costs (65%) will be $444 and $901, respectively, for a total of $2,730.

2) Incentives: The SHWQ is an optional questionnaire in PRESTO. PRESTO has enrolled 379 participants to date in 2023; 273 (72%) of these participants completed the optional SHWQ. To boost sample size and support data collection for the additional items added to the SHWQ (see above), we propose providing incentives to participants enrolling in PRESTO during this award (July 2024 — June 2025). We will offer a $10 gift card to ~350 participants who complete the SHWQ. Note that enrolling participants are also offered a $40 incentive to provide blood samples (in which PFAS are measured) using the mail-based protocol, which is currently funded by an NIH grant (see below). We therefore expect that the proposed incentives to complete the SHWQ will increase the current number of participants who provide both SHWQ and PFAS data.

3) Staff time for incentives: We will use this award to fund PRESTO administrative staff time to support the implementation of the proposed incentives. Specifically, PRESTO staff will identify newly enrolled participants that complete the SHWQ and disseminate gift cards to these participants. We anticipate that these activities will require 1 hour of staff time every other week (1.25% time), for a total direct cost of $625 ($50,000 base salary * 1.25% time). Fringe benefits (32%) and indirect costs (65%) will be $200 and $405, respectively, for a total of $1,230.

Ongoing PRESTO support: Ongoing data collection in PRESTO, including biospecimen collection, is supported by the NIH (R01-HD086742). Dr. Schildroth (co-PI) and Dr. Wise (mentor) are both funded under this award. Julia Bond (co-PI) is currently supported by a Ruth L. Kirschstein National Research Service Award Predoctoral Fellowship (F31-DE031969). Direct costs for this proposal are not currently funded. Dr. Wise certifies these funding sources.

X Lauren Wise

Dr. Lauren Wise, ScD

Career Development Plan (Julia Bond, MPH)

My career goal is to become an independent researcher at an academic institution researching women's reproductive and sexual health. I am particularly interested in the etiology of women's sexual dysfunction and plan to contribute high-quality epidemiologic research to support the development of new and effective treatments. My training to date has focused on advanced causal methods and reproductive epidemiology (**Figure 1**). Through my work with Pregnancy Study Online (PRESTO), the cohort in which the proposed research will be conducted, I have gained extensive experience in survey-based assessment of female sexual dysfunction. My experience and training have prepared me to successfully complete the proposed research alongside my co-applicant, Dr. Samantha Schildroth.

Figure 1. Overview of application's previous, current, and planned training



Both my short-term and long-term career goals are oriented towards advancing the etiologic study of sexual dysfunction and its clinical consequences. In the short term (~1 year), I am conducting my dissertation research focusing on preconception sexual dysfunction and reproductive outcomes. I have gained experience conducting etiologic research using sexual dysfunction as an exposure and understanding its reproductive consequences. I will also conduct the proposed research evaluating the association between per- and polyfluoroalkyl substances (PFAS) and sexual dysfunction (as outlined in this application), which will provide training in the study of sexual function as an outcome, as well as an opportunity to explore novel environmental determinants and biological mechanisms underlying sexual dysfunction.

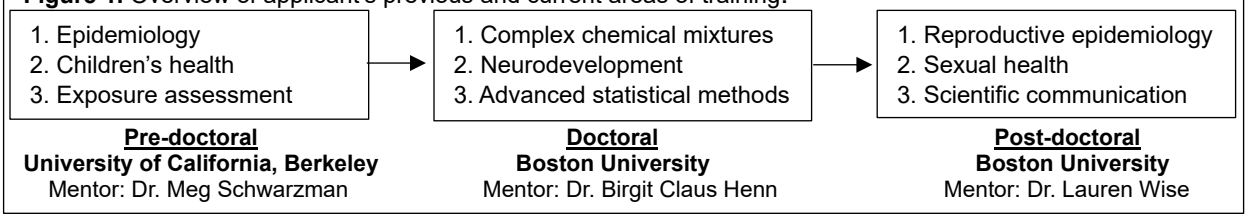
Long-term, Dr. Schildroth and I plan to submit grants to the National Institute of Environmental Health Sciences and National Institute of Human and Child Development using this proposed project as a basis for future research objectives. These grants will expand on this project by 1) proposing longitudinal data collection; 2) obtaining detailed information about menstrual cycle phases with relation to sexual function; and 3) expanding biomarker collection for additional environmental exposures that may have salience to sexual function. Longitudinal data will provide important insights, specifically the ability to isolate etiologically relevant exposure windows and to track changes in sexual functioning across the menstrual cycle and over time. Because PFAS affect hormones, detailed data on menstrual cycle timing in relation to both PFAS exposure and sexual functioning will be important to isolate the potential for effect modification by natural hormone cycling. These grants will help support my planned postdoctoral research, continuing my research on sexual function in the PRESTO cohort, as well as provide a foundation from which to pursue a faculty position. The outstanding research environment and mentorship at Boston University School of Public Health will also contribute to my success as an independent researcher.

My rigorous training in epidemiology and causal research methods has positioned me well to transition into an independent research career dedicated to identifying causes of female sexual dysfunction. Despite its relatively high prevalence, treatment options remain limited, particularly when contrasted with the treatments available for male sexual dysfunction. This proposal will support the first step in a planned body of research aiming to identify causes of sexual dysfunction, with the ultimate goal of informing policy and clinical decision-making and identifying potential targets for novel therapeutic options for female sexual dysfunction.

Career Development Plan (Dr. Samantha Schildroth)

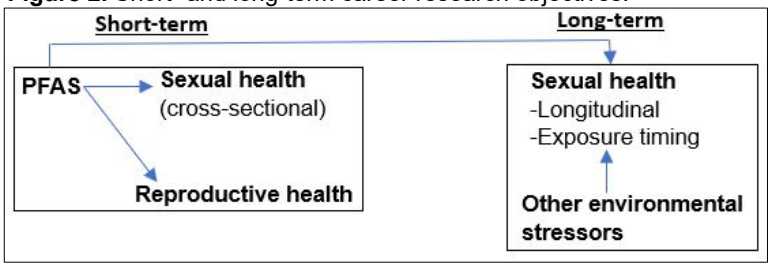
My ultimate career objective is to become an independent researcher at an academic institution investigating the impacts of chemical stressors on women's health. Exposure to environmental chemicals, including per- and polyfluoroalkyl substances (PFAS), is ubiquitous and poses a significant health risk for female sexual and reproductive health due to their endocrine disrupting and neurotoxic properties. My previous training and research experiences have focused on exposure assessment, epidemiology, chemical mixtures, neurodevelopment, and advanced statistical methods (**Figure 1**). Further, my training as a Postdoctoral Research Associate at Boston University under Dr. Lauren Wise has expanded my research profile to include reproductive and sexual health outcomes. As such, I have the necessary skills to conduct the research outlined in this proposal in conjunction with Julia Bond (co-applicant).

Figure 1. Overview of applicant's previous and current areas of training.



I have both short-term and long-term research and career goals (**Figure 2**). In the short-term (~2 years), I will gain training in my post-doctoral position that will allow for my successful transition into a faculty position; in addition to those training areas listed in **Figure 1**, I will further develop my analytic knowledge of novel statistical methods (e.g., multiple informant models) that will support the pursuit of my long-term research goals (e.g., exposure timing). My short-term research goals include investigating PFAS exposures in relation to female sexual health and reproductive outcomes (i.e., pregnancy outcomes, postpartum health). The research aims in this proposal are a key component of my short-term research goals and post-doctoral training. Therefore, this award will help propel my training and build my research portfolio so that I may ultimately pursue a career as an epidemiologist investigating environmental determinants of female sexual health.

Figure 2. Short- and long-term career research objectives.



In the long-term, my research objectives will focus on expanding on the aims in this proposal. Julia Bond and I will apply for grant funding from the National Institute of Environmental Health Sciences and National Institute of Human and Child Development to support longitudinal collection of female sexual health and biomarker data. In addition to establishing temporality (improving on the cross-sectional data in this proposal), longitudinal data collection will allow us to examine 1) exposure timing, and 2) other environmental stressors. Because PFAS affect hormonal systems, we hypothesize that the impact of chemical exposures on female sexual health may depend on the timing of exposure in relation to the menstrual cycle. Moreover, other endocrine disrupting chemicals (flame retardants, pesticides) also dysregulate hormonal systems, but these chemicals have not been examined in relation to female sexual function. In summary, my short- and long-term career objectives focus on elucidating environmental drivers of female sexual dysfunction. We are the first research group to investigate chemical exposures and female sexual dysfunction and our novel research will generate important findings for policy (e.g., chemical regulation) and clinical practice.

Julia C Bond, MPH
jcbond@bu.edu

EDUCATION

PhD Candidate, Epidemiology **Degree expected May 2024**
Boston University School of Public Health
MPH in Epidemiology—Maternal and Child Health **June 2018**
University of Washington, Seattle, WA
BA in Neuroscience, *cum laude* **May 2009**
Bowdoin College, Brunswick, ME

FUNDING

NIDCR: Ruth L Kirschtein National Research Service Award Predoctoral Fellowship (F31- DE031969)
Title: Women's oral health in the preconception period: correlates and consequences
Dates: 06/2022-11/2024
Role: PI
Objectives: Evaluate the association between preconception periodontitis, and its treatment, and reproductive health outcomes and assess predictors of poor preconception oral health.

CONTRIBUTIONS IN WOMEN'S SEXUAL HEALTH

PEER-REVIEWED PUBLICATIONS OF RELEVANCE TO GRANT

1. **Bond JC,** White KO, Abrams JA, Wesselink AK, Wise LA. Sexual dysfunction, distress, and care-seeking among females during the preconception period. Am J Obstet Gynecol. 2023 Jul;229(1):43.e1-43.e12. doi: 10.1016/j.ajog.2023.03.037. PMID: 37001576.
2. **Bond JC,** Abrams J, Wesselink AK, White KO, Rothman KJ, Wise LA. Predictors of Non-Response to a Sexual Health Survey in a North American Preconception Cohort Study. J Sex Med. 2022 Nov;19(11):1707-1715. doi: 10.1016/j.jsxm.2022.08.199. PMID: 36182572.
3. **Bond JC,** Geller RJ, White KO, Hatch EE, Rothman KJ, Wise LA. Concordance of self-reported sexual intercourse frequency between members of mixed-sex couples attempting conception. Can J Hum Sex. 2022;31(3):342-353. https://doi.org/10.3138/cjhs.2021-0059
4. Estibeiro V, Juntunen A, **Bond JC**, Harlow BL. Menstrual Cycle Characteristics and Vulvodynia. J Womens Health (Larchmt). 2022 Aug;31(8):1127-1136. doi: 10.1089/jwh.2020.9011. PMID: 35041490.
5. **Bond JC,** Harlow BL, White KO. Care Seeking for Chronic Vulvar Pain Among a Large, Population-Based Sample of Reproductive-Aged Women. J Womens Health (Larchmt). 2022 Apr;31(4):513-520. doi: 10.1089/jwh.2021.0086. PMID: 34520267.
6. **Bond JC,** Kachura JJ, Fox MP, Weuve J, Harlow BL. Potential for Selection Bias in Studies of the Association of Hormonal Contraception and Chronic Vulvar Pain. J Womens Health (Larchmt). 2022 Feb;31(2):194-201. doi: 10.1089/jwh.2020.8857. PMID: 34190629.
7. **Bond JC,** Morrison DM, Hawes SE. Sexual Self-Efficacy and Entitlement to Pleasure: The Association of the Female Sexual Subjectivity Inventory with Sexual Risk Taking and Experience of Orgasm. Arch Sex Behav. 2020 Apr;49(3):1029-1038. doi: 10.1007/s10508-019-01563-3. PMID: 31897825.

Under review

1. **Bond JC,** Ford JV. A call for sex-positive epidemiology. (under review at American Journal of Epidemiology)

CONFERENCE PRESENTATIONS OF RELEVANCE TO GRANT

1. **Bond JC**, White KO, Wesselink AK, Wise LA. Female orgasm frequency and time to pregnancy in pregnancy planners. Oral Presentation. Society for Pediatric and Perinatal Epidemiologic Research Annual Meeting. June 12-13, 2023. Portland, OR.
2. **Bond JC**, White KO, Wesselink AK, Wise LA. Female orgasm frequency and time to pregnancy in pregnancy planners. Poster presentation. Society for Epidemiologic Research Annual Meeting. June 13-16, 2023. Portland, OR.
3. **Bond JC**, White KO, Perkins RB, Wise LA. Cervical procedures for HPV and sexual function in pregnancy planners. Poster presentation. Society for Epidemiologic Research Annual Meeting. June 13-16, 2023. Portland, OR.
4. **Bond JC,** White KO, Wesselink AK, Wise LA. Factors related to participation in surveys of sexual health in a preconception cohort study. Poster presentation. Society for Pediatric and Perinatal Epidemiologic Research Annual Meeting. June 13-14, 2022. Chicago, IL.
5. **Bond JC,** White KO, Wise LA. Feasibility of adding a sexual function questionnaire to a preconception cohort study. World Meeting on Sexual Medicine. November 19-21, 2021. Online.

INVITED TALKS OF RELEVANCE TO GRANT

International Institute for Restorative Reproductive Medicine Grand Rounds Presentation Series. "Sexual function, female orgasm, and fecundity." October 26, 2023.

SELECTED OTHER PEER REVIEWED PUBLICATIONS

Complete list of published works**:**
https://www.ncbi.nlm.nih.gov/myncbi/julia.bond.1/bibliography/public/

1. **Bond JC**, Coleman CM, Yland JJ, Wesselink AK, Wang T, Willis M, Hatch EE, Rothman KJ, Savitz D, Eisenberg ML, Wise LA. Preconception self-reported sleep duration, non-daytime work, and spontaneous abortion in a prospective cohort study. Hum Reprod. [In Press].
2. **Bond JC**, Fox MP, Wise LA, Heaton B. Quantitative Assessment of Systematic Bias: A Guide for Researchers. J Dent Res. 2023. doi: 10.1177/00220345231193314. PMID: 37786916.
3. **Bond JC,** Wise LA, Fox MP, Garcia RI, Murray EJ, White KO, Rothman KJ, Hatch EE, Heaton B. Preconception Periodontitis and Risk of Spontaneous Abortion in a Prospective Cohort Study. Am J Epidemiol. 2023;192(9):1509-1521. doi: 10.1093/aje/kwad142. PMID: 37339008.
4. Heaton B*, **Bond JC***, Bae J, Cozier Y. Perceived experiences of racism linked to dental fear and anxiety among Black women. Community Dent Oral Epidemiol. 2023 Oct;51(5):896-907. doi: 10.1111/cdoe.12782. PMID: 35964228. (*Equal contributors)
5. **Bond JC,** McDonough R, Alshihayb TS, Kaye EA, Garcia RI, Heaton B. Edentulism is associated with increased risk of all-cause mortality in adult men. J Am Dental Assoc. 153 (7) 625-634. https://doi.org/10.1016/j.adaj.2021.11.009. PMID: 35241269
6. **Bond JC,** Wise LA, Willis SK, Yland JJ, Hatch EE, Rothman KJ, Heaton B. Self-reported periodontitis and fecundability in a population of pregnancy planners. Hum Reprod. 2021;36(8):2298-2308. doi: 10.1093/humrep/deab058. PMID: 33822056.
7. **Bond JC,** Mancenido AL, Patil DM, Rowley SS, Goldberg J, Littman AJ. Residence change during the first trimester of pregnancy and adverse birth outcomes. J Epidemiol Community Health. 2019;73(10):913-919. doi: 10.1136/jech-2018-211937. PMID: 31362943.

SELECTED HONORS

2023	Co-first author on a manuscript selected for the IADR Judith Albino Award for Outstanding Research in Health Equity
2017-2018	University of Washington Maternal and Child Health Program Thesis Award
2016-2017	University of Washington Maternal and Child Health Program Traineeship

CURRICULUM VITAE

Samantha Schildroth
Email: sschildr@bu.edu **Phone:** 207-710-3683

EDUCATION

Boston University School of Public Health, Boston, MA
Doctor of Philosophy, Environmental Health (Focus: Epidemiology) February 2023

University of California Berkeley School of Public Health, Berkeley, CA
Master of Public Health, Environmental Health Sciences May 2019

University of New England, Biddeford, ME
Bachelor of Science, Biomedical Sciences & Environmental Science May 2017

RESEARCH EXPERIENCE

Postdoctoral Training
Department of Epidemiology, Boston University School of Public Health 2023 – present
Supervisor: Dr. Lauren Wise

Ongoing Projects (selected)

1. **Per- and Polyfluoroalkyl Substances (PFAS) and Female Sexual Function**
2. **PFAS exposure and risk of Spontaneous Abortion**
3. **PFAS, Persistent Endocrine Disrupting Chemicals, and Psychosocial Health**
4. **Exposure to PFAS Mixtures, Metabolomics, and Pregnancy Outcomes**

Doctoral Training
Department of Environmental Health, Boston University School of Public Health 2019 – 2023

Research Projects (selected)

1. **Correlates of Exposure to Endocrine Disrupting Chemicals in Reproductive-aged Black Women**
2. **Per- and Polyfluoroalkyl Substances and Persistent Endocrine Disrupting Chemical Mixtures in Dust**

Master of Public Health Training
University of California, Berkeley, Berkeley, CA 2017 – 2019

Research Projects (selected)

1. **Impact of Proposition 65 on Chemical Exposures Relevant to Breast Cancer**

FUNDING SOURCES

NICHD Research Project (R01-HD086742)
Title: An Internet-Based Preconception Cohort Study in North America and Denmark
Dates: 3/1/2023 – present
Role: Postdoctoral trainee

NIEHS Pathway to Independence Award (submitted)
Title: A Prospective Study of Per- and Polyfluoroalkyl Substance (PFAS) Mixtures and Pregnancy Outcomes among Black Women
Dates: Submitted June 2023
Role: PI

NIEHS Ruth L. Kirschtein National Research Service Award Predoctoral Fellowship (F31-ES033507)
Title: Metal Mixtures and the Role of Iron Status in Early Adolescent Cognition
Dates: 7/1/2022 – 2/28/2023
Role: PI

NIEHS Predoctoral Training Grant (T32-ES014562)
Title: Environmental Epidemiology in Community Settings
Dates: 9/1/2019 – 6/30/2022
Role: Doctoral Trainee

PUBLICATIONS (selected)

Complete list of published works: **https://www.ncbi.nlm.nih.gov/myncbi/samantha.schildroth.2/bibliography/public/.**

Schildroth S, Valeri L, Kordas K, Shi B, Friedman A, Smith D, Placidi D, Wright RO, Lucchini RG, White RF, Horton M, Claus Henn B. Assessing the Mediating Role of Iron Status on Associations between an Industry-Relevant Metal Mixture and Verbal Learning and Memory in Italian Adolescents. *Sci. Tot. Environ.* 2023. PMID: 37774885.

Wise LA, Wang TR, Mikkelsen EM, Wesselink AK, Calafat AM, Wegienka G, Geller RJ, Coleman CM, Willis MD, Marsh EE, **Schildroth S**, Messerlian-Lambert G, Hatch EE. Per- and Poly-fluoroalkyl Substances and Anti-Mullerian Hormone Concentrations in Two Preconception Cohort Studies. *Environmental Health Perspectives, in press.*

Schildroth S, Friedman A, White RF, Kordas K, Placidi D, Bauer JA, Webster T, Coull BA, Cagna G, Wright RO, Smith D, Lucchini R, Horton M, Claus Henn B. Associations of an Industry-Relevant Metal Mixture with Verbal Learning and Memory in Italian Adolescents: The Modifying Role of Iron Status. *Environ. Res.* 2023; 224: 115457. PMCID: PMC10117691.

Schildroth S, Rodgers KM, Strynar M, McCord J, Poma G, Covaci A, Dodson RE. Per- and Polyfluroroalkyl Substances (PFAS) and Persistent Chemical Mixtures in Dust from U.S. colleges. *Environ Res* 2022;206: 112530. PMID: 34902383

Schildroth S, Wise LA, Wesselink AK, Bethea TN, Fruh V, Taylor KW, Calafat AM, Baird DD, Claus Henn B. Correlates of Non-Persistent Endocrine Disrupting Chemical Mixtures among Reproductive-aged Black Women in Detroit, Michigan. *Chemosphere.* 2022;28:134447. PMCID: PMC9215202.

Schildroth S, Wise LA, Wesselink AK, De La Cruz P, Bethea TN, Weuve J, Fruh V, Botelho JC, Sjodin A, Calafat AM, Baird DD, Claus Henn B. Correlates of Persistent Chemical Mixtures among Reproductive-aged Black Women. *Environmental Science and Technology.* 2021;55(20):14000-14014. PMCID: PMC9215200.

Wise LA, Wesselink AK, **Schildroth S**, Calafat AM, Bethea TN, Geller RJ, Coleman CM, Fruh V, Claus Henn B, Botelho JC, Harmon QE, Thirkill M, Wegienka GR, Baird DD. Correlates of Plasma Concentrations of Per- and Poly-fluoroalkyl Substances among Reproductive-aged Black Women. *Environ. Res.* 2021;203:111860. PMCID: PMC8616815.

Under review (selected):

Schildroth S, Wesselink AK, Bethea TN, Claus Henn B, Friedman A, Fruh V, Coleman CM, Lovett SM, Vines AI, Sjodin A, Botelho JC, Calafat AM, Wegienka G, Weuve J, Baird DD, Wise LA. A Prospective Cohort Study of Persistent Endocrine Disrupting Chemicals and Perceived Stress. *Under Review at American Journal of Epidemiology.*

Schildroth S, Bethea TN, Wesselink AK, Friedman A, Fruh V, Calafat AM, Wegienka G, Gaston S, Baird DD, Wise LA, Claus Henn B. Personal Care Products, Socioeconomic Status, and Endocrine Disrupting Chemical Mixtures in Black Women. *Under Review at Environmental Science and Technology.*

ORAL PRESENTATIONS (selected)

Schildroth S et al. 2023. Associations of Serum Per- and Polyfluoroalkyl Substances with Risk of Spontaneous Abortion in a Prospective Cohort of North American Women. *Society for Epidemiologic Research, Portland, OR.*

Schildroth S et al. 2023. Mediation Analysis in Chemical Mixtures Research: Application to Studies of Neurodevelopment and Reproductive Health. *NIEHS Mixtures Working Group, online.*

Schildroth S et al. 2022. Early Life Manganese Exposure is Associated with Attention-related Behaviors in Italian Adolescents: Evidence of Critical Periods of Susceptibility. *International Society for Exposure Science, Lisbon, Portugal.*

Buckley L, Grady S, **Schildroth S. 2021.** Novel Methods in Exposure Science. *Gijs Van Seventer Environmental Health Seminar, Boston MA*

Schildroth S & Webster T. 2020. Co-exposure Amplification Bias (CAB) in Chemical Mixture Models. *Powering Research through Innovative Methods for Mixtures in Epidemiology (PRIME) Program annual grant meeting.*

SERVICE AND STEM OUTREACH (SELECTED)

Boston University, Boston, MA

Antiracism Committee, *board member, Department of Epidemiology* 2023 (ongoing)
First Gen Mentor, *mentor* 2023 (ongoing)

Boston University School of Public Health
Office of the Dean
715 Albany Street
Boston, Massachusetts 02118

BOSTON UNIVERSITY

October 31, 2023

International Society for the Study of Women's Sexual Health
ISSWSH Scholars in Women's Sexual Health Research Grant

Dear Review Committee Members,

It is my pleasure to write this letter of recommendation in support of Dr. Samantha Schildroth and Julia Bond's application, titled "**Per- and Polyfluoroalkyl Substances (PFAS) and Female Sexual Function in a North American Cohort**", to the International Society for the Study of Women's Sexual Health (ISSWSH) Scholars in Women's Sexual Health Research Grant.

Dr. Schildroth and Ms. Bond propose to conduct the first study investigating the association of PFAS, a class of endocrine disrupting chemicals, with female sexual health, including individual domains (desire, lubrication, orgasm) of sexual function, in the Pregnancy Study Online (PRESTO). The research outlined in this proposal is the first of its kind and will further the current understanding of female sexual dysfunction, which has significant clinical and public health implications.

Dr. Schildroth (Post-Doctoral Research Associate) and Ms. Bond (Doctoral Candidate) are both members of the Department of Epidemiology at the Boston University School of Public Health (BUSPH) and have exceptional records of scholarly research. As a Professor of Environmental Health and the Associate Dean for Research and Faculty Advancement at BUSPH, I have known Dr. Schildroth since her time as a doctoral student in the Department of Environmental Health, where she stood out as an outstandingly motivated young investigator. In her time as a PhD student, and now as a Post-Doctoral Research Associate, she has consistently led novel research investigating chemical exposures in relation to women's and children's health. Dr. Schildroth has co-authored numerous peer-review publications, presented her work at international conferences, successfully completed an F31 NIH Predoctoral Fellowship, and recently submitted a K99/R00 Pathway to Independence Award focusing on PFAS exposure and women's health.

Ms. Bond has similarly stood out among her peers as an exceptionally bright, motivated, and rigorous researcher. She currently holds an F31 NIH Predoctoral Fellowship supporting her dissertation work in the PRESTO cohort and has a strong publication record. Moreover, she has shown immense skill and expertise in sexual health research, recently presenting her research on self-reported female orgasm and time to pregnancy at the Society for Perinatal and Pediatric Research. Ms. Bond leads sexual health research in the PRESTO cohort and has used these data to publish multiple epidemiologic studies, including a recent paper in *The American Journal of Obstetrics and Gynecology* about female sexual dysfunction in the preconception period (PMID: 37001576).

The culmination of Dr. Schildroth and Ms. Bond's expertise in investigating PFAS exposure and female sexual health, respectively, will ensure their successful completion of the proposed aims. Importantly, despite the strong biologic plausibility, no prior studies have investigated the potential role of PFAS exposure on female sexual dysfunction. The results will have the potential to influence both clinical practice and policies aimed at reducing PFAS exposure.

In summary, Dr. Schildroth and Ms. Bond are exceptionally rigorous junior investigators; their complementary skillsets in environmental epidemiology and sexual health research will support a synergistic collaboration leading to the successful completion of this award. I am confident that this proposed research will produce novel and relevant findings, and I am pleased to confer my highest recommendation on behalf of their application.

Thank you for your consideration.

Sincerely,



Michael D. McClean, ScD
Associate Dean for Research and Faculty Advancement
Professor of Environmental Health
Boston University School of Public Health

Boston University School of Public Health
715 Albany Street
Boston, Massachusetts 02118

BOSTON UNIVERSITY

International Society for the Study of Women's Sexual Health
ISSWSH Scholars in Women's Sexual Health Research Grant

October 31, 2023

Dear Review Committee Members,

It is with great enthusiasm that I write this letter in support of Dr. Samantha Schildroth and Julia Bond's application, entitled "Per- and Polyfluoroalkyl Substances (PFAS) and Female Sexual Function in a North American Cohort," to the International Society for the Study of Women's Sexual Health (ISSWSH) Scholars in Women's Sexual Health Research Grant. I am the Principal Investigator of Pregnancy Study Online (PRESTO), the cohort study that will be leveraged for this research proposal. Ms. Bond has led the collection and analysis of sexual health data in PRESTO since the launch of the Sexual Health and Well-Being Questionnaire (SHWQ) in 2019. Since the introduction of the SHWQ, we have collaborated on two publications (PMIDs: 37001576, 36182572), multiple conference presentations, and several ongoing analyses using these data. The SHWQ has provided a breadth of new research opportunities, including the aims of this proposal, and has inspired our research group to incorporate sexual health research into the broader investigative goals of the PRESTO team. Notably, the research aims proposed by Dr. Schildroth and Ms. Bond are extremely novel: no prior study has investigated the influence of endocrine disrupting chemicals on female sexual health. I am thrilled about the potential impact of the work proposed in this application.

Under this award, Dr. Schildroth and Ms. Bond propose to investigate associations between PFAS, a pervasive class of endocrine disrupting chemicals, and female sexual health. Additionally, they will evaluate individual domains of sexual function (e.g., orgasm, lubrication) in relation to biomarker concentrations of PFAS, which is itself a very novel approach. This research has the potential to provide critical insights into the influence of environmental stressors on female sexual and reproductive health, which has significant public health and policy implications.

I can attest to the fact that Dr Schildroth and Ms. Bond are an outstanding team to conduct this research, having worked extensively with each of them. Dr. Schildroth is a Postdoctoral Research Associate in the Department of Epidemiology and is actively leading several analyses investigating chemical exposures, perinatal, and postpartum health in PRESTO. Though she is new to the PRESTO team, having joined our research group in March of 2023, she has already proved herself an invaluable member of our team with expertise in chemical exposures, environmental epidemiology, and advanced statistical methods. I have worked with Dr. Schildroth since her time as a PhD student, where she led multiple projects in the Study of the Environment, Lifestyle, and Fibroids (of which I am a co-PI) related to environmental exposure, chemical mixtures, and psychosocial health. Dr. Schildroth's track record as a scholar is exceptional, having published many peer-reviewed publications in high-impact journals across disciplines; she has emerged as a leader on the PRESTO research team.

Boston University School of Public Health
715 Albany Street
Boston, Massachusetts 02118

Ms. Bond is a PhD Candidate and has been a member of the PRESTO research team since she joined the Department of Epidemiology at Boston University in 2019. In addition to leading the data collection and analysis of PRESTO's sexual health data, she has also led numerous impactful research projects spanning a wide range of topics, including oral health, sleep duration, and employment scheduling. Ms. Bond has demonstrated substantial leadership in the PRESTO research team; she further has a phenomenal publication record, and her dissertation research is currently supported by a National Institute of Health Ruth L. Kirschstein F31 Predoctoral Fellowship. She is an excellent scholar with capabilities well beyond her educational stage, and I consider her to be the sexual health expert in our PRESTO research group.

Dr. Schildroth and Ms. Bond each have demonstrated unique expertise in chemical exposures and female sexual health, respectively; their collaboration on this project has already proven synergistic, and I have no doubt that their fruitful collaboration will lead to the successful completion of the aims in this proposal. It is my pleasure to provide my strongest support for this application from these two extremely promising junior investigators. As the Principal Investigator of the PRESTO cohort, I welcome the opportunity to expand our portfolio of sexual health-related research projects and certify that this project will be implemented as described in the proposal. The proposed work is novel, innovative, and has the potential to contribute broadly to the etiologic understanding of female sexual function, as well as efforts to understand the health implications of wide-spread human exposure to environmental chemicals.

I appreciate your consideration.

Sincerely,

Lauren Wise

Lauren A Wise, ScD
Professor of Epidemiology
Boston University School of Public Health

KATHARINE O. WHITE, MD, MPH
Vice Chair of Academics
Director, Fellowship in Family Planning
Department of Obstetrics and Gynecology
Boston Medical Center

Associate Professor
Department of Obstetrics and Gynecology
Boston University Chobanian & Avedisian School of Medicine

International Society for the Study of Women's Sexual Health

ISSWSH Scholars in Women's Sexual Health Research Grant

September 30, 2023

Dear Review Committee Members,

I write to share my wholehearted support and strongest recommendation for Dr. Samantha Schildroth and Julia Bond's application, title "**Per- and Polyfluoroalkyl Substances (PFAS) and Female Sexual Function in a North American Cohort**," to the International Society for the Study of Women's Sexual Health (ISSWSH) Scholars in Women's Sexual Health Research Grant. Dr. Schildroth and Ms. Bond plan to conduct cutting-edge research investigating PFAS, a class of endocrine disrupting chemicals, and female sexual health. Importantly, they propose to evaluate individual domains of sexual function (e.g., orgasm, lubrication) in relation to PFAS exposure, which has the potential to generate novel insights into the biological underpinnings of women's sexual function. As a clinician-researcher with expertise in sexual wellness, I believe that the insights generated by this work will contribute towards a better understanding of certain types of sexual dysfunction and will help clinicians to support and treat their patients. Additionally, the work has important public health and policy implications in terms of understanding the human health consequences of PFAS exposure on the female reproductive tract.

Dr. Schildroth (Post-Doctoral Research Associate) and Ms. Bond (Doctoral Candidate) are an excellent research team. I have had the pleasure of working with Ms. Bond for four years since she approached me to collaborate on the development of the Sexual Health and Wellbeing Questionnaire to introduce to Pregnancy Study Online (PRESTO). She is an incredibly motivated, diligent, and creative researcher who has demonstrated skills well above her educational stage. She led the development of this questionnaire and numerous analyses using these data, many of which have resulted in peer-reviewed publications in high-impact journals. She is an exceptional scholar who will undoubtedly continue to contribute to the field of sexual health research at a high level. I recently began working with Dr Schildroth in the context of this project. She is skilled at crafting and implementing rigorous scientific questions, as well as effectively collaborating with researchers from other fields and communicating technical chemical data. Dr. Schildroth's outstanding publication record speaks for itself; she is a talented, motivated scientist.

I have absolutely no doubt that together Dr. Schildroth and Ms. Bond will effectively conduct the novel research proposed in this application. This research project has wide-ranging implications in terms of generating novel insights into environment influences on domain-specific elements of women's sexual function. As the Review Committee will

undoubtedly understand, research efforts investigating female sexual function lag well behind those focused on male sexual function, particularly in terms of the importance of environmental exposures, like PFAS. This research project represents an important first step towards building a body of research focused on the etiologic implications of environmental exposures on female sexual function.

In summary, Dr. Schildroth and Ms. Bond are truly exceptional junior investigators. Working together, each contributing unique skills, this project has the potential to initiate a novel and broadly impactful line of research. I am confident that they will be able to successfully complete the research as proposed, and, further, that the project will result in important findings that have far reaching implications. It is my pleasure to provide my strongest recommendation in support of this proposal.

Sincerely yours,



Katharine O'Connell White, MD, MPH