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Environmental impacts on women's health disparities and reproductive health: advancing environmental health equity in clinical and public health practice

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Environmental impacts on women's health disparities and reproductive health: advancing environmental health equity in clinical and public health practice

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Editorial: Environmental impacts on women's health disparities and reproductive health: advancing environmental health equity in clinical and public health practice

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Editorial on the Research Topic
Environmental impacts on women's health disparities and reproductive health: advancing environmental health equity in clinical and public health practice

Cumulative impacts of chemical and social factors challenge progress toward achieving equity and justice in the context of environmental exposures and somatic health, including reproductive well-being. As we work toward achieving justice in women's reproductive health, this Research Topic highlights studies that are designed to closely examine upstream factors to identify why disparate exposures and disproportionate adverse reproductive outcomes exist. Our intention for this editorial is to reiterate our continuing commitment to achieving environmental health equity and to call attention to the research impacts and lessons learned by the presenters at the National Institute of Environmental Health Sciences (NIEHS)-hosted workshop, "Environmental Impacts on Women's Health Disparities and Reproductive Health", held on 27–28 April 2022 (https://www.niehs.nih.gov/news/events/pastmtg/2022/ehdworkshop2022/index.cfm). The purpose of the workshop was to place emphasis on research examining the effects of chemical and non-chemical stressors on adverse maternal and fetal health outcomes, to discuss diseases specific to women and individuals assigned female at birth, and to assess the role of racial and ethnic disparities in environmental exposures.

We strongly encourage readers to thoughtfully consider the novel concepts proposed for conducting health disparity research to achieve health equity and environmental justice, the lessons learned, and the general knowledge gleaned from the workshop presentations, some of which are included in this Research Topic.

- To address health disparities, achieve health equity, and advance environmental justice it is essential that the research begins to closely examine upstream factors to identify why these disparate exposures and disproportionate adverse reproductive outcomes exist.
- To elucidate the role of the environment in reproductive health disparities, a shift is needed from the traditional concept of 'environment' to a contemporary lens that includes the built environment and place-based factors.
- Increasing research efforts toward translational environmental epidemiologic research frameworks, transdisciplinary community driven, comprehensive research that leads to action and informs policy will advance environmental health equity.
- The development of novel measures or the use of existing measures that other disciplines utilize to assess structural racism will be key as we continue to work toward achieving justice in reproductive health. Additionally, this means that there is room to be creative and inclusive of qualitative and mixed-method approaches to achieving equity in reproductive health.
- Most importantly, and often overlooked, is the need to create equal access to tools and opportunities to improve environmental health equity.

The selected papers in this Research Topic demonstrate the commitment that many in the field of environmental health sciences have made toward elucidating the intersecting systems that impact and marginalize many racial and ethnic populations at various stages of their life course. Specific examples of articles in this Research Topic include an assessment of racial/ethnic and educational differences in menstrual and intimate care product use among people who menstruate; a causal mediation analysis to examine whether racial and ethnic disparities in preterm birth may be partially explained by exposure to a class of chemicals used as flame retardants in the United States (polybrominated diphenyl ethers); the place-based impacts of environmental justice burdens (i.e., a neighborhood characterized by both increased environmental burden and socioeconomic deprivation) on racial disparities in spontaneous preterm birth; and investigating racial/ethnic differences in household food security status in the context of cardiometabolic health among pregnant people in the United States. Furthermore, some work focused on reproductive outcomes in offspring—racial disparities in the association between gestational exposure to a mixture of phthalates and fetal genital development.

We encourage readers of this special issue to consider their commitment to pursuing environmental and reproductive health equity. Specifically, to be intentional with the design of research studies to carefully consider the role of limited educational and employment opportunities; reduced residential options and hazardous residential characteristics; systemic barriers (e.g., redlining) and discriminatory policies (e.g., urban sprawl) that may increase the risk of adverse reproductive health outcomes.

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MS: Conceptualization, Writing – original draft, Writing – review & editing. KR: Conceptualization, Writing – original draft, Writing – review & editing. DD: Conceptualization, Supervision, Writing – original draft, Writing – review & editing.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Examining differences in menstrual and intimate care product use by race/ethnicity and education among menstruating individuals

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Introduction: United States consumers spend over two billion dollars a year on intimate care products. These products, along with scented menstrual products, are marketed for odor control, perceived "freshness," and vaginal/vulvar cleanliness. However, these scent-altering products may increase exposure to carcinogenic and endocrine-disrupting chemicals. Prior research has not adequately characterized demographic differences in product use. The objective of our study is to examine racial/ethnic and educational differences in menstrual and intimate care product use among people who menstruate.

Methods: We pooled data from two US-based cross sectional studies to examine demographic characteristics and product use in 661 participants aged 18–54 years. Participants reported use of scented and unscented menstrual products (tampons, sanitary pads, and menstrual cups) and intimate care products (vaginal douches, sprays, wipes, and powders). We examined differences by race/ethnicity and education using log-binomial regression and latent class analysis (LCA), which can identify groups based on product use patterns.

Results: Our sample was 33.4% Black, 30.9% Latina, 18.2% White, and 16.2% another identity. Approximately half the population had a bachelor's degree or more; 1.4% identified as transgender and 1.8% as non-binary. In adjusted models, scent-altering products (i.e., scented menstrual and intimate care products) were more likely to be used by those with less formal education ($p < 0.05$). Unscented menstrual products were more likely to be used by those with more formal education. Compared to Black participants, White participants were more likely to use unscented tampons and menstrual cups and less likely to use douches and wipes ($p < 0.05$). Using LCA we identified two groups: one more likely to use scent-altering products, and a second more likely to use unscented menstrual products. Less education and older age, but not race/ethnicity, was significantly associated with membership in the group more likely to use scent-altering products. While sex/gender composition did not statistically vary across groups, all non-binary participants fell in the unscented menstrual product group.

Discussion: Lower educational attainment was consistently associated with greater use of scent-altering menstrual and intimate care products. Future research should examine associations between body odor stigma, product use, and health risks at intersections of race, class, and gender.

KEYWORDS

personal care products, health disparities, women's health, endocrine disruptors, feminine care, feminine hygiene, chemical exposures, fragrance

Introduction

The feminine hygiene industry has been shaped by social, economic, and historical forces, which continue to impact contemporary product use. In the early to mid-20th century, there was rapid expansion in the commercial market for menstrual management. As indoor plumbing and disposable menstrual products became widely available, social expectations of bodily hygiene shifted to encourage the use of products that were marketed for odor control (1). Through curated advertisements that centered White, wealthy, and educated women, product manufacturers linked these "hygiene norms" with social mobility and privilege. The fear of stigma from body odor, and consequent menstrual and intimate care product use, was heightened after World War II when women entered male-dominated occupational settings (2). Adherence to these socially constructed "hygiene norms" was perceived as crucial to gaining access to professional opportunities, particularly for marginalized populations.

Today, sales of menstrual and intimate care products in the US are estimated at $3 billion dollars annually (3), and the global market is anticipated to reach $60 billion by 2030 (4). Yet, personal care products marketed for use near vaginal and vulvar tissues remain an understudied risk factor for reproductive health. Products of concern include: (1) menstrual products (e.g., tampons, sanitary pads, menstrual cups), which are used to manage menstrual bleeding, and (2) intimate care products (e.g., douches, vulvar sprays, wipes, powders), which are marketed for odor control and to help users attain perceived vaginal/vulvar cleanliness and freshness (2, 5, 6). Additionally, scented tampons and pads are marketed for both menstrual bleeding management and odor control. While product manufacturers commonly refer to menstrual and intimate care products as "feminine hygiene products" or "feminine care products," we choose to use language that is inclusive of all menstruators regardless of gender identity. Additionally, we choose not to use the word "hygiene" to describe this product category since many of these products are marketed to medicalize normal bodily functions and create unnecessary concerns about cleanliness.

Menstrual and intimate care product use is relevant to population health because these products may contain one or more ingredients associated with allergies, asthma, cancer, endocrine disruption, and/or poor pregnancy outcomes. **Table 1** summarizes the intended use and ingredients of concern of common products. There are now multiple studies that have quantified chemicals of concern in these products including asbestos, dioxins, per- and poly-fluoroalkyl substances, phthalates, parabens, metals, pesticides, volatile organic compounds (VOCs), and fragrance chemicals (e.g., alpha-isomethyl ionone, benzyl salicylate, hexyl cinnamaldehyde, linalool and piperonal) (13, 14, 22, 28, 34). Moreover, these products may represent an important source of human chemical exposure because they are used on highly permeable tissues that have high uptake rates and sensitivity to chemicals (34). Early data suggest that products marketed for odor control may be of particular concern. For example, scented tampons have higher concentrations of certain VOCs than unscented tampons, and the amount of fragrance chemicals leached from scented tampons has been demonstrated to exceed health protective thresholds for allergic reactions/skin sensitization (29, 35). Another study found that estimated cancer risks from VOCs exceeded health protective reference levels for sprays, washes, and powders (16).

Two separate analyses of nationally representative National Health and Nutrition Examination Survey (NHANES) data found that the practice of vaginal douching was associated with increased exposure to certain phthalates and VOCs, with evidence of positive dose-response (e.g., higher biomonitoring levels among those who douche more frequently) (22, 36). Epidemiologic studies suggest that douching may be associated with pelvic inflammatory disease (37), ectopic pregnancy (23), bacterial and fungal vaginosis (24, 25, 38), and ovarian cancer (39), and genital use of talc-based powders may be a risk factor for ovarian cancer (40). Furthermore, women who reported both douching and genital talc powder use have increased risks of uterine leiomyoma (fibroids), ovarian cancer, and pelvic inflammatory disease than those who only reported using one product, suggesting that cumulative product use may be critical to understanding health risks (39, 41). Despite the evidence of adverse health effects, these products remain poorly regulated with fragmented government oversight. In the USA, the US Food and Drug Administration (FDA) regulates tampons, menstrual pads, menstrual cups, and douching bag apparatuses and nozzles as medical devices whereas douching solutions, sprays, wipes, and powders are regulated as cosmetics (3).

Motivations underlying product choice and behavior are complex and driven by both proximate factors such as peers and family recommendations as well as more distal factors such as intersectional discrimination (e.g., combined discrimination from structural racism, sexism, and classism) (42, 43). In our prior scholarship, we argued that the greater uses of douches among Black women compared to White women may be a consequence of odor discrimination and contribute to the environmental injustice of beauty (43). Historically, perceived mal-odor of African American women by white enslavers has been linked with assertions of sexual immorality and to justify their oppression (44). Later, negative olfactory stereotypes and odor discrimination continued as Black women who failed to adhere to the middleclass archetype of a controlled and disciplined body were denied access to educational and occupational opportunities (1). As a result, Black women were more aggressively marketed products like douches with messaging that encouraged self-consciousness of potential vaginal and vulvar odors and implied healthfulness of product use, despite clinical guidance against douching (44, 45). This practice became embedded within families as a cultural norm, and now persist outside of marketing efforts (44). NHANES data from 2001 to 2004 suggest that more Black women use douches and other intimate care products than white or Mexican American women (36), and the practice of douching is more common among those with less education across all racial/ethnic groups (46). However, current demographic variations in product use are poorly understood

TABLE 1 Overview of menstrual and intimate care products: product type, category, indicated reasons of for use, and chemicals of concern reported in product types.

	Category	Product description	Chemicals of concern
Tampons	Menstrual	Inserted into the vagina to collect menstrual fluids	Parabens (7)
			Triclosan (7)
			Dioxins & Furans (8–11)
			Pesticides (12)
			PAHs[a] (11)
			Phthalates (7, 13, 14)
			Metals (15)
			VOCs[b] (16, 17)
			Fragrances (14, 18)
Pads	Menstrual	Placed on underwear to collect menstrual fluids and other vaginal secretions	Parabens (8, 14)
			Chlorine (19)
			Triclosan (7)
			Dioxins & Furans (10, 20, 21)
			Biocides (11, 20)
			PAHs (11, 20)
			Phthalates (1, 5, 7, 11, 13, 14, 17, 22–27)
			Fragrances (11, 14, 18)
			VOCs (16, 28, 29)
Menstrual cups	Menstrual	Inserted into the vagina to collect menstrual fluids	VOCs (30)
			Phthalates (30)
			PAHs (30)
			PFAS[c] (31)
Douches	Intimate care	Inserted into the vagina or anus to cleanse and prevent odor	Phthalates (32)
			VOCs (22)
			Fragrances (32)
Sprays	Intimate care	Sprayed onto genitals or underwear to reduce odor	VOCs (16)
			Phthalates (13)
			Parabens (13)
			Fragrances (18)
Powders	Intimate care	Sprinkled onto genitals, underwear, or menstrual products to absorb moisture and reduce odor	Talc (33)
			VOCs (13)
			Phthalates (27)
			Parabens (13) 11/2/23 2:20:00 PM
			Fragrances (18)
			Asbestos (33)
Wipes	Intimate care	Wiped on genitals or anus freshen up or removes odor	VOCs (14)
			Phthalates (13)
			Parabens (13)
			Ethanolamines (14)
			Fragrances (14, 18)

[a]Polycyclic aromatic hydrocarbon.
[b]Volatile Organic Compounds.
[c]Per- and polyfluoroalkyl substances.

given the expansion of the market, and the growth in public awareness about toxic chemicals in personal care products.

Given the socio-historical context, the unique route of chemical exposure, and the lack of regulatory oversight, the objective of our study is to evaluate racial/ethnic and educational differences in use of menstrual and intimate care products among menstruating individuals from two US-based cohort studies. While we examine a range of products, our particular emphasis is on scent-altering products that are marketed for odor control, perceived "freshness", and cleanliness. Our secondary objective is to examine demographic differences in motivations for product use. We also present descriptive data for non-binary and transgender populations.

Methods

Study population

Our analysis combines data from two separate studies of adults aged 18–54 years who reported menstruating in the past year. The Taking Stock Study (TSS) is a community-based participatory research initiative between Occidental College, Black Women for Wellness, local *promotores de salud* (community health workers), Silent Spring Institute, and Columbia University Mailman School of Public Health that examines racial/ethnic differences in consumer product use with a focus on Black women and Latinas using community-generated research questions and collaborative

methods of inquiry. We disseminated the TSS survey online to adult (≥18 years) women living in California of all races and ethnicities via online outreach, social media, a Qualtrics panel, and community networks. A detailed description of survey development and dissemination has been described elsewhere (47). The survey was available through Qualtrics between January 2019 and March 2020 in both English and Spanish and completed by 630 participants. Of the 630 participants, we excluded: 15 respondents who did not provide information about menstruating in the past year, and 81 respondents who reported not menstruating in the past year. Thus, data from 534 TSS survey participants are used in the current study. Protocols, including the survey, were reviewed, and approved by Occidental College's Institutional Review Board.

The second study, Fibroids Observational Research on Genes, and the Environment (FORGE), seeks to understand environmental, molecular, and social-structural determinants of gynecologic health conditions, with a specific emphasis on fibroids. In the FORGE study, we recruited and consented individuals who were seeking medical evaluation with the Minimal Invasive Gynecologic Surgery division of the Medical Faculty Affiliates in Washington D.C between 2018 and 2021. We recruited three different groups: (1) individuals who intended to undergo hysterectomy for treatment of non-cancerous, gynecologic conditions (e.g., fibroids, endometriosis); (2) individuals who intended to undergo hysterectomy for gender dysphoria; and (3) individuals newly diagnosed with fibroids. All eligible participants were nonpregnant, premenopausal, and ≥18 years of age. Of the 157 participants enrolled in FORGE, we excluded: 12 participants who did not provide information about menstruating in the past year, 17 participants who reported not menstruating in the past year, and 1 participant who was over 54 years of age. Thus, data from 127 FORGE participants were used in the current study. FORGE study protocols and survey instruments were approved by The George Washington University Institutional Review Board.

Menstrual and intimate care product use

Both studies used a similar survey design and structure to capture information about menstrual and intimate care product use. Both studies asked participants about their use of three menstrual products (tampons, sanitary napkins/pads, and menstrual cups) and four intimate care products (douches, feminine sprays, feminine powders, and feminine wipes). If the participant reported using a product, they were then asked how frequently they used the product in the past year (less than once a month; 1–3 times a month; during menstrual cycle; 1–5 times a week; 6 or more times per week; and more than once per day). If participants reported using tampons or sanitary pads, they were asked whether their products were scented or unscented. Frequency of menstrual cup use was asked in FORGE but not TSS.

We asked participants about factors that influence their product selection. Questions about participants' product selection influences were asked differently in the two studies. In FORGE, we asked participants about what influences their product use in a single question. In TSS, we asked two questions: (1) what characteristics are important when choosing a product and (2) where do you go to learn more about products.

Data harmonization

In addition to questions about product use, we asked several questions about the participants' demographics. All participants self-identified their race/ethnicity and gender, with an option not to disclose. Data from TSS and FORGE were harmonized to create a unified dataset for the analysis. In general, FORGE data were adjusted to match the survey structure and available responses from TSS survey prior to merging the data. For example, FORGE participants who identified as "Woman" were reported here as "Female" to be in parallel with the identities reported by TSS participants (and because all FORGE participants were assigned female at birth). Age was asked differently in the two studies; TSS participants selected an age category (i.e., 18–24 years, 25–34 years, 35–44 years, and 45–54 years) whereas age was calculated for FORGE participants based on their date of birth abstracted from medical records. As a result, age categories are used in the current analysis. We categorized self-identified race/ethnicity as non-Hispanic Black/African American ("Black"), Hispanic/Latinx ("Latinx"), non-Hispanic White/Caucasian ("White"), or some other identity. Latinx includes any participant who identified as Latinx even if they also reported another racial/ethnic identity. Some other identity captures those who identify with racial/ethnic groups other than Black, White, or Latinx (e.g., Asian, American Indian) as well as multiracial participants. We also asked participants about their level of formal education. We categorized self-reported formal education attainment into three categories: ≤high school graduate or GED credential (abbreviated as ≤high school diploma), some college, technical school or associate degree (abbreviated as some college), or ≥bachelor's degree. Lastly, we categorized self-identified sex/gender into three categories: female, transgender, and non-binary.

Data analysis

We summarized product use (yes vs. no) by participant demographics and evaluated differences in product use by each demographic variable using the Fisher's exact test. We used frequency of use data to determine whether participants used products largely during menstruation or as a more regular practice. To summarize and compare the frequency of product use, we collapsed the frequency data into three categories: occasionally (e.g., less than once a month or 1–3 times a month), during menstrual cycle, or regularly (e.g., 1–5 times a week, 6 or more times per week, or more than once per day). We assessed concordance in product use for each pair of products using the phi coefficient. We *a priori* identified race/ethnicity, education, age, sex/gender, and study (FORGE vs. TSS) as important covariates. To evaluate the association between product use and each covariate, we used relative risk (log-link) binomial

regression models. We first modeled each covariate of interest and product use (outcome variable) separately. We then combined education, race/ethnicity, age, and study within a multivariate model. Due to the small sample size of non-binary and transgender participants, we only examined differences in product use by sex/gender using descriptive statistics. We reported relative risks for each covariate from the mutually adjusted models. We used the fully adjusted log-binomial models to predict probabilities of use of each product for each category of race/ethnicity and education.

We used latent class analysis (LCA) to identify groups of participants with similar product use patterns, using an approach similar to Wang et al. (48) We used multiple criteria to assess the fit of the LCA model, including Bayesian Information Criterion and minimum class size (at least 10%). We selected the most parsimonious model, which was a model with two latent classes. We then categorized the two classes based on the probability of use of different products. Next, we summarized demographic characteristics for each latent class and assessed differences using Fisher's exact test. We further examined determinants of latent class assignment membership by regressing race/ethnicity, education, study, and age against the predicted class assignment in a multivariate model. Lastly, we examined differences in influences on product selection by LCA class assignment using Fisher's exact test.

We conducted sensitivity analyses to evaluate the relationship between educational attainment and product use in the subset because many population health and census studies only examine educational attainment as a risk factor among those who have completed their education and most US adults have completed their formal education by 25 years of age (49, 50). To explore the relationship between formal education and product use, we reran all mutually adjusted log-binomial models for individual product use among those ages 25–54. Additionally in this subset, we re-ran the LCA model and re-examined differences in probability of being in a certain LCA class by all demographic variables. In the case of scented tampon and scented pad use, 13 and 31 participants, respectively, were unsure about whether the products they used were scented. In the main analysis, we included unsure respondents with the "no" respondents. As a sensitivity analysis, we removed those who were unsure from the analysis. Since the results from the two analyses were similar, we only show results from models where the unsure participants are grouped with the "no" participants for scented menstrual product use.

Results

Descriptive characteristics of study population and product use

Our study population consisted of 661 participants aged 18–54 years (Table 2). Approximately 80% of the population were from TSS ($N = 534$) and 20% was from FORGE ($N = 127$). TSS participants were younger than FORGE participants, with 59.3% of TSS participants aged 18–34 years compared 12.5% of FORGE participants. Most respondents identified as female ($n = 640$); however, the population also included a small sample who identified as transgender ($n = 9$ or 1.4%) or non-binary ($n = 12$ or 1.8%). The most common racial/ethnic group was Black (33.4%) and followed by Latinx (30.9% of overall). Racial/ethnic composition varied by study with Black participants being the largest subpopulation in FORGE and Latinx participants being the largest subpopulation in TSS. Across both studies, 3.5% did not complete high school, 16.2% had a high school diploma or equivalent, 34.2% reported some college or an associate/technical degree, and 45.0% reported ≥bachelor's degree. The FORGE population had more formal education than the TSS population.

TABLE 2 Demographic characteristics of study participants by study (number and %).

	FORGE ($N = 127$)	TSS ($N = 534$)	Overall ($N = 661$)
Age (years)			
18–24	4 (3.1%)	185 (34.6%)	189 (28.6%)
25–34	12 (9.4%)	132 (24.7%)	144 (21.8%)
35–44	61 (48.0%)	154 (28.8%)	215 (32.5%)
45–54	50 (39.4%)	63 (11.8%)	113 (17.1%)
Race			
Black	88 (69.3%)	133 (24.9%)	221 (33.4%)
Latinx	6 (4.7%)	198 (37.1%)	204 (30.9%)
White	27 (21.3%)	93 (17.4%)	120 (18.2%)
Some other identity	6 (4.7%)	101 (18.9%)	107 (16.2%)
Missing	0 (0.0%)	9 (1.7%)	9 (1.4%)
Education			
Less than high school diploma	5 (3.9%)	18 (3.4%)	23 (3.5%)
High school diploma/GED	16 (12.6%)	91 (17.0%)	107 (16.2%)
Some college	31 (24.4%)	166 (31.1%)	197 (29.8%)
Technical school/associate degree	4 (3.1%)	25 (4.7%)	29 (4.4%)
Bachelor's degree	32 (25.2%)	129 (24.2%)	161 (24.4%)
Graduate degree	35 (27.6%)	101 (18.9%)	136 (20.6%)
Missing	4 (3.1%)	4 (0.7%)	8 (1.2%)
Sex/gender			
Female	116 (91.3%)	524 (98.1%)	640 (96.8%)
Transgender	7 (5.5%)	2 (0.4%)	9 (1.4%)
Non-binary	4 (3.1%)	8 (1.5%)	12 (1.8%)

Unscented menstrual products were the most used products; 70.0% of participants reported using unscented pads and 47.0% reported using unscented tampons (Table 3). Menstrual cups were used by 11.0% of the population. Scented pads were used more commonly than scented tampons (10.0% vs. 4.7%). Among intimate care products, wipes were the most common (22.0% of participants), followed by douches (8.8%), sprays (6.8%), and powders (2.4%). Figure 1 shows frequency of product use among users. While menstrual products were most used during menstruation, some participants reported more frequent use. For example, one-third of scented pad users reported using these products regularly (i.e., at least once per week). Relatedly, 7.1% of unscented tampon users and 12.9% of scented tampon users reported using these products regularly. In general, intimate care products were used more regularly than menstrual products. For example, wipes, sprays, and powders were used regularly by 30%–40% of users. In contrast, douches were more likely to be used occasionally (i.e., less than three times a month) (Figure 1).

TABLE 3 Product use (number and %) by demographic characteristics.

	Unscented pads	Unscented tampons	Menstrual cups	Scented pads	Scented tampons	Wipes	Douches	Sprays	Powders
Total ($N = 661$)	466 (70.0%)	310 (47.0%)	73 (11%)	68 (10%)	31 (4.7%)	145 (22.0%)	58 (8.8%)	45 (6.8%)	16 (2.4%)
Age (years)									
18–24 ($N = 189$)	125 (61.1%)	99 (52.4%)	**28 (14.8%)***	13 (6.9%)	7 (3.7%)	**21 (11.1%)***	**5 (2.6%)***	**5 (2.6%)***	2 (1.1%)
25–34 ($N = 144$)	109 (75.7%)	69 (47.9%)	**24 (16.7%)***	10 (6.9%)	4 (2.8%)	**34 (23.6%)***	**11 (7.6%)***	**12 (8.3%)***	2 (1.4%)
35–44 ($N = 215$)	150 (69.8%)	94 (43.7%)	**18 (8.4%)***	30 (14.0%)	13 (6.0%)	**58 (27.0%)***	**25 (11.6%)***	**23 (10.7%)***	9 (4.2%)
45–54 ($N = 113$)	82 (72.6%)	48 (42.5%)	**3 (2.7%)***	15 (13.3%)	7 (6.2%)	**32 (28.3%)***	**17 (15.0%)***	**5 (4.4%)***	3 (2.7%)
Race/ethnicity									
Black ($N = 221$)	150 (67.9%)	**83 (37.6%)***	**13 (5.9%)***	22 (10.0%)	13 (5.9%)	**72 (32.6%)***	**34 (15.4%)***	22 (10.0%)	8 (3.6%)
Latinx ($N = 204$)	154 (75.5%)	**86 (42.2%)***	**19 (9.3%)***	22 (10.8%)	9 (4.4%)	**42 (20.6%)***	**17 (8.3%)***	15 (7.4%)	2 (1.0%)
White ($N = 120$)	76 (63.3%)	**84 (70.0%)***	**27 (22.5%)***	10 (8.3%)	4 (3.3%)	**16 (13.3%)***	**3 (2.5%)***	4 (3.3%)	5 (4.2%)
Some other identity ($N = 107$)	80 (74.8%)	**52 (48.6%)***	**11 (10.3%)***	13 (12.1%)	5 (4.7%)	**15 (14.0%)***	**4 (3.7%)***	4 (3.7%)	1 (0.9%)
Education									
≤High school diploma ($N = 130$)	**80 (61.5%)***	**42 (32.3%)***	**5 (3.8%)***	**23 (17.7)***	10 (7.7%)	34 (26.2%)	**23 (17.7%)***	**17 (13.1%)***	4 (3.1%)
Some college, technical school, or associate degree ($N = 226$)	**156 (69.0%)***	**104 (46.0%)***	**23 (10.2%)***	**25 (11.1%)***	11 (4.9%)	50 (22.1%)	**18 (8.0%)***	**17 (7.5%)***	9 (4.0%)
≥Bachelor's degree ($N = 297$)	**226 (76.1%)***	**164 (55.2%)***	**45 (15.2%)***	**19 (6.4%)***	9 (3.0%)	58 (19.5%)	**14 (4.7%)***	**9 (3.0%)***	3 (1.0%)
Sex/gender									
Female ($N = 640$)	455 (71.1%)	297 (46.4%)	**66 (10.3%)***	67 (10.5%)	31 (4.8%)	141 (22.0%)	55 (8.6%)	45 (7.0%)	16 (2.5%)
Transgender ($N = 9$)	5 (55.6%)	5 (55.6%)	**0 (0.0%)***	1 (11.1%)	0 (0.0%)	2 (22.2%)	22 (22.2%)	0 (0.0%)	0 (0.0%)
Non-binary ($N = 12$)	6 (50%)	8 (66.7%)	**7 (58.3%)***	0 (0.0%)	0 (0.0%)	2 (16.7%)	1 (8.3%)	0 (0.0%)	0 (0.0%)
Study									
TSS ($N = 534$)	373 (69.9%)	248 (46.4%)	59 (11.0%)	52 (9.7%)	23 (4.3%)	**107 (20.0%)***	**38 (7.1%)***	35 (6.6%)	13 (2.4%)
FORGE ($N = 127$)	93 (73.2%)	62 (48.8%)	14 (11.0%)	16 (12.6%)	8 (6.3%)	**38 (29.9%)***	**20 (15.7%)***	10 (7.9%)	3 (2.4%)

Differences by demographic variable evaluated using a fisher test, with statistically significant differences ($p < 0.05$) in bold*.

Use of scented menstrual products (tampons and pads) was positively correlated with use of intimate care products (douches, sprays, wipes and powders), whereas use of unscented menstrual products was negatively correlated with intimate care product use (**Supplementary Figure S1**).

Associations between sociodemographic variables and product use

Product use varied by age, race/ethnicity, education, and sex/gender, and study in unadjusted, bivariate analyses (**Table 3**). Menstrual cup use was highest among the 18–24 years age group and significantly declined in the older age groups. Whereas use of wipes, douches, and sprays generally increased with age. Use of four products (unscented tampons, menstrual cups, douches, and wipes) varied by race/ethnicity. Use of unscented tampons and menstrual cups were most common among White participants with 70.0% and 22.5% reporting use, respectively. Whereas use of wipes and douches was highest among Black participants with 32.6% and 15.4% reporting use, respectively. Most products significantly varied by education; unscented menstrual product use was more common among those with ≥bachelor's degree whereas scented menstrual and intimate care product use was generally more common among those with ≤high school diploma. There were also significant differences in menstrual cup use by sex/gender with most non-binary participants (58.3%) reporting use compared to 10.3% among other female participants. None of the non-binary or transgender participants reported using scented tampons, sprays, or powders.

In mutually adjusted log-binomial models, age, race/ethnicity, and education remained important determinants of product use (**Table 4**). Compared to 18–24 year age group, there was decreased risk of menstrual cup use among 35–44 year age group (relative risk (RR) = 0.49, 95% confidence intervals (CI): 0.26, 0.93) and 45–54 year age group (RR = 0.16, 95% CI: 0.047, 0.52). However, there was increased risks of use of scented pads, wipes, douches, sprays, and powders among older participants, particularly in the 35–44 year age group compared to 18–24 age group. Compared to Black participants, White participants had a 1.8 (95% CI: 1.5, 2.2) and a 3.0 (95% CI: 1.1, 5.6) relative risk of using unscented tampons and menstrual cups, respectively. Black

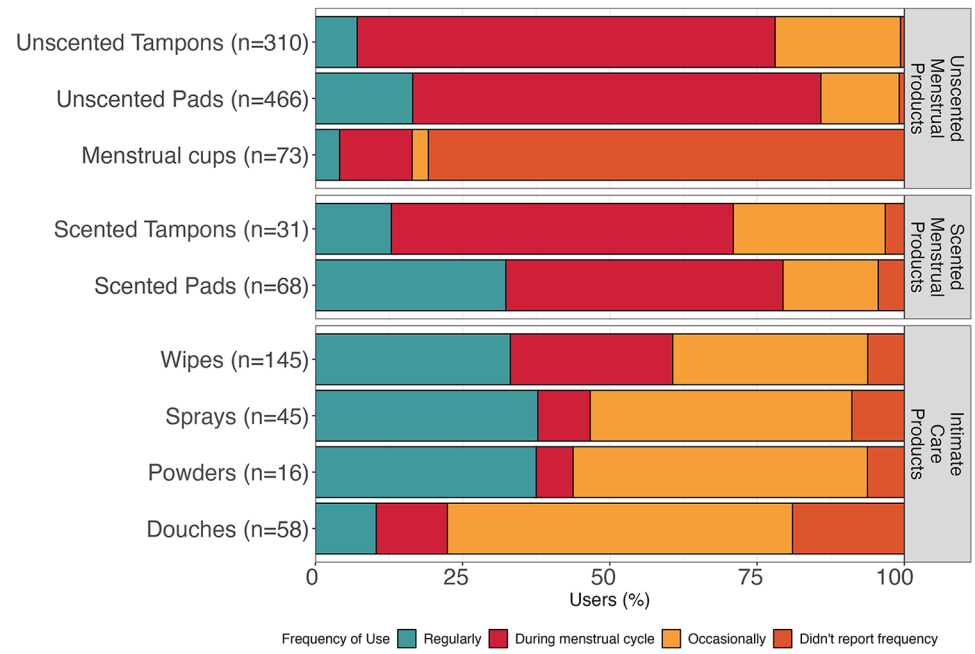

FIGURE 1
Reported frequency of use of menstrual and intimate care products for all participants. Occasionally indicates less than three times a month and Regularly at least once per week.

TABLE 4 Relative risks (95% CIs) from mutually adjusted log-binomial models.

Term	Unscented pads	Unscented tampons	Menstrual cups	Scented pads	Scented tampons	Wipes	Douches	Sprays	Powders
Age (years)									
18–24 ($N = 189$)	REF	REF	REF	REF	REF	REF	REF	REF	REF
25–34 ($N = 144$)	1.1 (0.95, 1.3)	**0.80 (0.66, 0.98)***	0.96 (0.55, 1.7)	1.4 (0.58, 3.2)	0.95 (0.27, 3.4)	**2.3 (1.4, 4)***	**3 (1.1, 8.7)***	**4.1 (1.4, 12)***	3.2 (0.43, 23)
35–44 ($N = 215$)	1 (0.89, 1.2)	**0.86 (0.72, 1)***	**0.49 (0.26, 0.93)***	**2.5 (1.3, 4.9)***	1.6 (0.6, 4.5)	**2.3 (1.4, 3.8)***	**2.9 (1.1, 7.9)***	**4.1 (1.5, 11)***	**7.8 (1.6, 38)***
25–54 ($N = 113$)	1 (0.87, 1.2)	0.87 (0.71, 1.1)	**0.16 (0.047, 0.52)***	**2.6 (1.2, 5.5)***	1.9 (0.61, 6)	**2.4 (1.4, 4.1)***	**4.4 (1.6, 12)***	1.5 (0.39, 5.8)	5.1 (0.81, 31)
Race									
Black ($N = 221$)	REF	REF	REF	REF	REF	REF	REF	REF	REF
Latinx ($N = 204$)	**1.2 (1, 1.3)***	1.3 (0.98, 1.6)	1.5 (0.75, 3)	1.1 (0.56, 2)	0.77 (0.3, 2)	**0.65 (0.45, 0.93)***	**0.5 (0.27, 0.94)***	0.54 (0.26, 1.1)	**0.2 (0.039, 0.98)***
White ($N = 120$)	0.96 (0.81, 1.1)	**1.9 (1.5, 2.3)***	**3 (1.6, 5.6)***	1.1 (0.54, 2.4)	0.7 (0.22, 2.2)	**0.53 (0.32, 0.87)***	**0.25 (0.076, 0.8)***	0.49 (0.17, 1.4)	1.5 (0.46, 4.5)
Some other identity ($N = 107$)	1.1 (0.96, 1.3)	**1.3 (1, 1.8)***	1.5 (0.68, 3.3)	1.6 (0.8, 3.4)	0.99 (0.32, 3)	**0.58 (0.34, 0.97)***	0.37 (0.13, 1.1)	0.48 (0.17, 1.4)	0.3 (0.036, 2.5)
Education									
≤High school diploma ($N = 130$)	**0.81 (0.69, 0.94)***	**0.53 (0.39, 0.7)***	**0.27 (0.11, 0.67)***	**3.1 (1.7, 5.6)***	**2.6 (1, 6.4)***	**1.5 (1, 2.2)***	**4.3 (2.3, 8.2)***	**5.3 (2.4, 12)***	**4.7 (1.1, 21)***
Some college, technical school, or associate degree ($N = 226$)	0.94 (0.84, 1.1)	**0.79 (0.67, 0.94)***	0.64 (0.38, 1.1)	**2.1 (1.1, 3.7)***	1.7 (0.69, 4.1)	**1.4 (1, 2)***	**2.1 (1.1, 4.2)***	**3.3 (1.5, 7.2)***	**5 (1.4, 18)***
≥Bachelor's degree ($N = 297$)	REF	REF	REF	REF	REF	REF	REF	REF	REF
Study									
TSS ($N = 534$)	REF	REF	REF	REF	REF	REF	REF	REF	REF
FORGE ($N = 127$)	1.1 (0.96, 1.3)	1.2 (1.0, 1.4)	1.5 (0.82, 2.6)	1.2 (0.62, 2.2)	0.94 (0.35, 2.5)	0.96 (0.67, 1.4)	0.96 (0.51, 1.8)	0.73 (0.33, 1.6)	0.41 (0.11, 1.5)

CIs, Confidence Interal; REF, Referent Group.
Statistically significant differences ($p < 0.05$) from the referent group are indicated by an asterisk and bold ($N = 644$).

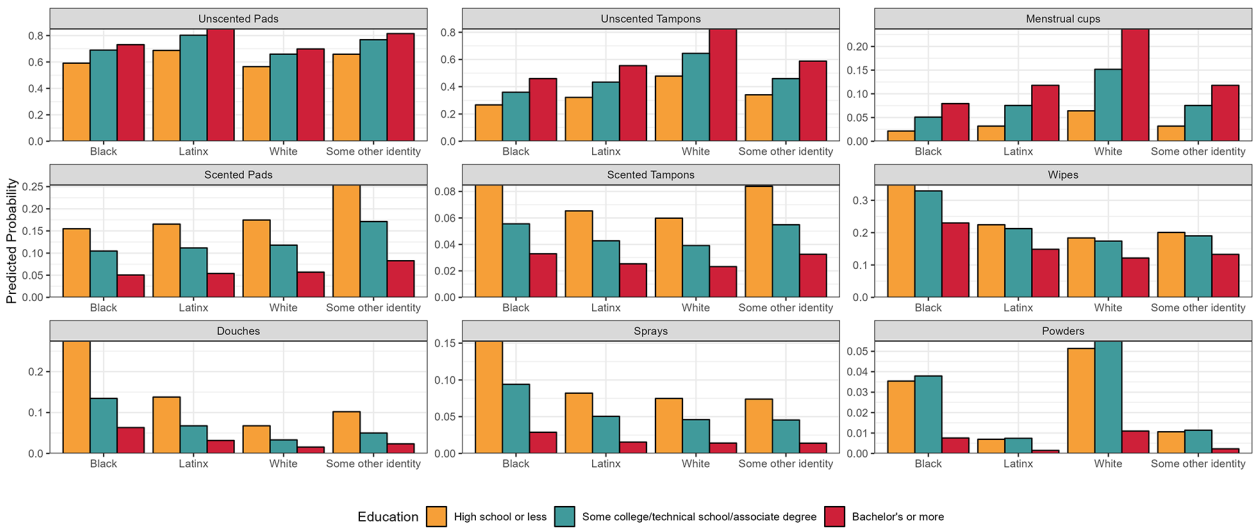

FIGURE 2
Predicted probability of product usage by educational attainment and by race ($N = 644$).

participants had significantly higher relative risks of using wipes compared to all other racial/ethnic groups. Similarly, Black participants had higher risks of douche use compared to White (RR = 0.25, 95% CI: 0.076, 0.80) and Latinx (RR = 0.5, 95% CI: 0.27, 0.94) participants. Black participants also had higher risk of use of powders compared to Latinx participants. Furthermore, in adjusted models, educational attainment became a significant determinant of each product used. There were increased risks of use of unscented pads, unscented tampons, and menstrual cups among those with ≥bachelor's degree compared to those with those with ≤high school diploma. In contrast, use of scented menstrual and intimate care products showed an inverse relationship with formal education with the greatest risks of use among those with the least formal education. For example, use of scented pads (RR = 3.1, 95% CI: 1.7, 5.6), scented tampons (RR = 2.6, 95% CI: 1.0, 6.4), wipes (RR = 1.5, 95% CI: 1.0, 2.2), douches (RR = 4.3, 95% CI: 2.3, 8.2), sprays (RR = 5.3, 95% CI: 2.4, 12), and powders (RR = 4.7 (1.1, 21) was associated with increased risks among ≤high school diploma compared to ≥bachelor's degrees. In most cases, those with some college had an intermediate risk of use between those with ≤high school diploma and those with ≥bachelor's degree. Figure 2 shows the predictive probability of product use by race/ethnicity and education. Study was not associated with any product use in mutually adjusted models.

Unscented and scent-altering product use

We next sought to understand whether product use could distinguish groups of participants (i.e., do respondents cluster based on their reported product use) and if those groups varied by demographic characteristics. The LCA identified two distinct classes or groups of product users. The first group ($n = 84$) was more likely to use scent-altering products, including scented menstrual care products as well as the four intimate care products. The second group ($n = 577$) was more likely to use unscented tampons, unscented pads, and menstrual cups (Figure 3). There were clear differences in age and formal education between the two groups (Table 5). Most participants in the scent-altering product use class were between the ages of 35–54 (64.3%) and had less than a bachelor's degree (71.0%). Age and formal education remained significant determinants of membership in scent-altering product class in log-binomial regression models after adjustment for race/ethnicity and study. For example, compared to those with ≥bachelor's degree, those with ≤high school diploma and those with some college had relative risks of 3.2 (1.8, 5.4) and 2.1 (1.2, 3.6), respectively, of having membership in the scent-altering product class. None of the other demographic factors varied by class assignment. While sex/gender did not statistically vary between the two groups, all the respondents who identified as non-binary fell within the group less likely to use scent-altering products. Those who belonged to the scent-altering LCA class were more likely to report choosing products based on their scent compared to the other class (Figure 4). Whereas those in the unscented product class were more likely to report choosing products based on effectiveness. Figure 5 shows the distribution of number of scent-altering product use among those who reported using at least one product by three education categories. Those with ≤high school diploma reported using more scent-altering products than those with more formal education. Among those with ≤high school diploma, 9.5% reported using four or more scent-altering products.

Sensitivity analysis

As a sensitivity analysis, we further examined the association between education and product use among those 25 years and older, when most US adults have typically completed their

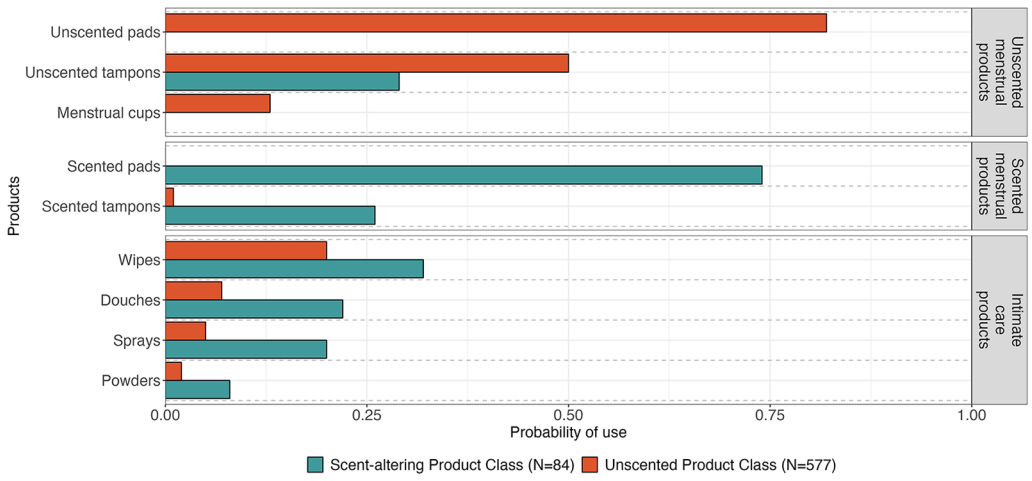

FIGURE 3
Product use probability by latent class.

TABLE 5 Demographic differences by latent class.

Characteristic	Scent-altering product class		
	Yes ($N = 84$)	No ($N = 577$)	Adjusted RR (95% CI)
Age (years)			
18–24 ($N = 189$)	17 (20.2%)	172 (29.8%)	REF
25–34 ($N = 144$)	13 (15.5%)	131 (22.7%)	1.4 (0.67, 2.9)
35–44 ($N = 215$)	36 (42.9%)	179 (31.0%)	**2.3 (1.2, 4.1)***
45–54 ($N = 113$)	18 (21.4%)	95 (16.5%)	**2.4 (1.2, 4.7)***
Race/ethnicity[a]			
Black ($N = 221$)	31 (37.3%)	190 (33.4%)	
Latinx ($N = 204$)	26 (31.3%)	178 (31.3%)	0.79 (0.45, 1.4)
White ($N = 120$)	13 (15.7%)	107 (18.8%)	0.98 (0.53, 1.8)
Some other identity ($N = 107$)	13 (15.7%)	94 (16.5%)	1 (0.52, 1.9)
Education[b]			
≤High school diploma ($N = 130$)	28 (34.1%)	102 (17.9%)	**3.2 (1.8, 5.4)***
Some college, technical school, or associate degree ($N = 226$)	31 (37.8%)	195 (34.2%)	**2.1 (1.2, 3.6)***
≥Bachelor's degree ($N = 297$)	23 (28.0%)	274 (48.0%)	REF
Sex/gender			
Female ($N = 640$)	83 (98.8%)	557 (96.5%)	NA
Transgender ($N = 9$)	1 (1.2%)	8 (1.4%)	NA
Non-binary ($N = 12$)	0 (0.0%)	12 (2.1%)	NA
Study			
TSS ($N = 534$)	66 (78.6%)	468 (81.1%)	REF
FORGE ($N = 127$)	18 (21.4%)	109 (18.9%)	0.82 (0.46, 1.4)

RR, Relative Risk; CI, Confidence Intervals; REF, Referent Group.
Adjusted RRs (95% CI) are for relative risk of having membership in the scent-altering product class. Significant differences ($p < 0.05$) in bold, ($N = 661$).
[a]9 participants did not report race/ethnicity.
[b]8 participants did not report education.

formal education. We first examined the relative risks of each individual product use from mutually adjusted log-binomial models. Associations between education and individual product use were generally consistent with those from the main analysis except for scented tampons, which was not associated with education in the main analysis. In the sensitivity analysis, there was a significant association between scented tampon use and education. Compared to those with ≥bachelor's degree, there is an increased risk of use of scented tampons among those with ≤high school diploma (RR = 4.6, 95% CI: 1.6, 13) and some college (RR = 3.0, 95% CI: 1.1, 8.3) (**Supplemental Table S1**). We also reran the LCA and re-examined demographic determinants of LCA class assignment in the older subset. The adjusted association between educational attainment and scent-altering product class assignment was more pronounced in the sensitivity analysis. Compared to

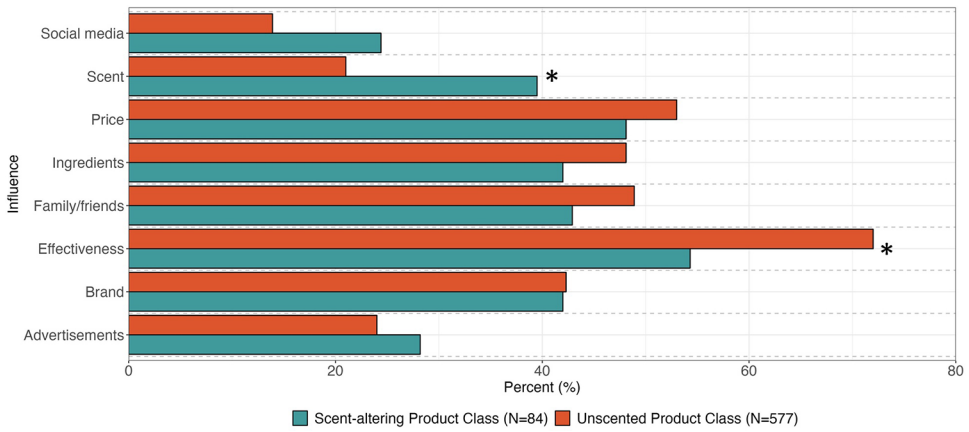

FIGURE 4
Influences impacting product selection stratified by latent class assignment. Significant differences ($p < 0.05$) indicated with asterisk.

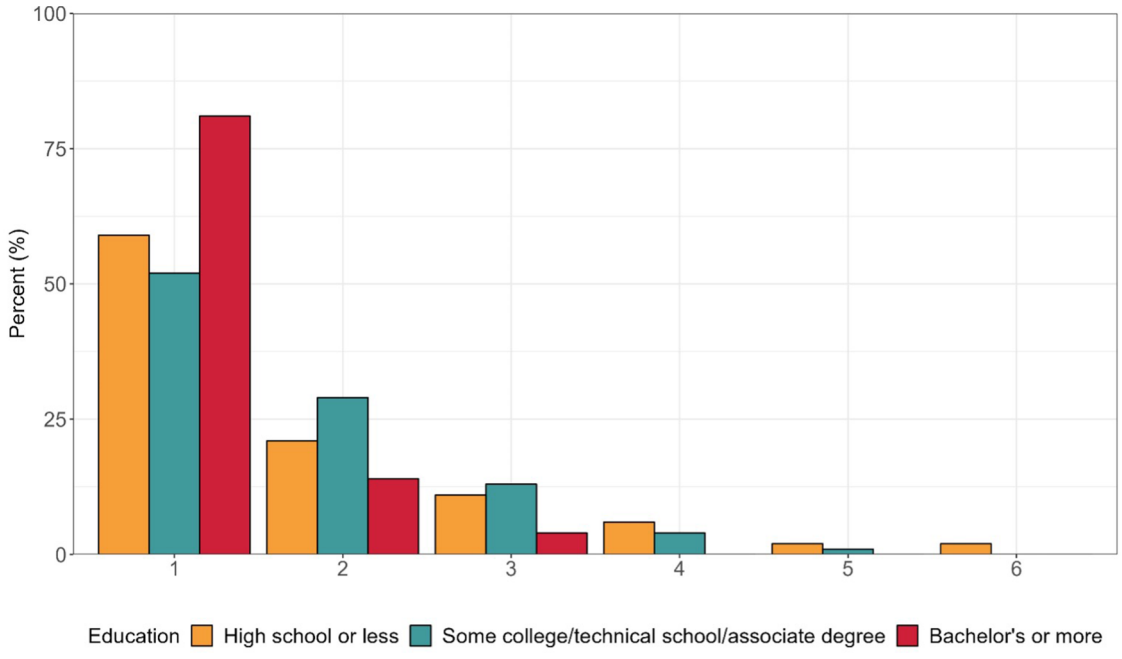

FIGURE 5
Number of scent-altering products used among those who reported using at least one scent-altering product stratified by education: high school or less ($n = 63$), some college/technical school/associate degree ($n = 75$) and bachelor's or more ($n = 91$).

those with ≥bachelor's degrees, those with ≤high school diploma had a relative risk of 4.4 (95% CI: 2.4, 7.9), compared to a relative risk of 3.2 (95% CI: 1.8, 5.4) in the main analysis. Age was not a significant determinant of scent-altering product class membership in the restricted analysis.

Discussion

In this pooled analysis of two US-based study populations, we found a consistent relationship between level of formal education and use of menstrual and intimate care products: those with the less formal education were more likely to use multiple scent-altering products and those with more formal education were more likely to use unscented tampons and menstrual cups. We also found racial/ethnic differences in product use; compared to Black participants, White participants were more likely to use unscented tampons and menstrual cups and less likely to use douches and wipes. We observed important differences by age; those who were ages 18–24 were more likely to use menstrual cups and less likely to use intimate care products. Lastly, we present some of the first data on product use among gender

minorities with descriptive statistics on transgender and nonbinary respondent product usage. Among the small sample of non-binary participants, there was a high prevalence of use of menstrual cups and no reported use of scented menstrual products, powders, or sprays. Collectively, our findings suggest importance differences in menstrual and intimate care product use by measures of social identity (e.g., race/ethnic, socioeconomic, and gender identities) further underscoring the significance of the menstrual and intimate care industry to the environmental injustice of beauty.

Consistency with prior literature

There is limited prior research upon which we can contextualize our research findings. To our knowledge, no prior studies have characterized demographic differences in usage of menstrual cups, scented tampons, or scented pads aside from Dodson et al. who examined racial/ethnic differences in personal care products use among TSS participants ages 18–34. (47) Among the products included in this study, sociodemographic patterns in douching are the most well characterized. Prior literature suggests that douching is most common in Black women, specifically among those who are lower socioeconomic status, as reflected by their education or income (46, 51, 52). Our findings are consistent with those from previous studies. Moreover, the douching prevalence for Black participants in our study (data collected from 2018 to 2021) was similar to estimates from Branch et al. (NHANES 2001–2004) (34% vs. 37%) despite efforts by the clinical community to discourage this practice (36). Branch et al. also reported that Black women used significantly more wipes, sprays, and powders than White or Mexican American women. We found similar patterns although some of the differences between racial/ethnic groups in our study did not reach statistical significance.

We found significant differences in racial/ethnic patterns of use of unscented tampons and menstrual cups, both of which were more likely to be used by White, more highly educated, and younger participants. In contrast, there were no racial/ethnic differences in use of scented pads or tampons. Previous literature supports our findings on unscented tampons and menstrual cups: one study demonstrated that White women are more likely to report using tampons as adolescents compared to Black and Latina peers, which was credited to differences in household and cultural norms (53). Similarly, menstrual cup usage has been reported to be higher amongst younger populations with greater educational attainment among participants ages 18–55 in Spain (54). We also found menstrual cup use was highly prevalent among our small sample of non-binary participants, despite this product generally having lower reported usage rates across literature (55). While our study cannot elucidate upstream drivers of product use within this group, an ethnographic study of 19 trans and non-binary participants found that respondents chose menstrual products with respect to their gender identities and body politics, with many opting for products that minimized gender dysphoria during menstruation (56).

Educational variation in scent-altering product use

We found that use of all six scent-altering products were separately associated with less education in the fully adjusted relative risk models, and that combined use of these products was also more common in those with less education. Consistent with the product use findings, those who belonged to the "scent-altering" latent class were also more likely to report scent as an influential factor in product choice and selection. To our knowledge, ours is the most in-depth examination of educational variation of menstrual and intimate care product use.

The cultural marketing and use of menstrual products in the US shifted menstruation from a natural function and aspect of fertility into a hygiene crisis that needed to be managed by scientists, the medical community, and menstrual product manufacturers (1). The vagina has been historically described by advertisers as having a negative odor and in need of deodorizing, disinfecting, and cleaning, promoting sales of douching products to women for "freshness" and marital harmony. From the earliest commercial menstrual products in the early twentieth century, ads reinforced two notions—that menstruation was a hygiene issue and an odor issue. Tampon and pad manufacturers added perfume and scents to their products to "protect against odor." (57) The rise of synthetic fragrance manufacturing intersects with the post war rise of the petrochemical industry, and the marketing of a range of products to US consumers, including single use products, plastics, and other throw away items (58, 59).

Our study cannot directly disentangle how formal education interacts with the cultural history around scent and odor in the U.S. It is possible that attainment of formal education could be a proxy for differences in cultural norms and social taboos by socioeconomic status. While we did not measure socioeconomic status during childhood, extensive prior data demonstrates an association between socioeconomic status during childhood and adulthood (60). Social taboos surrounding menstruation and odor can come from media, religion, and cultural norms, and can largely influence what types of products people use (61). Most women report that guidance on menstrual hygiene is shaped during their adolescent years and are strongly influenced by their mother and other family members (62). As such, the relative importance of social taboos around body odor could vary across the socioeconomic spectrum. Alternatively, our results suggest that college and post-graduate education can expose menstruating populations to additional information about reproductive and menstrual health beyond what they learned in high school, including broader exposure to menstrual activism and other social movements that have sought to reframe the symbolism of menstruation and messages in menstrual product marketing (63). Social movements surrounding the normalization of menstruation have inspired art, humor, legislation, and campus activism. For example, in recent years activists have successfully drawn critical attention to 35 states which impose a sales tax on menstrual hygiene products, while products such as those for erectile dysfunction are tax-free. This "tampon tax" has become emblematic of gender inequality, as it imposes a

burden on top of the purchase of biologically necessary products that menstruating individuals require to attend work, school, and participate in public life (64). Furthermore, for many, college might be the first time living with non-family members. The most recent data available from the National Center for Education Statistics suggests that the majority of bachelor's degree seeking students live outside of their family home, either on campus (29.1%) or off campus with roommates (42.6%) (65). Comparatively, 40.0% of students enrolled in 2-year associate degree programs report residing with parents. For many, college might be the first exposure to broader menstrual equity conversations and residing with non-family members, which can potentially create opportunities for dialogue about alternative menstrual management products and dispel myths about odor and hygiene (66, 67). Future research should further investigate the mechanisms underlying our observed association between education and scent-altering product use.

Exposure and health implications

The potential health implications of our findings warrant further consideration. Few toxicologic or epidemiologic studies have considered the adverse health risks of menstrual and intimate care product use in relation to racial/ethnicity or education. Available risk assessments are limited since most have only estimated health risks from one class of chemicals in one product (e.g., cancer risks of VOCs in sprays) (16, 35). Our study importantly highlighted that some menstruating individuals are using multiple (up to six) scent-altering products in and around vaginal and vulvar tissues. Many of these products contain fragrance chemicals. Use of fragranced products on vulvar tissue warrants unique consideration since vulvar tissue differs from cutaneous epithelia in structure, morphology, and biophysical characteristics. For example, the skin of the labia majora exhibits unique hydration, occlusion, and frictional properties, which may increase susceptibility to irritants and contact sensitizers. Furthermore, the nonkeratinized vulvar vestibule is likely to be more permeable than keratinized regions found in other parts of the body. These differences heighten vulvar susceptibility to topical agents including chemicals in intimate care products, which have been reported sources of allergic contact dermatitis of the vulva (34). In addition to more acute conditions, menstrual and intimate care product use may be associated with increased cancer risk of sexual and reproductive organs (e.g., uterine cancer, cervical cancer, ovarian cancer) as well as other gynecologic conditions such as fibroids (39, 41, 68–70). These products could affect chronic health risks through several possible pathways, including inflammation response, microbiota changes, or endocrine disruption (70). Future research should further examine exposure and health consequences of chemicals in menstrual and intimate care products using a combination of *in vitro* and epidemiologic models. Future research should also consider newer, alternative products, such as period underwear, which was reported by several of our study participants in the "other product" category.

Strengths and limitations

Our analysis has many strengths. Importantly, this work builds upon the environmental injustice of beauty, an intersectional framework that seeks to understand how interlocking systems of power and oppression, and related social identities, shapes beauty norms, product use, chemical exposures, and health across the life course (42, 43). Our data further underscore the importance of the social politics of body odor and personal aroma as upstream drivers of product use, particularly scent-altering products that may contain fragrance chemicals. Our study included a comprehensive examination of nine different menstrual and intimate care products within a diverse cohort. We also examined demographic variations in individual product use as well as analyzed patterns of use across products. Lastly, we included trans and non-binary participants in our study, who have been understudied and under-recognized in environmental and reproductive health research (71).

The study also has some important weaknesses. We relied on cross-sectional surveys that only asked about product use at one time point; product use can change by life stage. We did not ask for information on brands or specific product ingredients, which are critical to evaluating the environmental health risks of reported product use. We lacked adequate statistical power to evaluate multiplicative interactions between race/ethnicity and education, which would better approximate an intersectionality framework. We did not have household income data across both studies. Our only proxy for socioeconomic status was education, which creates a limitation to our socioeconomic analysis, as income may play an important role in determining product use and selection. Our data highlights some important, potential differences in product use by non-binary and transgender populations; however, the size of these subpopulations was small so it is difficult to generalize the findings. Lastly, there were some important differences in the two underlying study populations. While TSS sought to capture product use information among the general, female population in California, FORGE was a clinical epidemiologic study that recruited participants who had gynecologic morbidities (e.g., fibroids, endometriosis) or who were undergoing gynecologic procedures (e.g., hysterectomy). Nonetheless, there were few meaningful differences in product use by study, and adjustment for study in our LCA model did not change associations between product use and our demographic variables of interest. However, because of the unique nature of our study populations, these findings may have limited generalizability, and warrant replication in other study populations.

Conclusion

We found meaningful differences in menstrual and intimate care product use by race/ethnicity, education, age, and sex/gender, which has important implications for both reproductive and environmental health equity. Importantly, lower educational attainment was consistently associated with greater use of scent-altering menstrual and intimate care products Given the clustered use of scent-altering products by some respondents,

which can lead to greater cumulative exposures to fragrance chemicals, regulatory bodies should place greater scrutiny on toxicological evaluation of fragrance chemicals, particularly products used in or near sensitive tissues. In addition to enhanced regulatory actions around product ingredients, there should be greater transparency so that consumers can more easily obtain information on ingredient safety. Future research should examine associations between body odor stigma, product use, and health risks at different intersections of race, class, and gender. The medical community, particularly obstetricians and gynecologists, should be informed on the evolving environmental public health literature on menstrual and intimate care products to provide clearer guidance to their patients on potential health risks. Menstrual activism as a component of feminist politics has increasingly focused on equitable access to menstrual products and promotion of education about menstruation. Our findings suggest that the movement should expand beyond product-focused activism to include examination of root causes of menstrual stigma. Reducing environmental health risks from intimate care and scented menstrual products will require explicitly addressing social norms around menstruation and body odor beginning at an early age. To accomplish this bold task, we will need to shift discourses about menstruation from private to the public sphere, from sanitization and medicalization towards an intersectional lens.

Data availability statement

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Occidental College Institutional Review Board and George Washington University Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

ARZ – Conceptualized the study, supervised data analysis and visualization, contributed to funding acquisition for both FORGE and Taking Stock, supervised data collection for FORGE, and led the writing of the initial draft of the manuscript. ETF led the data analysis and visualization and contributed to writing and editing of the manuscript. EBW contributed to data analysis, visualization, writing and editing of the manuscript. BS contributed to the conceptualization and funding acquisition of the Taking Stock Study (parent study), supervised data collection for the Taking Stock Study, and contributed to writing and editing of the manuscript. AW contributed to data collection and editing of the manuscript. ELS contributed to study design and editing of the manuscript. RED contributed to the conceptualization and funding acquisition of the Taking Stock Study (parent study), supervised data analysis and visualization, helped design the data analysis methodology, and contributed to writing and editing of the manuscript. All authors approved the submitted version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/frph.2023.1286920/full#supplementary-material

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Racial disparities affect the association between gestational urinary phthalate mixtures and infant genital measures

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Background: Phthalates are ubiquitous anti-androgenic endocrine disrupting chemicals found in personal care products, medications, and many plastics. Studies have shown a racial disparity in phthalates exposure among U.S. women, which may also impact fetal development.
Methods: We conducted a prospective cohort study of gestational exposure to a phthalates mixture in a racially-diverse population to determine their association with genital development. Mid-gestation (18–22 weeks) urine was collected from 152 women who self-identified as non-Hispanic Black and 158 women who self-identified as non-Hispanic White in Charleston, South Carolina between 2011 and 2014. We measured eight phthalate monoester metabolites in urine using liquid chromatography tandem-mass spectrometry. Mid-gestational penile dimensions were measured using ultrasound and anogenital distances were measured postnatally. We used Bayesian kernel machine regression to estimate the associations among the mixture of phthalate metabolites and mid-gestation penile dimensions and postnatal anogenital distance measures among singleton male ($n = 179$) and female ($n = 131$) infants, adjusted for urinary specific gravity, maternal age, body mass index, education level, cigarette smoking, and gestational age at enrollment or birth weight z-score.
Results: We found a stronger association between greater phthalates and decreased anopenile distance among infants born to women who self-identified as Black. Mono (2-ethylhexyl) phthalate (MEHP) was the driving mixture component among Black women, and monobutyl phthalate (MBP) and monoethyl phthalate (MEP) were drivers among White women. We also identified a non-linear association between phthalates and lesser ultrasound penile volume among women who self-identified as Black with monoisobutyl phthalate (MiBP) and MBP being most important. We also found an association between greater phthalates and shorter anoclitoral distance among infants born to women who self-identified as Black, with MEP and monobenzyl phthalate (MBzP) contributing most to this association.
Conclusion: Our results suggest a disparity in the association between gestational exposure to a mixture of phthalates and fetal genital development among women who self-identified as Black compared to White.

KEYWORDS

anogenital distance, BKMR, penile measures, phthalates mixture, race disparity

1. Introduction

Phthalates are ubiquitous endocrine disrupting chemicals used in personal care products and cosmetics, plastic food and beverage packaging, toys, and other consumer products (1). Human exposure to phthalates is widespread (2) and occurs via dermal absorption, ingestion, or inhalation of volatized phthalates (3). Low molecular weight phthalates are used as solvents and fragrance carriers in personal care products, such as lotions, soaps, and perfumes, including diethyl phthalate (DEP) and dibutyl phthalate (DBP). High molecular weight phthalates, like di-(2-ethylhexyl) phthalate (DEHP), tend to be used in plastics, especially polyvinyl chloride packaging (4). In the U.S., minoritized groups experience greater levels of exposure to many phthalates compared to White populations (5). Some phthalates have anti-androgenic properties in experimental studies (6) and cross the placental barrier to potentially affect a developing fetus. Gestational phthalates exposure caused male reproductive organ malformations, diminished testosterone and inhibited Leydig cell steroidogenesis in experimental animal models (7, 8), although the evidence from human testicular explant studies was mixed (9, 10). Some phthalates are shown to have estrogenic effects in experimental studies (11, 12). Phthalates can act as estrogen receptor agonists (13) and androgen receptor antagonists (14), which may result in reduced testosterone and sperm production in males (15). While most work has focused on the effects of individual phthalates, more recent studies suggest that the biological effects of phthalates may differ in the context of a mixture (16), prompting the U.S. National Academy of Sciences to call for cumulative risk assessment approaches to the endocrine disrupting effects of phthalates (17). For example, phthalate mixtures elicited meaningful dose-additive anti-androgenic effects in male rats (18–20). Another study found that gestational exposure to an environmentally-relevant mixture of phthalates [DEHP, DEP, DBP, benzyl butyl phthalate (BBP), di-isobutyl phthalate (DiBP), and diisononyl phthalate (DiNP)], was associated with decreased anogenital distance (AGD) in female mice, although at a greater dose than typically experienced by human populations (21). Furthermore, dose-response associations may be non-linear. For example, there was a stronger positive association between AGD and DEHP at low doses (0.5 μg/kg/day) than at higher doses (500,000 μg/kg/day) in gestationally-exposed male mice (22).

Results from human studies of gestational phthalates exposure and fetal genital development have been inconsistent. Previous studies have examined associations between individual phthalates and measures of AGD, the length from the anus to the genitalia, though results were discordant (3, 23). A longer AGD is a biomarker of greater fetal exposure to androgens during early pregnancy and has been correlated to reproductive health endpoints in adults (24, 25). In our previous work, we reported inverse associations between anopenile distance (APD) and maternal urinary mono(2-ethylhexyl) phthalate (MEHP), monobutyl phthalate (MBP), monobenzyl phthalate (MBzP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), monoethyl phthalate (MEP), monoisobutyl phthalate (MiBP), and monomethyl phthalate (MMP) among male infants (26). Among female infants, we reported a positive association between maternal urinary MBzP and anoclitoral distance (ACD), but inverse associations for maternal urinary MBP, MiBP, MEHP, MEOHP, MEHHP, MEP, and MMP with ACD (26). We also found inverse associations between maternal urinary MiBP, MBzP, MEHP, MEOHP, MEHHP, MEP, and MMP with ultrasound-derived penile volume (PV); however, a positive association between maternal urinary MBP and ultrasound PV (27). Our results suggested a differential association between gestational urinary phthalates among women who self-identified as Black (including African American) and White (26, 27), and for female and male infants. However, to our knowledge, no studies have investigated the potential effects of gestational exposure to a phthalates mixture on fetal genital development, which may differ from the effects of individual phthalates in isolation (28).

Therefore, our aim was to estimate associations between gestational exposure to a mixture of eight urinary phthalate metabolites with ultrasound-derived penile volumes and postnatal AGD measurements among mother-infant pairs. These results will help to inform risk assessments of the fetal developmental health risks of gestational phthalates exposure as called for by the National Academy of Sciences (17).

2. Methods

2.1. Study population

From 2011 to 2014, we enrolled 407 women with a viable singleton pregnancy into a birth cohort study during a routine fetal anatomic ultrasound visit between 18 and 22 weeks' gestation. Women were eligible if they were 18 years of age or older, had no obvious fetal anomalies by fetal ultrasound, agreed to identification of the fetal sex, and planned to deliver at the Medical University of South Carolina (MUSC) (26, 27, 29). Women were excluded with multiple gestations, did not want to learn the fetal sex, had fetal congenital anomalies or endocrine diagnoses, and used steroids or other medications. At enrollment, women provided a spot urine specimen and completed an interviewer-administered study questionnaire to collect information about sociodemographic and lifestyle factors. Clinical data were extracted from the electronic medical record. This study includes 310 women with live deliveries who self-identified as non-Hispanic Black ($n = 152$), including African American, or non-Hispanic White ($n = 158$) (subsequently referred to as Black and White, respectively), and had a urine phthalates analysis. We use racial grouping as a proxy for individual and societal experiences driven by ongoing historical processes based on one's identify, presumably reflecting skin pigmentation (30). All participants in this study completed written informed consent and the study protocol was approved by the MUSC Institutional Review Board.

2.2. Measures of postnatal anogenital distance and prenatal ultrasound penile dimensions

Measures of AGDs, the length from the anus to the genitalia, were completed within 48 h of delivery using a caliper as previously described in detail (26). Briefly, each AGD was measured in triplicate and averaged, with infants lying on their back and legs in the frog position. For males, we measured APD and anoscrotal distance (ASD) as the distance from the anterior margin of the anus to the base of the penis or to the base of the scrotum where the skin changes from smooth to rugated, respectively. For females, ACD and anofourchette distance (AFD) were measured as the distance from the anterior margin of the anus to the clitoral hood or posterior convergence of the fourchette, respectively.

Ultrasound penile length (PL) and penile width (PW) measures were made in women with male fetuses between 18 and 22 weeks gestation, as previously described in detail (27). Briefly, American Institute of Ultrasound in Medicine (AIUM)-certified sonographers used freeze-frame images and electronic calipers to measure PL from the scrotal junction to the tip of the glans, and penile width (PW) was measured mid-shaft. Each dimension was measured in triplicate and the values averaged together. Penile volume (PV) was estimated as $(PW/2)^2$ *PL.

2.3. Urinary phthalates analysis

Urine samples were processed and frozen at −20°C immediately after collection. Specific gravity was determined at room temperature using a handheld refractometer (Atago U.S.A., Inc., Bellevue, WA, USA) (26, 27). Urinary specimens were transferred, on dry ice, to Hollings Marine Laboratory, National Institute of Standards and Technology (Charleston, SC, USA). For analysis of phthalates, urinary concentrations of eight phthalate monoester metabolites were determined using a method based on liquid chromatography coupled to tandem mass spectrometry after solid phase extraction, as previously described in detail (26), including: MBP, MiBP, MBzP, MEHP, MEOHP, MEHHP, MEP, and MMP.

Limits of detection (LOD) ranged from 0.10 ng/ml for MMP to 1.00 ng/ml for MBzP. Instrument-reported phthalate values were used for values less than the LOD without imputation to minimize bias in the regression models (31). For descriptive analysis, we corrected phthalate concentrations for urinary dilution using specific gravity as $P_c = P_i[(1.016–1)/SG_i\text{-}1]$, where P_c = specific gravity-corrected phthalate concentration (ng/ml), P_i = individual urinary phthalate concentration (ng/ml); 1.016 = mean urinary specific gravity for all women in the study population, and SG_i = individual specific gravity. However, we used urinary phthalate metabolites uncorrected for specific gravity during regression analysis, and included urine specific gravity as a covariate in the regression models (32), to prevent propagation of measurement error in phthalate values and bias that may be introduced by conventional standardization approaches in regression models.

2.4. Statistical analysis

We summarized the distribution of covariates, overall and according to Black and White racial identity group, and used Student's *t*-tests and Chi-square tests of the differences between the racial groups. Phthalate concentrations were natural log transformed after adding a constant (=1), to normalize the distributions and stabilize the variances prior to analysis.

We used Bayesian kernel machine regression (BKMR) (33) to estimate associations between gestational exposure to the mixture of eight urinary phthalate metabolites as a predictor and postnatal AGDs and ultrasound penile dimensions as outcomes in individual models. The BKMR approach was selected because it allows for inter-phthalate interactions and non-linear dose-response associations. Based on previous studies, we adjusted the models for maternal age (years) (34), body mass index (BMI, kg/m^2) (35), education ("did not complete college" or "completed college or higher") (35), cigarette smoking (never smoked or current smoker/quit smoking during pregnancy) (36), urinary specific gravity, and either gestational age at enrollment (weeks) for penile dimensions or birth weight standardized to World Health Organization (WHO) growth charts (*Z*-score) for AGDs (37). We used multiple imputation by chained equations (MICE) to create 10 datasets with missing covariates imputed for $n = 22$ and $n = 1$ for MEP and MMP (38). For each outcome, we estimated 10 individual BKMR models using the MICE imputed datasets (39, 40). We averaged the posterior inclusion probabilities (PIPs) from the 10 imputed datasets, and we visually inspected the trace plots to ensure convergence of the imputed datasets and the BKMR models. We implemented 50,000 to 200,000 iterations, removed 50% burn-in iterations, and retained 10% of the remaining chains to ensure stable estimates of the associations (39, 40).

Statistical significance was defined as $p < 0.05$ for a two-tailed hypothesis test. All analyses were conducted using R software version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Demographic, lifestyle, and clinical characteristics of the study population

Table 1 shows the distributions of demographic characteristics and infant genital measures for the $n = 310$ women included in this analysis ($n = 152$ women who identified as Black and $n = 158$ women who identified as White). The mean overall age was 27.61 years and the pre-pregnancy BMI was 29.14 kg/m^2. Women who identified as Black were younger and had a greater BMI than women who identified as White. More women who identified as Black (77.30%) had less than a college education compared to women who identified as White (36.42%). A greater number of male infants were included in this study than female infants because only mothers carrying male fetuses were initially

TABLE 1 Demographic characteristics and anogenital distance measures of women and offspring from Charleston, South Carolina, overall and by racial identity.

Characteristic	Overall ($n = 310$)	Black ($n = 152$)	White ($n = 158$)	p-value
Age (years), mean (SD)[a]	27.61 (5.64)	26.07 (5.62)	29.09 (5.26)	<0.001
Pre-pregnancy BMI (kg/m^2), mean (SD)[a,b]	29.14 (7.14)	31.27 (7.94)	27.09 (5.56)	<0.001
Education, n (%)[c,d]				<0.001
< College	164 (56.16)	109 (77.30)	55 (36.42)	
≥ College	128 (43.84)	32 (22.70)	96 (63.58)	
Infant sex, n (%)[d]				0.452
Male	179 (57.74)	84 (55.26)	95 (60.13)	
Female	131 (42.26)	68 (44.74)	63 (39.87)	
Smoking status, n (%)[d,e]				0.648
Never smoked	270 (87.95)	131 (86.75)	139 (89.10)	
Current smoker[f]	37 (12.05)	20 (13.25)	17 (10.90)	
Birth measures (mm), mean (SD)				
APD[a,g]	44.47 (5.61)	44.07 (5.27)	44.80 (5.88)	0.392
ASD[a,g]	22.53 (4.81)	23.27 (4.56)	21.89 (4.95)	0.060
ACD[a,h]	33.60 (4.07)	33.59 (3.67)	33.61 (4.50)	0.979
AFD[a,h]	12.88 (2.50)	13.33 (2.50)	12.39 (2.44)	0.034
Ultrasound measures (mm), mean (SD)				
PV (mm^3)[a,b]	48.04 (20.34)	52.79 (18.48)	43.89 (21.06)	0.003
PW[a,b]	5.23 (0.70)	5.34 (0.64)	5.13 (0.74)	0.046
PL[a,b]	6.77 (1.32)	7.19 (1.26)	6.34 (1.24)	<0.001
WHO standardized birth weight z-score[a]				
Male infants, mean (SD)	−0.13 (1.20)	−0.54 (1.36)	0.23 (0.92)	<0.001
Female infants, mean (SD)	−0.04 (1.17)	−0.36 (1.00)	0.31 (1.23)	0.001
Gestational age, (weeks), mean (SD)[a,i]	20.07 (0.71)	20.21 (0.65)	19.92 (0.74)	<0.001

ACD, anoclitoral distance; AFD, anofourchette distance; ASD, anoscrotal distance; APD, anopenile distance; PL, ultrasound penile length; PV; ultrasound penile volume; PW, ultrasound penile width.
[a]Student's t-test.
[b]$n = 1$ missing.
[c]$n = 18$ missing.
[d]Chi-Square test of independence.
[e]$n = 3$ missing.
[f]Current smoker or quit since learning of pregnancy.
[g]$n = 8$ missing among male infants.
[h]$n = 3$ missing among female infants.
[i]Gestational age at enrollment.

eligible to participate in our study. Ultrasound PL, PW, and PV were significantly greater among infants born to women who identified as Black, although with significantly lesser birth weight and shorter gestational age at delivery.

Table 2 shows the distributions of specific-gravity corrected urinary phthalate metabolite concentrations. Most values exceeded the LOD for all measured phthalates (86.1–100%) The mean concentrations of MBP, MiBP, MEHP, and MEP were greater among women who identified as Black. However, the mean concentrations of MBzP, MEOHP, MEHHP, and MMP were greater among women who identified as White.

3.2. Associations among a mixture of urinary phthalate metabolites, AGDs, and penile dimensions among male infants

Figure 1 shows the association between the overall phthalates mixture and APD, stratified by maternal racial identity. Greater levels of the urinary phthalate mixture were associated with lesser APD in the Black and White groupings although the association was stronger among women who identified as Black. For example, relative to the 25th percentile of the urinary phthalates concentration distribution, APD was −4.29 mm [95% credible interval (CI): −9.83 mm, 1.24 mm] shorter at the 90th percentile among the Black male newborns, but −2.78 mm (95% CI: −6.70 mm, 1.13 mm) shorter at the 90th percentile in the White male newborns. As shown in Figure 2 and Supplementary Table S1, the association between the gestational urinary phthalate metabolite mixture and APD was driven primarily by MEHP and MEOHP among women who identified as Black, whereas MBP was most important among women who identified as White.

The univariate exposure response plots in Supplementary Figure S1 show the associations between individual urinary phthalate metabolite concentrations with APD in the Black male newborns, fixing all other urinary phthalate metabolite concentrations at the 50th percentile. There was a nonlinear negative association suggested between both MEHP and MEOHP and APD in the women who identified as Black. Supplementary Figure S2 shows the associations between an interquartile range difference in the urinary concentrations of each phthalate

TABLE 2 Distribution of maternal urinary specific gravity-corrected phthalate concentrations (ng/ml), among women from Charleston, South Carolina, overall and by racial identity.

Phthalate	LOD	*n* (%) > LOD	Mean	SD	Minimum	Median	Maximum
Overall (*n* = 310)							
MBP	0.950	305 (98.4)	28.2	80.2	1.57	16.5	1.35×10^3
MiBP	0.170	310 (100.)	18.6	38.4	1.20	10.8	6.10×10^2
MBzP	0.100	304 (98.1)	44.8	3.90×10^2	0.0141	12.1	6.87×10^3
MEHP	0.350	297 (95.8)	6.08	14.7	0.306	2.96	211
MEOHP	0.100	310 (100.)	9.96	30.2	0.853	5.78	517
MEHHP	0.100	310 (100.)	12.8	35.3	0.960	7.08	591
MEP[a]	1.00	306 (98.7)	204	555	2.88	46.7	4.81×10^3
MMP[a]	0.340	267 (86.1)	7.26	48.3	−2.75	2.10	772
Black (*n* = 152)							
MBP	0.950	152 (100.)	32.2	33.9	2.30	22.6	191
MiBP	0.170	152 (100.)	23.1	22.8	2.11	15.8	169
MBzP	0.100	152 (100.)	31.3	44.5	0.644	17.1	308
MEHP	0.350	151 (99.3)	6.37	9.68	0.454	3.34	91.7
MEOHP	0.100	152 (100.)	8.71	8.89	1.22	5.78	51.9
MEHHP	0.100	152 (100.)	11.9	13.7	0.960	7.09	84.1
MEP[a]	1.00	151 (99.3)	268	631	10.7	58.7	4.81×10^3
MMP[a]	0.340	143 (94.1)	4.78	6.04	−0.049	3.01	43.2
White (*n* = 158)							
MBP	0.950	153 (96.8)	24.4	107	1.57	12.8	1.35×10^3
MiBP	0.170	158 (100.)	14.2	48.6	1.20	8.28	6.10×10^2
MBzP	0.100	152 (96.2)	57.9	545	0.0141	7.61	6.87×10^3
MEHP	0.350	146 (92.4)	5.81	18.4	0.306	2.78	211
MEOHP	0.100	158 (100.)	11.2	41.5	0.853	5.78	517
MEHHP	0.100	158 (100.)	13.7	47.6	1.29	7.06	591
MEP	1.00	155 (98.1)	142	466	2.88	29.5	3.90×10^3
MMP	0.340	124 (78.5)	9.63	67.3	−2.75	1.67	772

LOD, limit of detection; MBP, monobutyl phthalate; MBzP, monobenzyl phthalate; MEHHP, mono(2-ethyl-5-hydroxyhexyl) phthalate; MEHP, mono(2-ethylhexyl) phthalate; MEOHP, mono(2-ethyl-5-oxohexyl) phthalate; MEP, monoethyl phthalate; MiBP, monoisobutyl phthalate; MMP, monomethyl phthalate; SD, standard deviation.
[a]*n* = 1 missing.

metabolite and APD, with the other urinary phthalate metabolite concentrations fixed at the 25th percentile, 50th percentile, and 75th percentile, among women who identified as Black; there was no evidence of heterogeneity of the associations.

Supplementary Figure S3 shows the univariate exposure response plot between the individual urinary phthalate metabolite concentrations and APD among the white male newborns, fixing all other urinary phthalate metabolite concentrations at the 50th percentile. There was a negative linear association between MBP and APD, a modest nonlinear negative association suggested between greater MEHP and APD, and a positive linear association between MiBP and APD. Supplementary Figure S4 shows the associations between an interquartile range difference in the urinary concentrations of each phthalate metabolite and APD, with the other phthalate metabolite concentrations fixed at the 25th percentile, 50th percentile, and 75th percentile among women who identified as White; there was no evidence of heterogeneity of the associations.

Differences in ASD were small and imprecise at the 90th percentile compared to the 25th percentile of the urinary phthalates mixture distribution; approximately 1.70 mm (95% CI: −1.61 mm, 5.58 mm) among women who identified as Black and −1.62 mm (95% CI: −6.00 mm, 1.63 mm) among women who identified as White (Supplementary Figure S5).

Figure 3 suggests a non-linear association between the urinary phthalates mixture and ultrasound-derived PV among women reporting a Black identity. Relative to the 25th percentile, PV was greatest at the 10th percentile (5.57 mm^3; 95%CI: 0.07 mm^3, 11.07 mm^3) and the 90th percentile (3.25 mm^3; 95% CI: −10.11 mm^3, 16.60 mm^3), and least at the 60th percentile (−6.14 mm^3; 95% CI: −13.61 mm^3, 1.34 mm^3). In contrast, no association was suggested among the women reporting a white racial identity. As shown in Figure 2 and Supplementary Table S1, the association between the gestational urinary phthalate metabolites mixture and PV was driven primarily by MiBP among women who identified as Black.

Supplementary Figure S6 shows the univariate exposure responses between urinary phthalate metabolites and ultrasound-derived PV among infants born to women who identified as Black. There was a nonlinear "U-shaped" association between MiBP and mid-gestation fetal ultrasound PV, although the associations appeared to be null for the other urinary phthalate metabolites. There was no evidence of heterogeneity in the associations between urinary phthalate metabolites and ultrasound-derived PV among women who identified as Black (Supplementary Figure S7). Similar non-linear trends were suggested for the association between the urinary phthalate metabolites mixture and ultrasound measured PW

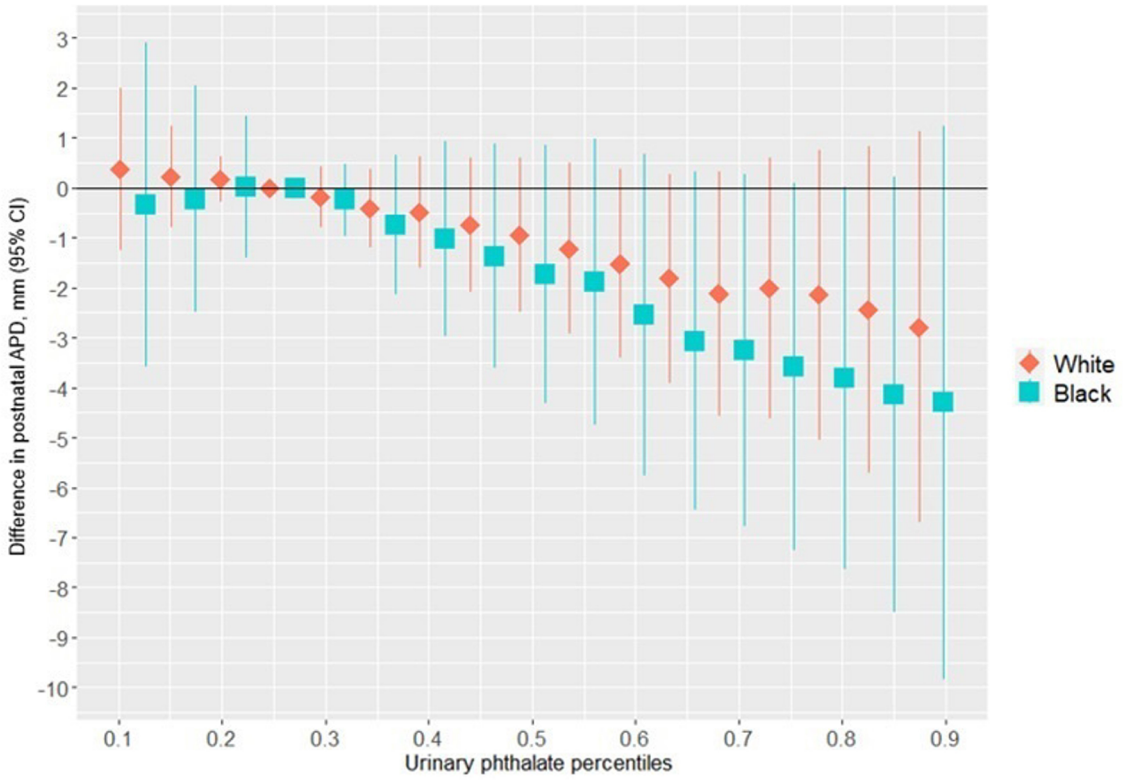

FIGURE 1
Differences in postnatal APD associated with percentiles of a urinary phthalate metabolites mixture (with the 25th percentile as the reference), adjusted for maternal specific gravity, maternal age, maternal BMI, maternal cigarette smoke, maternal education level, and WHO standardized birth weight as *z*-scores, among male infants born to women in Charleston, South Carolina, by racial identity ($n = 171$).

(Supplementary Figure S8) and ultrasound measured PL (Supplementary Figure S9), although the differences were small and close to the null hypothesis.

3.3. Associations between the mixture of urinary phthalate metabolites and AGDs among female infants

Figure 4 shows the association between the overall phthalates mixture and ACD, stratified by racial identity. Greater levels of the urinary phthalate metabolite mixture were associated with lesser ACD in women who identified as Black, but not in women who identified as White. For example, relative to the 25th percentile of the urinary phthalate metabolites concentration distribution, ACD was −3.40 mm (95% CI: −6.78 mm, −0.08 mm) shorter at the 90th percentile in the infants of women who identified as Black, but with little difference in the infants of women who identified as White (0.06 mm; 95% CI: −3.95 mm, 4.07 mm). As shown in Figure 5 and Supplementary Table 2, the association between the gestational urinary phthalate metabolite mixture and ACD was driven primarily by MEP among women who identified as Black.

Supplementary Figure S10 shows the univariate exposure responses between urinary phthalate metabolites and postnatal ACD among female infants born to women who identified as Black. There was an inverse association for MEP with ACD and a positive association for MBzP and ACD, with other phthalates fixed at the 50th percentile concentrations. There was no evidence of heterogeneity in the associations between urinary phthalate metabolites and postnatal ACD among women who identified as Black (Supplementary Figure S11).

Supplementary Figure S12 shows the association between the overall phthalates mixture and AFD, stratified by racial identity. Differences in AFD were small and imprecise at the 90th percentile compared to the 25th percentile of the urinary phthalate metabolites mixture distribution; approximately 0.77 mm (95% CI: −2.44 mm, 3.97 mm) among women who identified as Black and 0.14 mm (95% CI: −1.90 mm, 2.19 mm) among women who identified as White.

4. Discussion

4.1. Key findings

In this prospective birth cohort study, we found that greater maternal urinary concentrations of a phthalates mixture was associated with lesser APD in male infants. This change in the APD is considered a feminization or anti-androgenic effect. Among women who identified as Black, the association with APD was driven mostly by MEHP and MEOHP, but among women who identified as white the association was driven

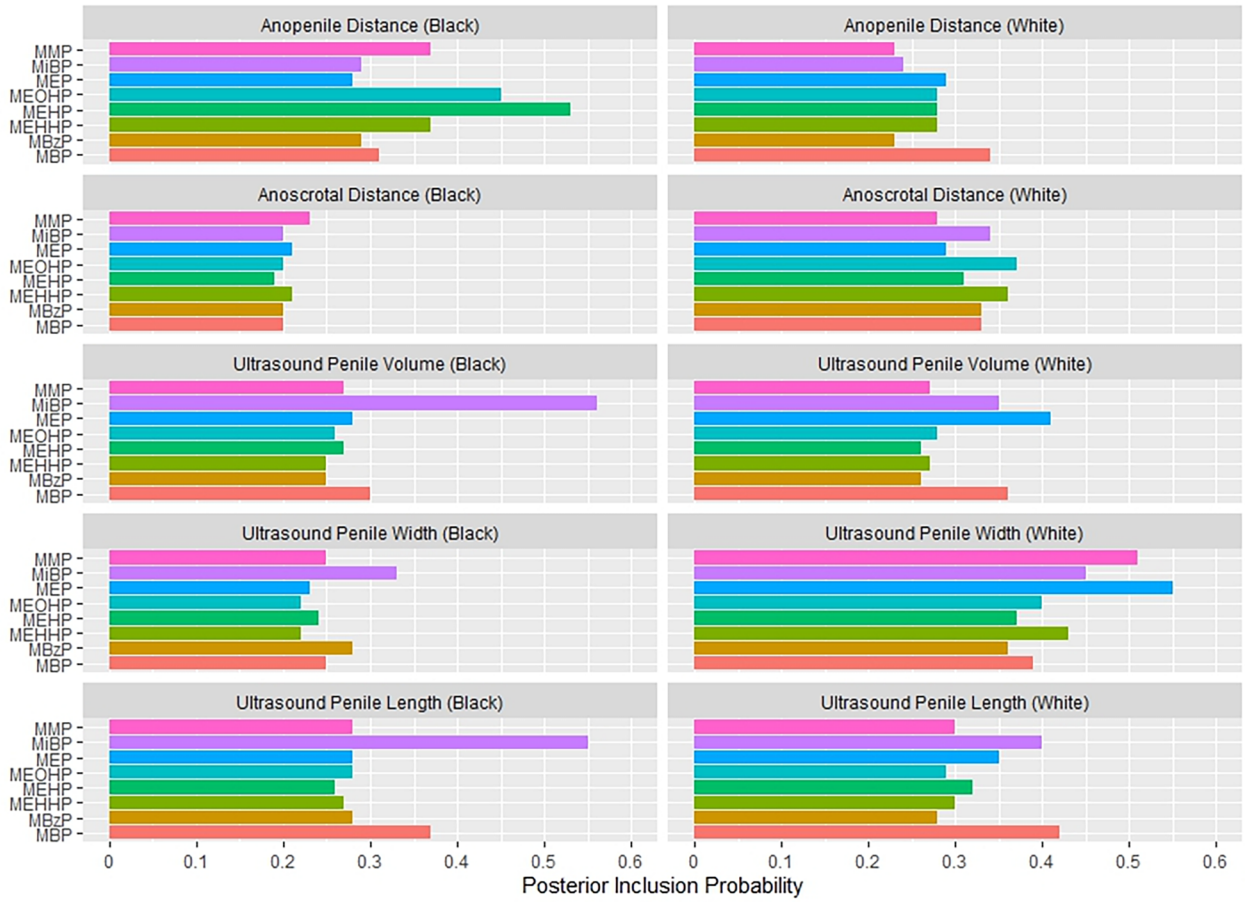

FIGURE 2
Posterior inclusion probabilities for urinary phthalate metabolite predictors of prenatal ultrasound penile dimensions and postnatal anogenital distance measures among male infants born to women in Charleston, South Carolina, by racial identity (n = 179).

primarily by MBP. There was a non-linear association between gestational exposure to the phthalates mixture and a lesser ultrasound-derived mid-trimester PV among women who identified as Black, primarily driven by MiBP. Among women who identified as Black, we also found an inverse association of maternal urinary phthalates with ACD in female infants, which was driven primarily by MEP. The shorter ACD in female infants in association with a greater urinary phthalate mixture concentration would also suggest a feminizing effect of such exposure. These results show a racial disparity in the associations between infant genital measures and gestational exposure to a mixture of urinary phthalate metabolites in a racially-diverse population.

4.2. Associations between gestational phthalates exposure, AGDs, and penile dimensions in male infants

Several studies have previously investigated associations between gestational exposure to individual phthalates and male AGDs in the offspring. Many of these studies have identified inverse associations between metabolites of DEHP, but with mixed results for other phthalates (3). However, few previous studies have estimated associations between gestational exposure to a mixture of phthalates and male AGDs. A small study in Mexico (41) found an inverse association between APD and MEHP (mean difference = −0.025 mm per μg/l, p-value = 0.840) and with the sum of MEHP, MBzP, MEP, and MBP (mean difference = −0.191 mm per μg/l, p-value = 0.037). In their seminal work, Swan and colleagues (42) reported a decrease in child anogenital index (i.e., AGD divided by body weight) associated with greater gestational urinary concentration of a phthalate summary score incorporating MBP, MBzP, MEP, and MiBP (mean difference = −0.095 per $\log_{10}$ ng/ml; 95% CI: −0.17, −0.03; p-value = 0.009) in the multi-city U.S.-based Study of Future Families (SFF) birth cohort. We found similar inverse associations between a mixture of maternal urinary phthalate metabolites and APD in offspring using BKMR, an approach that does not place strong assumptions on the additivity of the component phthalates and allows for non-linear dose-response associations.

Previously, we reported associations between maternal urinary concentrations of individual phthalate metabolites and AGD

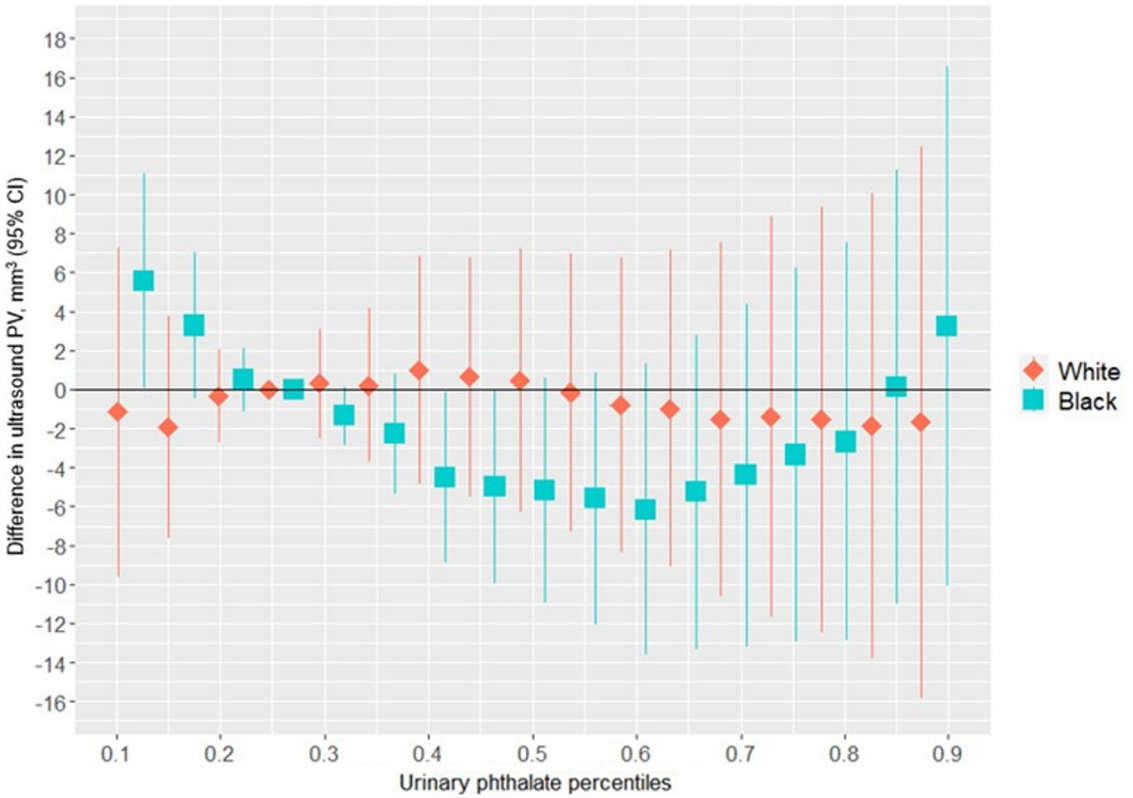

FIGURE 3
Differences in ultrasound PV associated with percentiles of a urinary phthalate metabolites mixture (with the 25th percentile as the reference), adjusted for maternal specific gravity, maternal age, maternal BMI, maternal cigarette smoke, maternal education level, and gestational age at enrollment, among male infants born to women in Charleston, South Carolina, by racial identity (n = 178).

measures in male infants from this same study population (26). We found inverse associations between APD and MBP, MiBP, MBzP, MEHP, MEOHP, MEHHP, MEP, and MMP. The strongest associations were with MEHP [mean difference = −2.07 mm per $\log_e$ ng/ml, 95% confidence interval (CI): −4.05, −0.08] and MEOHP (mean difference = −1.45 mm per $\log_e$ ng/mL, 95% CI: −3.41, 0.52) in the Black grouping, and MBP (β = −1.47 mm per $\log_e$ ng/ml, 95% CI: −3.13, 0.18) and MEHP (β = −1.23 mm per $\log_e$ ng/ml, 95% CI: −3.18, 0.73) in the White grouping (26). In our earlier work, a change in MEHP and MEOHP concentrations from the 25th percentile to the 90th percentile correspond to APD differences of −2.80 mm and −2.60 mm, respectively, among the Black grouping (i.e., vs. −4.29 mm for the mixture in our current work), and APD differences of −2.18 mm and −1.51 mm with MBP and MEHP, respectively among the White grouping (i.e., vs. −2.78 mm for the mixture in our current work). Thus, we identified similarly important urinary phthalates, but generally stronger associations with APD and a clearer racial disparity in the context of a phthalates mixture than when considered as individual phthalates. However, in the current study, there was no evidence of synergy between metabolites in the phthalates mixture with respect to APD.

Contradictory to our *a priori* hypothesis, we found small positive and negative differences in the associations between the urinary phthalates mixture and ASD in the Black and White racial groupings, respectively. We also found positive and negative associations between individual urinary phthalates and ASD in our previous work (26), although without a consistent pattern. The mechanism driving the discordant APD and ASD results is unclear, but may in part reflect unmeasured associations with scrotal volume, a hypothesis that we were unable to test in our study. A future study that incorporates scrotal volume measures and comprehensive psychosocial stress information will be necessary to confirm our results.

Few previous studies have estimated associations between gestational urinary phthalates exposure and penile dimensions among offspring (43). The aforementioned SFF reported inverse associations between a child's PW and greater maternal urinary MEHP (mean difference = −0.78 mm per $\log_{10}$ ng/ml, p-value = 0.005), MEHHP (mean difference = −0.53 mm per $\log_{10}$ ng/ml, p-value = 0.080), and the sum of DEHP metabolites (mean difference = −0.57 mm per $\log_{10}$ ng/ml, p-value = 0.072) among 106 mother-infant pairs (43). We previously reported both positive and inverse associations between individual maternal urinary phthalate metabolites and fetal ultrasound PL, PW, and PV that differed according to maternal racial identity, in the same study population used here (27). The associations for maternal urinary MiBP and the sum of DBP metabolites (MBP

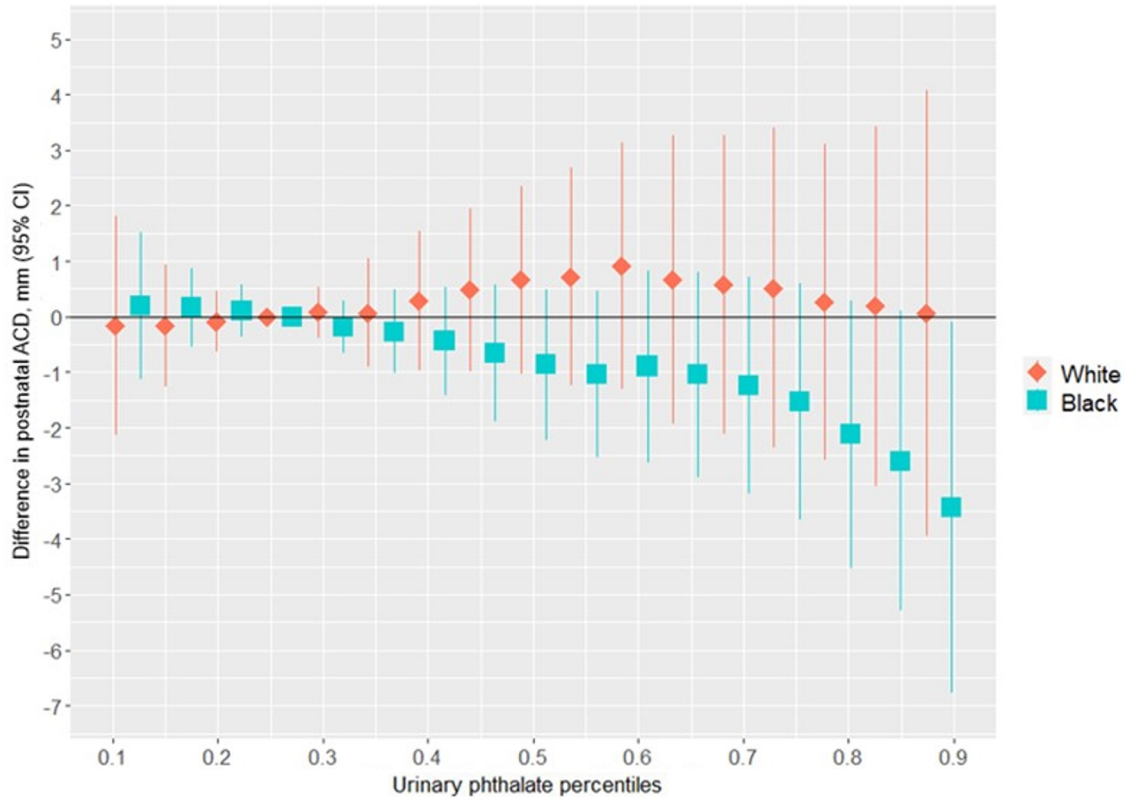

FIGURE 4
Differences in postnatal ACD associated with percentiles of a urinary phthalate metabolites mixture (with the 25th percentile as the reference), adjusted for maternal specific gravity, maternal age, maternal BMI, maternal cigarette smoke, maternal education level, and birth weight *z*-score, among female infants born to women in Charleston, South Carolina, stratified by racial identity ($n = 128$).

and MiBP) showed negative and positive associations with fetal ultrasound PL in our prior work, among the women who identified as Black and White, respectively. In contrast, maternal urinary MEHP, MEHHP, MMP, and the sum of DEHP metabolites (MEHP, MEOHP, and MEHHP) had mixed and discordant associations with fetal ultrasound measured PW in our prior work, among women who identified as Black and White. In our prior study, the sum of DBP metabolites was also associated with lesser fetal ultrasound-derived PV among women who identified as Black (mean difference = −1.71 mm^3 per log_e ng/ml, 95% CI −6.39, 2.96) and greater fetal ultrasound-derived PV among women in the White racial grouping (mean difference = 3.84 mm^3 per log_e ng/ml, 95% CI: −0.62, 8.29) (27). In contrast to our prior work, our current results in the same study population suggested a non-linear "U-shaped" dose-response association between gestational exposure to the mixture of eight urinary phthalate metabolites and fetal ultrasound-derived PV among the women who identified as Black, without an association among the women who identified as White. We did not find evidence of synergy between component phthalates within the mixture. These new results underscore the importance of evaluating gestational phthalates exposure in a mixture to identify non-linear dose-response patterns and to disentangle potentially complex environmental reproductive health race disparities.

4.3. Associations between gestational phthalates and AGDs in female infants

Few investigators have reported on associations between gestational urinary phthalate exposure and AGDs among female infants (26, 44). The Maternal-Infant Research on Environmental Chemicals (MIREC) study, a prospective birth cohort study of 196 mother-infant pairs in Canada, reported inverse (mean difference = −1.24 mm per log_e µg/l; 95% CI: −1.91, −0.57; *p*-value = 0.0004) and positive (mean difference = 0.65 mm per log_e µg/l; 95% CI: 0.12, 1.18, *p*-value = 0.02) associations for ACD with first-trimester maternal urinary MBzP and MEP concentrations, respectively, although without a significant association for AFD (23). However, the study population consisted mostly (>90%) of women who identified as White. Another multi-city U.S. birth cohort study of 373 mother infant pairs, The Infant Development and Environment Study (TIDES) found no association between 12 first-trimester maternal urinary phthalates and ACD or AFD, however, the results were not stratified by racial identity although 33.6% of the study population identified as non-White (44).

In our previous work in the same study population used here, we found statistically significant differences in the associations between ACD and maternal urinary MEP and the sum of urinary DBP metabolites among the female newborns of women

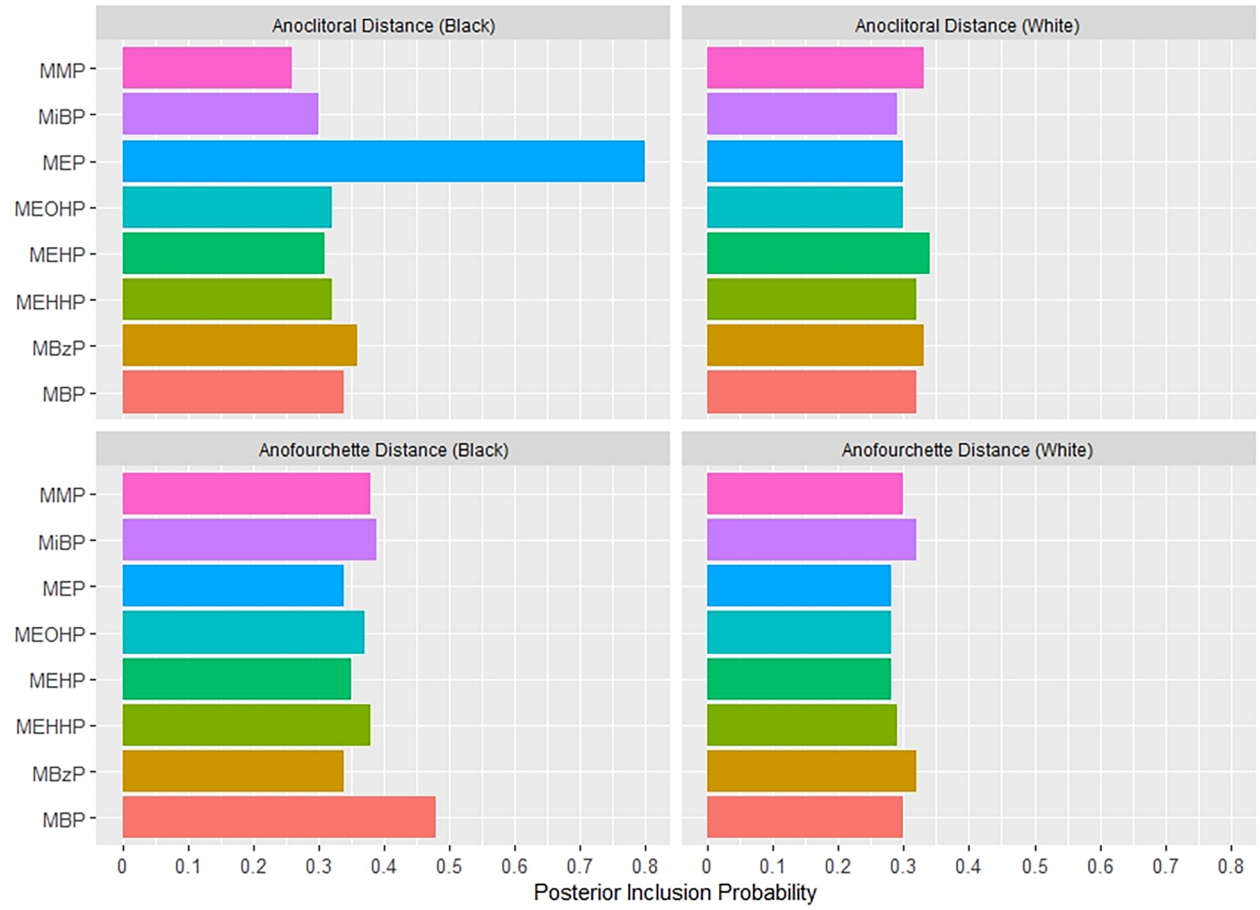

FIGURE 5
Posterior inclusion probabilities for urinary phthalate metabolite predictors of postnatal anogenital distance measures among female infants born to women in Charleston, South Carolina, by racial identity ($n = 131$).

who identified as Black (mean difference = −1.13 mm per $\log_e$ ng/ml; 95% CI: −1.90, −0.35 and mean difference = −0.77 mm per $\log_e$ ng/ml; 95% CI: −2.06, 0.51, respectively) as well as among the female newborns of women who identified as White (mean difference = 0.63; 95% CI: −0.42, 1.68 and mean difference = 1.22 mm; 95% CI: −0.66, 3.09, respectively) (26). In our earlier work, a change in MEP and the sum of DBP metabolite concentrations from the 25th percentile to the 90th percentile corresponded to ACD differences of −2.86 mm and −1.08 mm, respectively, among the Black grouping (i.e., vs. −3.40 mm for the mixture in our current work), and ACD differences of +1.33 mm for MEP and +1.80 mm and the sum of DBP, among the White grouping (i.e., vs. 0.06 mm for the mixture in our current work). We did not find evidence of synergism among mixture components. In the current study we found that MEP was an important driver of an inverse, potentially non-linear, association between the mixture of maternal urinary phthalate metabolites and ACD among women who identified as Black, but not for DBP metabolites (MBP and MiBP). The associations between the phthalates mixture and ACD appeared to be stronger than with individual phthalates among the Black grouping, whereas the estimate for the White grouping was closer to the null hypothesis. While our null results for ACD among the White racial identity grouping is consistent with the TIDES results (44), they differ from the individual phthalate exposure model results reported by MIREC (23). The associations between maternal urinary phthalates and offspring AFD have been consistently null, using individual maternal urinary phthalates as predictors in prior studies and a mixture of maternal urinary phthalate metabolites in the current study. The reason for discordant effect estimates between urinary phthalates and measures of ACD and AFD is unclear and results of experimental studies of gestational exposure to endocrine disrupting chemicals and female AGDs is mixed (24). A future study that measures fourchette-clitoral distance may offer further insight into the nature of the discrepancy.

4.4. Potential mechanisms

We found gestational phthalate mixtures tended to have stronger associations with infant genital measures among mothers who self-identified as Black compared to White. The racial disparity might be attributed in part to differences in dose

levels as women in the Black racial grouping had greater urinary MBP, MiBP, MEHP, and MEP concentrations. However, women in the Black and White groupings had similar MEOHP concentrations. Unaccounted differences in maternal factors (24), including allostatic load and structural racism (45) may also play a role in "potentiating" gestational phthalate exposures. A future study that incorporates comprehensive psychosocial stress and lived experiences data will be necessary for a more definitive interpretation of the results.

4.5. Strengths and limitations

Our study has several notable strengths. Most saliently, we used a mixtures-based approach to estimate the associations of infant genital measures with simultaneous gestational exposure to eight urinary phthalate metabolites, an approach that more closely approximates "real world" exposure scenarios compared to that achieved using single phthalate predictor models in previous studies (28). We implemented BKMR, which allows for interactions among the phthalate mixture components and for non-linear associations with the study endpoints (33). Because our study population included a substantial proportion of women who self-identified as Black, we were also able to conduct a stratified analysis to estimate racial disparities in the associations between gestational exposure to a mixture of phthalates and fetal genital measures. We adjusted regression models for important confounding factors and all outcome measures were performed in triplicate, using a standardized protocol, to ensure quality control and minimize outcome misclassification. Finally, our prospective birth cohort design ensured temporality between mid-gestation exposure to a phthalates mixture and postnatal genital measurements among infants.

There are also important limitations to this study. The masculinization programming window (MPW) that governs fetal genital development is believed to occur primarily between 8 and 14 weeks' gestation (46), so our urine collection at 18–22 weeks' gestation may have misclassified exposure in some participants with a bias towards the null hypothesis. Phthalates have a short half-life *in vivo*, on the order of hours, and tend to vary across time within person, which may have further misclassified exposure in some women (47, 48). We also considered a limited panel of eight phthalate metabolites, which were highly prevalent in the U.S. population at the time of our study. However, additional phthalates found in common exposure sources, such as personal care products, may have biased our study results, so a future study with a more comprehensive phthalates mixture is necessary to confirm our results (49).

5. Conclusions

We found mostly inverse associations between gestational exposure to a mixture of maternal urinary phthalates and genital measure outcomes except for the measures of ASD and AFD, especially in male and female infants born to women who self-identified as Black. We also found a "U-shaped" association between ultrasound-derived PV and a mixture of phthalates among male infants in the Black racial grouping. However, the racial groupings had small sample sizes and wide credible intervals. Collectively, our results suggest a potential feminizing, anti-androgenic effect of phthalate mixture exposure during gestation. In addition, we also identify a potential racial disparity in the association between gestational phthalate exposure and fetal genital development. To our knowledge, this is the first study to report on the associations between gestational exposure to a mixture of urinary phthalate metabolites and fetal genital developmental measures among a racially diverse population. Further studies should estimate the associations between gestational exposure to a more comprehensive mixture of phthalates with multiple specimen collections across pregnancy to provide more definitive evidence for policy makers and regulators in order to guide appropriate interventions.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Institutional Review Board of the Medical University of South Carolina. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

MV: Writing – original draft, Data curation, Formal Analysis, Methodology, Visualization. MB: Writing – review & editing, Conceptualization, Funding acquisition, Methodology, Project administration, Supervision. AW: Investigation, Validation, Writing – review & editing. JB: Conceptualization, Resources, Supervision, Writing – review & editing. JK: Conceptualization, Resources, Supervision, Writing – review & editing. RW: Investigation, Writing – review & editing. RN: Conceptualization, Funding acquisition, Project administration, Resources, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/frph.2023.1304725/full#supplementary-material

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Environmental justice burden and Black-White disparities in spontaneous preterm birth in Harris County, Texas

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Introduction: Given limited evidence of previous studies, we evaluated the role of environmental justice (EJ) burden (i.e., a neighborhood characterized by both increased environmental burden and socioeconomic deprivation) in Black-White disparities in spontaneous preterm birth (sPTB) in Harris County, Texas and compared results that evaluated neighborhood-level socioeconomic deprivation alone.

Methods: We conducted a retrospective analysis using PeriBank, a database and biospecimen repository of gravidae giving birth at two hospitals in the Texas Medical Center. We included 3,703 non-Hispanic Black and 5,475 non-Hispanic white gravidae who were U.S.-born, delivered from August 2011-December 2020, and resided in Harris County, TX. We used data from the U.S. EPA EJScreen to characterize the EJ burden of participant's zip code of residence from fine particulate matter ($PM_{2.5}$), ozone, and proximity to National Priorities List (NPL) sites and calculated zip-code level Area Deprivation Index (ADI). We assessed the contribution of neighborhood-level variables to the Black-White disparity in sPTB by evaluating attenuation of the odds ratio (OR) representing the effect of race in multivariable logistic regression models, controlling for individual-level characteristics. We also conducted race-stratified analyses between each neighborhood variable and sPTB. Exposure indices were treated as continuous variables; in stratified models, ORs and 95% Confidence Intervals (CIs) are presented per 10-unit increase in the neighborhood variable.

Results: Accounting for individual-level variables, Black gravidae had 79% higher odds of sPTB than white gravidae (OR = 1.79, 95%CI = 1.32, 2.44); the disparity was moderately attenuated when accounting for EJ burden or ADI (ORs ranged from 1.58 to 1.69). Though we observed no association between any of the EJ burden indices and sPTB among white gravidae, we found increased risks among Black gravidae, with ORs of similar magnitude for each EJ variable. For example, Black gravidae experienced 17% increased odds of sPTB associated with a 10-unit increase in the EJ burden index for $PM_{2.5}$ (OR = 1.17, 95%CI = 0.97, 1.40). No racial differences were observed in the association of ADI with sPTB.

Discussion: Though we observed limited evidence of the contribution of living in EJ neighborhoods to the Black-White disparity in sPTB, our study suggests living in an EJ neighborhood may differentially impact Black and white gravidae.

KEYWORDS

environmental justice, neighborhood, socioeconomic deprivation, preterm birth, health disparities, racial disparities

1. Introduction

Preterm birth (i.e., the delivery of a neonate prior to 37 weeks gestation) has broad economic and social implications, for both maternal and newborn health. The economic burden of preterm birth in the United States (U.S.) was estimated to be more than $25 billion in 2016; while the majority of these costs were associated with newborn and early childhood medical care, more than $5 billion was attributed to lost productivity in adulthood (1). Pregnant gravidae who deliver a preterm neonate are more likely than their counterparts to develop significant medical co-morbidities later in life, particularly cardiac complications, and preterm neonates are at increased risk of complications ranging from neurologic deficits to pulmonary, cardiac, or metabolic disorders (2–5). Moreover, preterm birth is not borne equally among racial and ethnic groups in the U.S. In 2018, the prevalence of preterm birth among non-Hispanic Black gravidae in this country was 14.1% compared with 9.1% among non-Hispanic white gravidae; further, the prevalence of preterm birth among Black individuals is increasing at a steeper rate than their white counterparts (6) and the burden of the Black-White preterm birth disparity is largely limited to gravidae born in the U.S (7).

Though there are a number of individual-level risk factors associated with the occurrence of preterm birth including maternal age, marital status, parity, maternal smoking, and access to healthcare, these factors alone do not explain the majority of the observed Black-White disparity in prevalence of preterm birth in the U.S (8–13). Thus, there is a need to consider the broader social context within which women live. Following the Ecosocial Theory as outlined by Krieger (14), social inequalities in health and wellbeing are embodied through simultaneous and diverse routes involving, for example, exposure to social inequality and economic deprivation, exogenous hazards (e.g., environmental chemical exposures), and historic trauma. Stressors in the neighborhood environment activate the hypothalamic pituitary adrenal (HPA) axis (15), resulting in release of cortisol that can cross the placenta and adversely impact pregnancy (16, 17). This stress response provides a potential route through which neighborhood features may impact preterm birth risk and potentially mediate racial disparities in preterm birth.

It is also possible that, due to systemic and structural racism, Black and white women "embody" the neighborhood context differently, providing a pathway for race to modify associations between neighborhood contextual factors. Previous U.S.-based studies have attempted to quantify maternal risks associated with living in a socioeconomically deprived neighborhood though results have been mixed (18–21). Further, previous reviews of the U.S.-based literature provide evidence that this association may vary by maternal race (18, 19, 21). In the most recent meta-analysis of the topic published in 2016, Ncube et al. (19) reported a 27% increased risk of preterm birth associated with living in the most socioeconomically deprived neighborhoods compared with the least deprived neighborhoods [odds ratio (OR) = 1.27, 95% confidence interval (CI) = 1.16, 1.39]. However, there was no association between neighborhood socioeconomic deprivation and preterm birth for the sub-set of studies that adjusted for race (OR = 1.01, 95% CI = 0.94, 1.09). Further, this meta-analysis found that the magnitude of ORs representing associations between living in neighborhoods with higher vs. lower levels of socioeconomic deprivation was greater among white (OR = 1.61, 95% CI = 1.30, 2.00) than Black gravidae (OR = 1.15, 95% CI = 1.09, 1.21).

Beyond socioeconomic deprivation, other features of the neighborhood, such as environmental toxicant exposures like air pollution, may adversely impact perinatal health (22, 23). Unfortunately, some communities are doubly burdened by both socioeconomic disadvantage and environmental exposures and are deemed environmental justice (EJ) communities. Hence, measures of neighborhood-level environmental exposure alone do not fully capture the dual dimensions of EJ. In an analysis applying formal decomposition methods, zip-code level air pollution exposure provided only a modest contribution to observed racial disparities in preterm birth in California, pointing to the need to evaluate the impact of the neighborhood context beyond environmental exposure burden to further our understanding of key drivers of racial differences in perinatal health outcomes (10). Yet, few studies, to our knowledge, have explored the impact of living in an EJ communty (i.e., a neighborhood characterized not only by socioeconomic deprivation but also by increased environmental burden) on racial disparities in preterm birth and those investigations have reported equivocal findings. In one study using data for the period 2000–2005, inverse associations were reported between county-level prevalence of preterm birth and county-level environmental quality (considering factors related to both environmental contamination and socioeconomic deprivation) [Rappazzo et al. (24)]. In contrast, a more recent investigation using data from the U.S-based ECHO Cohort found moderately increased odds of preterm birth associated with living in a census tract with higher combined burden of environmental and social stressors (25). Moreover, in a stratified analysis, the association persisted only for Black women, suggesting that living in an EJ neighborhood may differentially impact risk of preterm birth among Black and white women.

Given equivocal and limited evidence of previous studies, we aimed to evaluate the role of EJ burden in Black-White disparities in preterm birth in Harris County, Texas, home to the fourth largest and most diverse city in the U.S. (Houston, TX). A secondary objective was to compare results to the impact of neighborhood-level socioeconomic deprivation alone.

2. Methods

2.1. Study population

We conducted a retrospective data analysis of deidentified data from gravidae enrolled in PeriBank, an IRB-approved perinatal database and biospecimen repository maintained by trained full-time research coordinators at Baylor College of Medicine in Houston, Texas. All gravid patients who are at least 18 years of age (or at least 16 years of age if emancipated) who deliver at our

two institutional hospitals (Ben Taub Hospital and Texas Children's Pavilion for Women) are approached and offered participation in PeriBank, which began recruitment on August 1, 2011 (26). The rate of enrollment into PeriBank among qualified patients has not changed significantly with consent rates ranging from 86% to 90% over the study interval. Regular quarterly audits are done to ensure data accuracy. Maternal sociodemographic characteristics, zip codes in which gravidae lived and worked during the preconception period and in the 1st and 2nd/3rd trimesters during pregnancy, comorbidities, previous pregnancy history, and delivery data are collected and stored in PeriBank via abstraction of electronic medical records and participant interviews. PeriBank and the current study were approved by the Baylor College of Medicine Institutional Review Board.

The present analysis was based on data from self-identified non-Hispanic Black and non-Hispanic white (hereafter referred to as Black and white) gravidae who delivered a singleton live birth with no identified congenital anomaly between August 2011 and December 2020. If gravidae had more than one eligible pregnancy, we randomly selected one pregnancy for the present analysis resulting in 14,043 pregnancies from 5,864 (41.8%) Black and 8,179 (58.2%) white gravidae. We then assessed eligibility based on residence in Harris County using the self-reported zip code of domicile residence in the 2nd/3rd trimester. If this zip code was missing, we relied on the 1st trimester ($n = 22$) or the preconception ($n = 4$) zip code. We excluded 2,466 (17.6%) gravidae with reported zip codes outside of Harris County and 161 (1.4%) gravidae who were missing information on all residential zip codes. We further excluded 1,851 (13.2%) gravidae born outside the U.S. and those missing nativity information ($n = 380$; 3.3%), resulting in 9,181 gravidae (Figure 1).

2.2. Neighborhood-level EJ burden and socioeconomic deprivation

To evaluate the impact of living in EJ communities, we utilized U.S. Environmental Protection Agency's (EPA's) Environmental Justice Screening and Mapping Tool (EJScreen) to generate zip-code level EJ indices for ozone, fine particulate matter ($PM_{2.5}$), and proximity to National Priority List (NPL) sites (i.e., Superfund sites) for Harris County (27). An EJ index combines area-level information for both the specific environmental exposure (e.g., ozone) and population characteristics (e.g., percentages of low income and persons of color). Hence, each EJ index provides a measure of pollution burden due to a particular environmental contaminant or source through a social equity lens. EJ indices are highest in areas where there is both a large pollution burden and high proportion of socioeconomically disadvantaged individuals and are represented as percentile rankings (ranging from 0 to 100) relative to data from the entire state of Texas. The zip code-level EJ indices for ozone, $PM_{2.5}$, and proximity to NPL sites were linked to gravidae based on

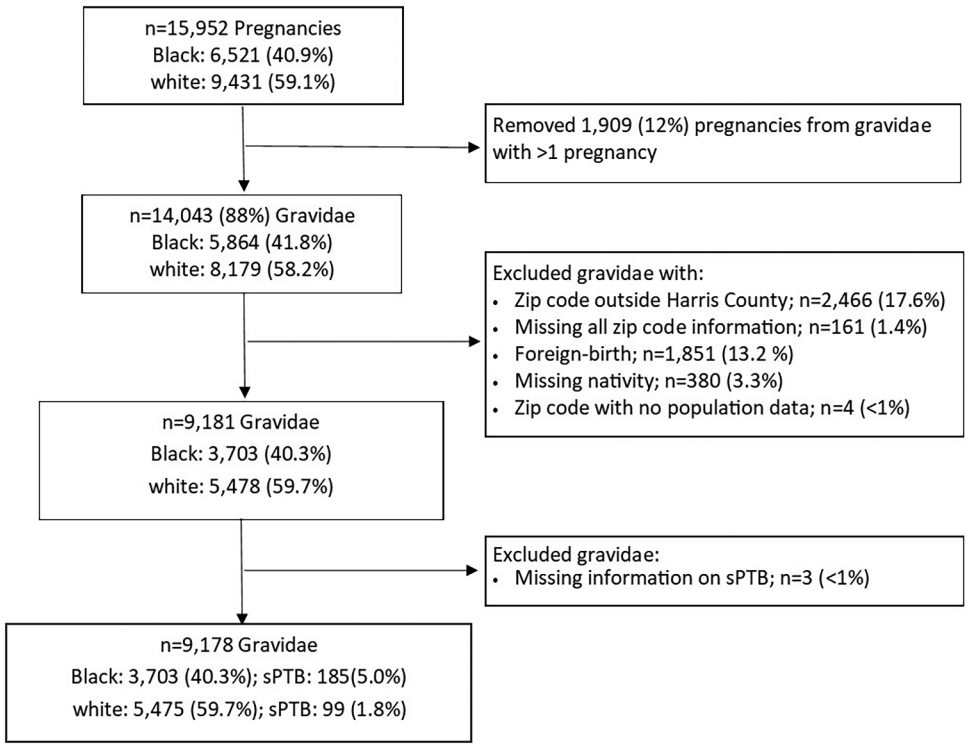

FIGURE 1
Flow chart of study inclusion among non-Hispanic gravidae in PeriBank (2011–2020).

their reported zip code of residence. We excluded four gravidae from two zip codes with no population data (Figure 1).

We also computed the area deprivation index (ADI), a composite metric of 17 indicators from the U.S. Census (28). Higher values of ADI indicate more socioeconomically deprived areas. We obtained zip code tabulation area (ZCTA)-level data from the American Community Survey 5-year estimates (2014–2018) to calculate ADI for all ZCTAs in Harris County and assigned ADI scores to each participant in our study using a ZCTA-to-zip code crosswalk.

2.3. Spontaneous preterm birth

We obtained an indicator of whether a participant experienced spontaneous preterm birth (sPTB; i.e., delivery of an infant prior to 37 weeks of gestation and resulting from preterm premature rupture of the membranes or spontaneous labor) from PeriBank records. Gravidae with indicated preterm birth were excluded from this analysis. Three gravidae (<1%) were missing this outcome information (Figure 1).

2.4. Covariates

We abstracted several covariates from PeriBank records for each study participant including: maternal age (continuous), parity (0, 1, ≥ 2), maternal education (less than a college degree, college degree or higher), marital status (married, unmarried), alcohol consumption (ever, never), insurance (private, other), pre-pregnancy BMI (<25, 25–30, ≥ 30 kg/m^2), smoking (ever, never), adequacy of prenatal care (inadequate/intermediate, adequate, adequate plus) (29). We also calculated a binary variable indicating whether a participant had a history of any of the following previous pregnancy complications: preterm birth, intrauterine growth restriction, macrosomia, stillbirth, preeclampsia, congenital anomaly, gestational diabetes, preterm premature rupture of the membranes, hemorrhage, endometriosis, placental abruption or placenta previa, chorioamnionitis, or oligohydramnios.

2.5. Statistical analysis

We conducted descriptive statistics for the study population as a whole and separately among Black and white gravidae. To explore the impact of ADI and EJ indices on Black-White disparities in the occurrence of sPTB, we conducted a series of complete case logistic regression models using generalized estimating equations to account for clustering among gravidae residing in the same zip code. First, we assessed the crude association between race (Black vs. white) and sPTB (Model 1) to quantify the extent of the Black-White disparity. We then added maternal age, insurance, alcohol use, marital status, adequacy of prenatal care, and history of pregnancy complications) to Model 2 to evaluate the combined contributions of these individual-level sociodemographic and medical characteristics to the Black-White disparity in preterm birth. These covariates were included based on *a priori* knowledge regarding their association with sPTB. Finally, to evaluate whether neighborhood-level factors further attenuated this disparity, we separately included each EJ Index or ADI in Model 2. A comparison of the odds ratio (OR) describing the Black-White disparity in sPTB between models with or without each neighborhood-level variable informs the extent to which each factor contributes to the observed racial disparity. In addition to this approach, which utilizes a mediation framework to evaluate the contribution of neighborhood-level factors on racial disparities, we conducted stratified analyses (adjusted for the same set of covariates as Model 2) to explore whether race modifies associations of neighborhood-level factors with sPTB (30). In all models, the EJ index or ADI was modeled continuously. In the race-stratified models, ORs and 95% confidence intervals are presented based on a 10-unit increase in each neighborhood-level metric.

As a sensitivity analysis, we repeated all analyses excluding variables for adequacy of prenatal care and history of pregnancy complications because they have the potential to mediate associations between neighborhood-level factors and adverse pregnancy outcomes. We then made comparisons to the full models to evaluate whether they obscured the impact of EJ burden or neighborhood-level socioeconomic deprivation on Black-White disparities in sPTB. All analyses were conducted using SAS (version 9.4, SAS Institute Inc., Cary, NC, USA).

3. Results

Our study included 9,178 gravidae: 3,703 (40.3%) Black gravidae and 5,475 (59.7%) white gravidae (Figure 1). Table 1 highlights several differences between these two groups with Black gravidae generally experiencing greater disadvantage than white gravidae. The prevalence of sPTB was 3.1% overall and was more than twice among Black gravidae than among white gravidae (5.0% vs. 1.8%). Compared with their white counterparts, fewer Black gravidae were married (46.3% vs. 91.7%), held at least a college degree (28.5% vs. 78.6%) or had private insurance (24.6% vs. 82.5%). A greater proportion of Black compared with white gravidae had a pre-pregnancy BMI ≥30 kg/m^2 (32.1% vs. 14.8%) or were classified as having received inadequate/intermediate prenatal care (31.8% vs. 9.5%). With the exception of pre-pregnancy BMI and adequacy of prenatal care, the proportion of missing observations for each variable was <5%. The final analytic sample size in our study was 8,086 gravidae, including 121 sPTB among Black gravidae and 80 sPTB among white gravidae.

Among women included in our analytic sample, we observed that the neighborhoods in which Black gravidae live were characterized by greater EJ burden and sociodemographic deprivation, as demonstrated in Figure 2, displaying the cumulative distribution functions for each of the neighborhood-level variables, by race. In all cases, there was a shift in the distribution of values for the neighborhood-level indicator towards higher values among Black as compared with white gravidae. The distributions of neighborhood-level factors are also

TABLE 1 Individual-level maternal sociodemographic characteristics of 9,178 US-born non-Hispanic white and Black gravidae with singleton livebirths in Harris County, Texas, PeriBank (2011–2020).

	All Gravidae (n = 9,178) n (%)	White Gravidae (n = 5,475) n (%)	Black Gravidae (n = 3,703) n (%)
Age			
Mean ± SD	29.8 ± 5.6	31.4 ± 4.7	28.5 ± 6.2
Missing	11 (0.1)	7 (0.1)	4 (0.1)
Pre-pregnancy BMI (kg/m^2)			
<25	4,505 (49.1)	3,284 (60.0)	1,221 (33.0)
25–30	2,002 (21.8)	1,146 (20.9)	856 (23.1)
≥30	1,995 (21.7)	808 (14.8)	1,187 (32.1)
Missing	676 (7.4)	237 (4.3)	439 (11.9)
Parity			
0	4,422 (48.1)	2,716 (49.6)	1,706 (46.1)
1	2,861 (31.2)	1,813 (33.1)	1,048 (28.3)
≥2	1,886 (20.6)	941 (17.2)	945 (25.5)
Missing	9 (0.1)	5 (0.1)	4 (0.1)
Married			
No	2,389 (26.0)	432 (7.9)	1,957 (52.9)
Yes	6,731 (73.3)	5,018 (91.7)	1,713 (46.3)
Missing	58 (0.6)	25 (0.5)	33 (0.9)
Highest level of education			
<College degree	3,521 (38.4)	1,020 (18.6)	2,501 (67.5)
College degree or higher	5,355 (58.4)	4,301 (78.6)	1,054 (28.5)
Missing	302 (3.3)	154 (2.8)	148 (4.0)
Smoking			
Ever	2,032 (22.1)	1,263 (23.1)	769 (20.8)
Never	7,141 (77.8)	4,209 (76.9)	2,932 (79.2)
Missing	5 (0.1)	3 (0.1)	2 (0.1)
Alcohol Consumption			
Ever	6,854 (74.7)	4,518 (82.5)	2,336 (63.1)
Never	2,318 (25.3)	954 (17.4)	1,364 (36.8)
Missing	6 (0.1)	3 (0.1)	3 (0.1)
Insurance			
Private	5,429 (59.2)	4,519 (82.5)	910 (24.6)
Other	3,484 (38.0)	814 (14.9)	2,670 (72.1)
Missing	265 (2.9)	142 (2.6)	123 (3.3)
Adequacy of prenatal care			
Inadequate/ intermediate	1,695 (18.5)	518 (9.5)	1,177 (31.8)
Adequate	3,727 (40.6)	2,651 (48.4)	1,076 (29.1)
Adequate plus	2, 927 (31.9)	1,950 (35.6)	977 (26.4)
Missing	829 (9.0)	356 (6.5)	473 (12.8)
Previous pregnancy complications			
Yes	3,110 (33.9)	1,747 (31.9)	1,363 (36.8)
No	6,066 (66.1)	3,728 (68.1)	2,338 (63.1)
Missing	2 (0.02)	0 (0.0)	2 (0.04)
Spontaneous Preterm Birth			
Yes	284 (3.1)	99 (1.8)	185 (5.0)
No	8,894 (96.9)	5,376 (98.2)	3,518 (95.0)

presented in Supplementary Table S1. The median and interquartile range (IQR; 25%, 75%) for the EJ Index for $PM_{2.5}$ was 88 (85, 92) for Black and 69 (59, 85) for white gravidae, respectively. The race-specific distributions of the EJ Index for ozone were similar to that of the EJ Index for $PM_{2.5}$. The median EJ Index for NPL sites was 86 (79, 92) among Black and 66 (57, 80) among white gravidae. The median (IQR) of ADI was 109.8 (103.2, 115) and 90.7 (69.8, 102.8) for Black and white gravidae, respectively. The spread in the distribution of values for each neighborhood-level variable was much smaller for Black than for white gravidae as evidenced by the relatively narrow interquartile ranges and steep rise of the cumulative distribution functions, particularly for the EJ $PM_{2.5}$ and ozone indices.

3.1. Evaluation of EJ burden and ADI as mediators of Black-White disparities in sPTB

Overall, we found more than twice the odds of sPTB among Black compared with white gravidae [Table 2, Model 1: OR = 2.46, 95% CI = 1.89, 3.19]. Adjusting for individual-level sociodemographic variables attenuated, but did not diminish, this disparity (Table 2, Model 2: OR = 1.79, 95% CI = 1.32, 2.44). The Black-White disparity in sPTB after accounting for individual-level variables was only moderately attenuated when further accounting for EJ burden of $PM_{2.5}$ (OR = 1.68, 95% CI = 1.21, 2.32), ozone (OR = 1.68, 95% CI = 1.22, 2.32), NPL sites (OR = 1.69, 95% CI = 1.25, 2.29) or ADI (OR = 1.58, 95% CI = 1.14, 2.18).

3.2. Race as a modifier of associations between EJ burden or ADI and sPTB

In the race-stratified analyses (Table 3) we observed an increased odds of sPTB in association with each EJ index among Black gravidae and no association between each EJ index and sPTB among white gravidae. The ORs describing the association of a 10-unit increase in the neighborhood-level EJ Index for $PM_{2.5}$ with sPTB was 1.17 (95% CI = 0.97, 1.40) for Black and 1.02 (95% CI = 0.86, 1.21) for white gravidae. Similar associations were observed between the EJ indices for ozone and NPL sites with sPTB. The association between living in a neighborhood with a higher ADI (i.e., a more socioeconomically deprived neighborhood) was the same for both racial groups (Black: OR = 1.11, 95% CI = 0.95, 1.30; white: OR = 1.11, 95% CI = 0.98, 1.25).

In our sensitivity analyses, models that did not include prenatal care and previous pregnancy complication produced similar conclusions (Supplementary Tables S2 and S3).

4. Discussion

Our study utilized data from an existing and well curated perinatal data repository to explore the role of EJ burden in Black-White disparities in sPTB birth in Harris County, Texas, home to the fourth largest and most diverse city in the U.S.—Houston. We additionally evaluated the role of neighborhood socioeconomic deprivation alone, via ADI. In our study, set in an area characterized by a network of dense, heavily trafficked

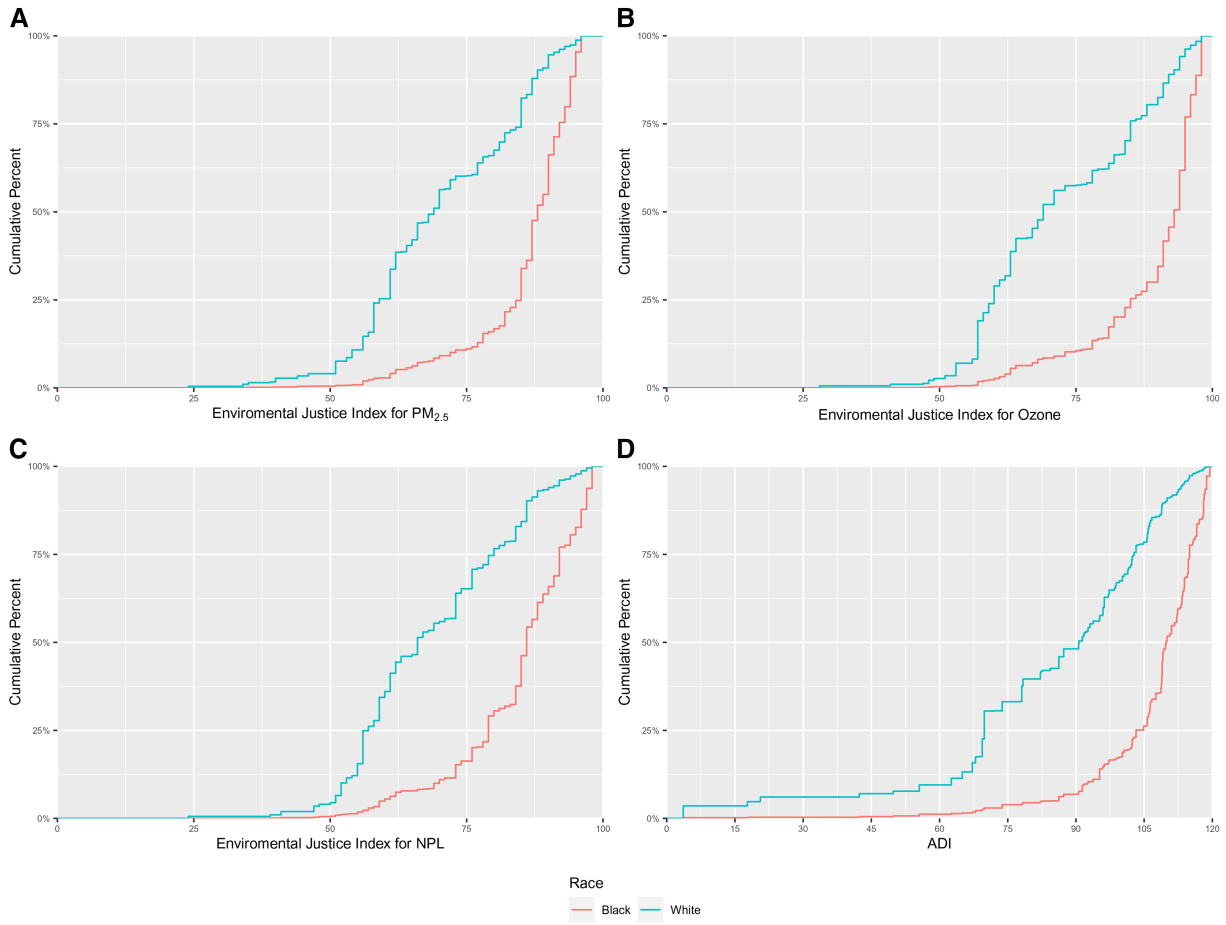

FIGURE 2
Cumulative distributions of (**A**) environmental justice (EJ) index for fine particulate matter ($PM_{2.5}$); (**B**) EJ index for ozone; (**C**) EJ index for national priority list (NPL) sites; and, (**D**) area deprivation index (ADI) among 8,086 US-born non-Hispanic Black and white gravidae in Harris County, Texas, PeriBank (2011–2020).

TABLE 2 Odds ratios describing the Black-White disparity in spontaneous preterm birth among 8,086 US-born non-Hispanic Black and white gravidae in Harris County, Texas, PeriBank (2011–2020).

	OR (95% CI)
Model 1[a]	2.46 (1.89, 3.19)
Model 2[b]	1.79 (1.32, 2.44)
Model 2[b] + EJ index for $PM_{2.5}$	1.68 (1.21, 2.32)
Model 2[b] + EJ index for ozone	1.68 (1.22, 2.32)
Model 2[b] + EJ index for NPL sites	1.69 (1.25, 2.29)
Model 2[b] + ADI	1.58 (1.14, 2.18)

ADI, area deprivation index; CI, confidence interval; EJ, environmental justice; NPL, national priorities list; OR, odds ratio; $PM_{2.5}$, fine particulate matter.
[a]Crude association between race (Black vs. white) and spontaneous preterm birth.
[b]Association between race (Black and white) and spontaneous preterm birth adjusted age, insurance, alcohol use, marital status, adequacy of prenatal care, and previous pregnancy complications.

TABLE 3 Associations[a] between EJ indices and ADI and spontaneous preterm birth among 8,086 US-born non-Hispanic Black and white gravidae in harris county, Texas, periBank (2011–2020).

	White Gravidae	Black Gravidae
	OR (95% CI)	OR (95% CI)
EJ index for $PM_{2.5}$	1.02 (0.86, 1.21)	1.17 (0.97, 1.40)
EJ index for ozone	1.01 (0.86, 1.18)	1.18 (0.99, 1.41)
EJ index for NPL sites	0.97 (0.82, 1.15)	1.16 (0.98, 1.39)
ADI	1.11 (0.98, 1.25)	1.11 (0.95, 1.30)

ADI, area deprivation index; CI, confidence interval; EJ, environmental justice; NPL, national priorities list; OR, odds ratio; $PM_{2.5}$, fine particulate matter.
[a]Adjusted for age, insurance, alcohol use, marital status, adequacy of prenatal care, and previous pregnancy complications.

roadways, many hazardous waste sites, no zoning laws, and the largest seaport in the nation, U.S.-born Black gravidae had substantially greater odds of sPTB compared with U.S.-born white gravidae. Though we found only a modest contribution of neighborhood factors (either EJ burden or ADI) to Black-White disparities in sPTB among women in our study, our analyses suggest racial differences in the magnitude of associations between neighborhood measures of EJ burden and sPTB.

Because individual-level characteristics do not fully explain observed Black-White disparities in preterm birth (8, 9, 11), we must look to other factors, including the neighborhood context, to evaluate their role as key drivers of disparities. While the

physiology and timing of initiation of labor persists as largely poorly understood, aspects of the neighborhood environment may increase psychosocial stress experienced by pregnant persons (31). For example, it has been suggested that chronic stress exposures are associated with the release of catecholamines and activation of the HPA-axis, triggering downstream events such as the release of cortisol, which is transported across the placenta (16, 17, 32). While previous reviews provide evidence of the adverse perinatal impact of living in socioeconomically disadvantaged neighborhoods (18, 19), other investigations have attempted to assess the specific contribution of the neighborhood-level socioeconomic context to racial and ethnic health disparities—that is, whether consideration of such factors attenuates the risk of adverse perinatal health outcomes among Black compared with white gravidae. For example, Benmarhnia et al. (10) found zip code-level neighborhood socioeconomic characteristics (i.e., unemployment, poverty, linguistic minority, educational attainment) explained 16.1% of the observed Black-White disparity in preterm birth, nearly equal to the proportion (17.5%) of the disparity explained by individual-level factors (i.e., maternal education, age at delivery, Medicaid enrollee, and missing paternal information).

However, we are aware of only a handful of studies evaluating perinatal health impacts of living in an EJ neighborhood (that is, a neighborhood jointly characterized by increased pollution burden and socioeconomic deprivation) (24, 25, 33–36). In a county-level analysis, Rappazzo et al. (24) reported lower prevalence of preterm birth among counties with poorer overall environmental quality, assessed via a county-level composite index of variables from four environmental domains: air, water, built, and sociodemographic (37). However, the authors also reported differences in the direction and magnitude of associations when they evaluated domain-specific associations and within urban-rural strata (24). Additionally, in a follow-up study, there was evidence of interactions among domain-specific effects on county-level prevalence of preterm birth (36). On the other hand, Martenies et al. (25) constructed a census-tract level exposure index incorporating information relating to air pollution, built environment, and social exposures, and found increased risk of preterm birth among women living in areas with greater combined environmental and social exposures. We are unaware of studies that have explicitly evaluated whether Black-White disparities in perinatal health outcomes are mediated through residence in an EJ neighborhood. Although accounting for EJ burden (or ADI) attenuated the observed Black-White disparity in sPTB in the present study, the attenuation was modest, pointing to potential (as yet) unmeasured determinants of this disparity in our population.

To fully explore how the neighborhood context might influence health disparities, stratified analyses may provide insight into the potential differential impact that living in a disadvantaged context may have among gravidae of different racial groups (30). The only previous study of which we are aware that has evaluated racial differences in the impact of living in an EJ neighborhood is the study by Martenies et al. (25) which included pregnant individuals across the U.S. who were enrolled in the national ECHO Cohort. When stratified by race, the authors found no evidence of an association between a one standard deviation increase in the census tract-level combined cumulative exposure index and risk of preterm birth among white participants (RR = 0.99; 95% CI = 0.95, 1,03) although they report an 8% increased risk of preterm birth among Black participants (RR = 1.08, 95% CI = 1.00, 1.16). In the current study, we also found suggestive evidence that the impact of living in an EJ neighborhood is limited to Black gravidae. Metrics of EJ burden may capture evidence of systemic or structural racial inequities which amplify adverse effects of environmental toxicant exposure amongst Black and other vulnerable and marginalized populations (31).

Interestingly, our evaluation of living in neighborhoods characterized by socioeconomic deprivation (without regards to increased environmental exposure burden) revealed a different pattern of association. In the current study, we observed identical effect estimates representing the association between ADI and sPTB among Black and white gravidae, in contrast to the results of the analyses of EJ Indices, where associations were only observed among Black gravidae. Although the literature is generally supportive of associations between neighborhood socioeconomic deprivation and adverse perinatal health outcomes overall (18, 19), results of previous studies investigating race-specific associations between neighborhood socioeconomic deprivation and preterm birth have been mixed (18–20, 38–40), with some studies indicating larger effect estimates associated with living in a socioeconomically disadvantaged neighborhood among white compared with Black gravidae (19) while others report the opposite (18). Given mixed results, future analyses using data from studies that allow the characterization of specific aspects of the neighborhood context as well as individual-level stressors and buffers may help further inform mechanisms through which the neighborhood environment may (or may not) differentially impact Black and white gravidae and result in disproportionate perinatal health outcomes.

Our study included a relatively large number of births, spanning nine years and including more than 8,000 women. Even so, given the low prevalence of sPTB, our analysis suffered from small numbers. Because there were few cases of sPTB in several strata when data were stratified by both race and categories of exposure, we present associations based on 10-unit increases in each neighborhood factor, which was around a single standard deviation in the distributions of the EJ indices and less than 1 standard deviation in the distribution of ADI; this approach to analyzing environmental justice burden variables is also similar to that utilized in a previous investigation (25). However, it is possible that the relation between living in a deprived neighborhood and sPTB would be better characterized through a comparison of gravidae who live in areas with relatively higher vs. lower socioeconomic deprivation or environmental justice burden. Interestingly, the distributions of indices representing environmental justice burden due to $PM_{2.5}$, ozone, and NPL sites were very similar and thus, it is likely that these metrics were all measuring generalized EJ burden. It is also possible that the neighborhood measures we used did not fully capture the scope of EJ burden or socioeconomic deprivation experienced by gravidae in our study, in part due to the exposure misclassification resulting from the relatively large geographic area covered by zip codes. In

contrast, smaller geographical units would better capture dimensions of the neighborhood context. Although our analysis was constrained to the use of zip codes to define participant's neighborhood environment, we recommend future studies to further investigate the present findings using data sources that allow for a more spatially resolved neighborhood assessment.

In this study of retrospectively collected data from a large number of U.S.-born gravidae living in the third most populous county in the U.S. with myriad sources of environmental exposure and demonstrated environmental injustice, we observed clear evidence of Black-White disparities in sPTB, an outcome with immense public health implications. Though we observed only moderate evidence of the contribution of living in EJ neighborhoods to this disparity, our study suggests living in an EJ neighborhood may differentially impact Black and white gravidae.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: PeriBank data are available for any investigator to access with appropriate approvals by the PeriBank Governing Board and their local Institutional Review Board. Requests to access these datasets should be directed to Jia Chen (jiac@bcm.edu).

Ethics statement

The studies involving humans were approved by Baylor College of Medicine Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

KW: Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Supervision, Writing – original draft. IM: Data curation, Writing – review & editing. HS: Conceptualization, Writing – review & editing. AC: Data curation, Writing – review & editing. MS: Data curation, Writing – review & editing. KA: Data curation, Writing – review & editing. ES: Conceptualization, Funding acquisition, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

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Racial and ethnic disparities in preterm birth: a mediation analysis incorporating mixtures of polybrominated diphenyl ethers

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Background: Racial and ethnic disparities persist in preterm birth (PTB) and gestational age (GA) at delivery in the United States. It remains unclear whether exposure to environmental chemicals contributes to these disparities.
Objectives: We applied recent methodologies incorporating environmental mixtures as mediators in causal mediation analysis to examine whether racial and ethnic disparities in GA at delivery and PTB may be partially explained by exposures to polybrominated diphenyl ethers (PBDEs), a class of chemicals used as flame retardants in the United States.
Methods: Data from a multiracial/ethnic US cohort of 2008 individuals with low-risk singleton pregnancies were utilized, with plasma PBDE concentrations measured during early pregnancy. We performed mediation analyses incorporating three forms of mediators: (1) reducing all PBDEs to a weighted index, (2) selecting a PBDE congener, or (3) including all congeners simultaneously as multiple mediators, to evaluate whether PBDEs may contribute to the racial and ethnic disparities in PTB and GA at delivery, adjusted for potential confounders.
Results: Among the 2008 participants, 552 self-identified as non-Hispanic White, 504 self-identified as non-Hispanic Black, 568 self-identified as Hispanic, and 384 self-identified as Asian/Pacific Islander. The non-Hispanic Black individuals had the highest mean ∑PBDEs, the shortest mean GA at delivery, and the highest rate of PTB. Overall, the difference in GA at delivery comparing non-Hispanic Black to non-Hispanic White women was −0.30 (95% CI: −0.54, −0.05) weeks. This disparity reduced to −0.23 (95% CI: −0.49, 0.02) and −0.18 (95% CI: −0.46, 0.10) weeks if fixing everyone's weighted index of PBDEs to the median and the 25th percentile levels, respectively. The proportion of disparity mediated by the weighted index of PBDEs was 11.8%. No statistically significant mediation was found for PTB, other forms of mediator(s), or other racial and ethnic groups.

Conclusion: PBDE mixtures may partially mediate the Black vs. White disparity in GA at delivery. While further validations are needed, lowering the PBDEs at the population level might help reduce this disparity.

KEYWORDS

health disparities, race and ethnicity, preterm birth, gestational age, chemical stressors, polybrominated diphenyl ethers, mediation analysis, environmental mixtures

1 Introduction

Preterm birth (PTB) affects 9%–10% of pregnancies in the United States, and is associated with increased risk of maternal and neonatal morbidity and mortality (1, 2). There are pronounced racial and ethnic disparities in PTB in the United States, with rates disproportionately higher in non-Hispanic Black women than non-Hispanic White women (14% vs. 9%) (3, 4). These disparities may further contribute to higher infant mortality (4) among non-Hispanic Black relative to non-Hispanic White infants. For other groups, studies showed no significant difference in PTB rate comparing Asian or Hispanic women to White women, although the risk appeared higher in certain Asian subgroups (5). Therefore, identifying the potentially modifiable risk factors of PTB, especially those that are unevenly distributed across racial and ethnic groups, is important, to help understand and reduce the disparities in PTB.

The existing literature suggests that disparities in PTB are largely attributable to environmental factors rather than genetic variation (3, 6, 7). These include social stressors, physical stressors (such as environmental chemicals and pollutants), neighborhood variation, healthcare access/quality, and individual cultural practices (8). One study suggested that certain sociodemographic and perinatal health factors contributed to the Black vs. White disparity in PTB, although they reported that more than 60% of the disparities in PTB remained unexplained (9). Other studies also showed that the Black vs. White disparities in PTB persisted after accounting for socioeconomic status, access to care, or medical interventions (10–12). For environmental pollutants, multiple studies revealed associations of air pollution, lead, phthalates, and other chemicals with increased risk of PTB, and found higher exposure levels among non-Hispanic Black women compared with the non-Hispanic White women (13–20). However, it remains unclear whether and what proportion of racial and ethnic disparities in PTB is attributable to different exposures to these environmental factors. A causal mediation analysis (21) is needed to further explore the role of multiple environmental factors on the racial and ethnic disparities in PTB.

There have been recent calls for and developments in the methodology of evaluating environmental factors as potential mediators of health disparities (22–24). Furthermore, given that people are often simultaneously exposed to multiple environmental factors (25, 26), a growing body of conceptual models and statistical methods integrating the joint effects of multiple pollutants into a mediation analysis framework has been proposed, especially in the field of environmental health disparities (27–30). These methods can help quantify the proportion of disparity due to environmental factors, as well as the proportion of disparity that would remain if interventions were made to reduce the levels of these environmental factors. Despite the discussions on this framework and the related methods, a real-world, population-based application of these methods in evaluating the contribution of environmental chemicals/pollutants as a mixture to a health disparity question remains lacking.

One class of environmental chemicals, known as polybrominated diphenyl ethers (PBDEs), has been used as a flame retardant since the 1970s and remains to be detected in the US population even a decade after the voluntary phase out that began in 2004 (31–33). PBDEs have the potential to shed or volatilize into the environment (34). Human beings are exposed to PBDEs via inhalation of contaminated air, ingestion of contaminated food, and contact with indoor dust. We hypothesize that PBDEs might be potential mediators for the racial and ethnic disparities in PTB given the following evidence: (1) multiple studies showed higher exposure levels to PBDEs among non-Hispanic Black women compared with non-Hispanic White women (35–37); (2) studies have found associations between certain PBDE congeners and elevated risk of PTB (38–42). In this study, we aimed to use real-world data from a large, multicenter, multiracial/ethnic cohort of singleton pregnancies in the United States to evaluate whether and the extent to which exposure to PBDEs may contribute to the racial and ethnic disparity in PTB and gestational age at delivery, through applying causal mediation analyses incorporating these chemicals (individually and as mixtures) as potential mediators. Race and ethnicity are socially constructed, and racial/ethnic health disparities are driven by the root cause of structural/institutional racism. With that in mind, we present a causal diagram (43) of our research questions in Figure 1.

2 Methods

2.1 Study population

The study used data from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Fetal Growth Studies—Singleton Cohort, a multicenter, multiracial/ethnic prospective study of 2,802 pregnant women recruited during 2009–2013 from 12 US clinical sites (44). Women aged 18–40 years with a singleton pregnancy were enrolled during 8–13 weeks of gestation and followed through delivery. Further

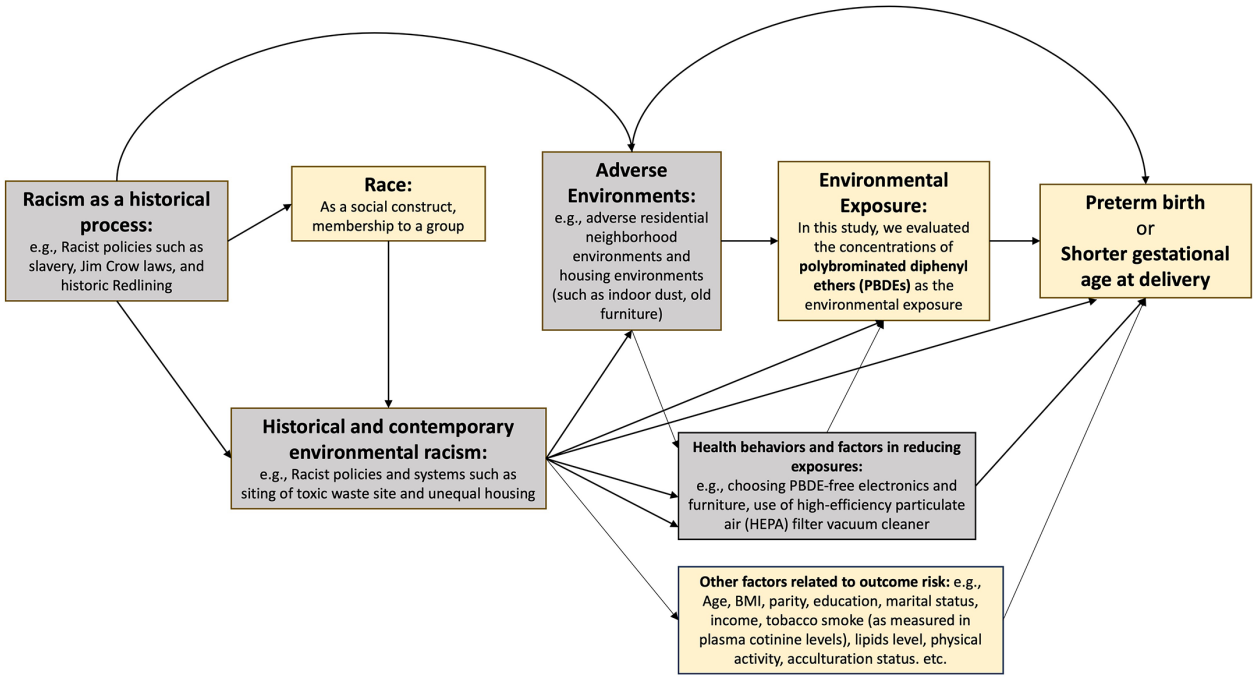

FIGURE 1
Causal diagram for studying racial and ethnic disparities in preterm birth and gestatonal age at delivery, mediated by polybrominated diphenyl ethers. The boxes in yellow correspond to the variables that we were able to measure with available data in this study. The boxes in gray correspond to the variables on the causal pathway that we were not able to measure in this study.

details of the cohort can be found elsewhere (44, 45). For this study, we restricted to a subcohort of 2008 eligible women with a low-risk pregnancy (i.e., those with certain pre-existing medical conditions such as systemic diseases or past pregnancy complications were excluded from enrolling in the study) (44, 45) and without obesity [i.e., individuals whose body mass index (BMI) < 30 kg/m^2], who had available data on gestational age at delivery and measurements of PBDEs from blood specimens. The rationale of these criteria and the numbers excluded are summarized in the Supplementary Material (Supplemental eMethod). Approval for human subjects' research was obtained from the institutional review boards at all participating sites, and all participants provided informed consent.

2.2 Race and ethnicity

Self-identified race and ethnicity were collected at baseline in four categories: non-Hispanic White, non-Hispanic Black, Hispanic, and Asian/Pacific Islander. Further specifications such as self-reported Hispanic origin or Asian background were evaluated in secondary analyses. Non-Hispanic White was defined as the reference group. Too few Hispanic White ($n = 4$) and Hispanic Black ($n = 4$) participants were included to consider these groups separately. We use the self-identified race and ethnicity as the "predictor" parameter in the mediation analysis, while recognizing that race is a social construct (46) that may through racism impact differences in exposures to PBDEs and their sources, as well as differences in factors contributing to PTB or shorter gestational age at delivery, including pathophysiology and access to/quality of prenatal care (7) (Figure 1). As race and ethnicity are non-manipulable, the effect estimates from the mediation analysis should be interpreted as associations reflecting disparity-related (instead of causal/biological) information (23), but we maintained the usage of "effects" when describing these measures to be consistent with common causal mediation terminologies.

2.3 Outcomes

The primary outcomes of interest were: (1) gestational age at delivery (weeks), calculated as the difference between date of delivery (abstracted from medical records) and self-reported date of first day of last menstrual period (LMP) as validated by ultrasound (47); and (2) a binary outcome of PTB, defined as delivery prior to 37 weeks of gestation. As secondary outcomes, PTB was further categorized as very early or moderate (<34 weeks) and late (34 to <37 weeks) PTB.

2.4 Mediators

A set of potential mediators was determined based on prior knowledge (42), which included plasma concentrations of polybrominated biphenyl (PBB) 153 and 9 PBDEs (PBDE 28, 47,

85, 99, 100, 153, 154, 183, and 209) collected upon enrollment (median: 11 weeks of gestation). Details of the processing, measurement, and limits of quantification (LOQs) of these chemicals have been reported previously (48). All chemical concentrations were reported as ng/mL plasma. For this analysis, we restricted to six PBDEs with quantification rates >30% in this population, including PBDE 28, 47, 99, 100, 153, and 154. Machine-observed values were used for all chemicals in the analysis without substitution, including concentrations below the LOQ (49).

2.5 Covariates

The following covariates (collected from the baseline questionnaire unless otherwise specified) were incorporated into our mediation analyses, based on a priori knowledge of being potential confounders for the mediator-outcome associations: maternal age (years); prepregnancy BMI (kg/m^2), calculated from self-recalled prepregnancy weight divided by measured height squared (50); parity (0, 1, 2+); education level (college degree, some college/undergraduate, graduate/postgraduate); marital status (married or living with partner, not married); family income during last year (<$30,000, $30,000–$49,999, $50,000–$99,999, ≥$100,000, not reported); plasma cotinine level (ng/mL), measured in specimens collected at enrollment (35); plasma total lipids (non-fasting) (ng/mL) at enrollment, quantified using commercially available enzymatic methods (51), and calculated as total cholesterol × 2.27 + triglycerides + 62.3 (52); total and sedentary activities [metabolic equivalent of task (MET) hours/week]; and acculturation status (US-born, recent immigrant, long-term immigrant) based on previous definitions (53). It is possible that race and ethnicity are associated with various downstream risk factors, which might violate the assumption of no mediator-outcome confounders affected by the exposure (54). To address this, we conducted sensitivity analyses using more generalized approaches (23), with details described in the statistical analysis.

2.6 Statistical analysis

2.6.1 Descriptive analysis

The characteristics of the study population were summarized with means ± standard deviations or numbers (percentages). Geometric means (GMs) and 95% confidence intervals (CIs) of lipid-adjusted PBDE congener concentrations and their molar sum (∑PBDEs) were calculated, stratified by race and ethnicity and by PTB status.

2.6.2 Mediation analysis

For mediation analysis, we natural log-transformed the machine-observed values of the chemical concentrations to account for skewedness of their distributions, and then performed standardization (subtracted the mean and divided by the standard deviation) to generate comparable scales. The total racial and ethnic (denoted by X) disparity in PTB or gestational age at delivery (denoted by Y) accounting for a set of covariates (denoted by C) was calculated using: $E[Y|X,\ C] = \alpha_0 + \alpha_1 X + \alpha_2 C$ (when Y represents continuous gestational age at delivery, in weeks), or $logit\{Pr[Y = 1|X,\ C]\} = \alpha_0 + \alpha_1 X + \alpha_2 C$ (where $Y = 1$ represents PTB and $Y = 0$ represents non-PTB). The following forms of mediator(s) were then evaluated within a counterfactual framework using causal mediation models (for simplicity, we use a continuous variable Y as an illustration).

2.6.2.1 Reducing the PBDEs mixtures to a single mediator—weighted quantile sum

As the first approach, we reduced the dimensions of the PBDEs mixtures to a single summary index score via the weighted quantile sum (WQS) approach, which is a method that constructs a weighted index estimating the mixture effect associated with all predictor variables on an outcome (55). The weights for each PBDE were empirically determined using a 40%/60% split of training/validation sets from the data and 500 bootstrap samples for parameter estimation. Next, the WQS index was treated as a single summary measure of the PBDE congeners, and was included as a single mediator in the following models:

$$E[Y|X,\ \mathrm{WQS}, C] = \alpha_0' + \alpha_1' X + \alpha_2' \mathrm{WQS} + \alpha_3' C$$

$$E[\mathrm{WQS}|X,\ C] = \beta_0' + \beta_1' X + \beta_2' C$$

The direct and indirect effects through this single mediator were estimated using standard regression-based methods (56).

2.6.2.2 Reducing the number of mediators—select specific mediator(s)

As the second approach, we reduced the number of mediators by selecting a single specific mediator based on the results of a previous study utilizing data from the same cohort of individuals, where multiple statistical approaches [including generalized linear models, principal component analysis, and Bayesian kernel machine regression (BKMR) (57)] have consistently demonstrated PBDE 153 being the main congener associated with shorter gestation and higher risk of PTB, after adjusting for race/ethnicity and other covariates (42). In this study, we further utilized a hierarchical BKMR variable selection approach based on correlation structures of PBDEs in this cohort (which address the potential bias introduced by highly correlated chemicals) to re-evaluate that PBDE 153 is the most important contributor that is associated with gestational age at delivery.

In this approach, we used a single mediator (PBDE 153 as an example) in the following models:

$$E[Y|X,\ \mathrm{PBDE\ 153}, C] = \alpha_0^* + \alpha_1^* X + \alpha_2^* \mathrm{PBDE\ 153} + \alpha_3^* C$$

$$E[\mathrm{PBDE\ 153}|X,\ C] = \beta_0^* + \beta_1^* X + \beta_2^* C$$

The direct and indirect effects through this single mediator were estimated using regression-based methods (56).

2.6.2.3 Modeling all six PBDE congeners as multiple mediators—multiple regression

As the third approach, we included PBDE 28, 47, 99, 100, 153, and 154 simultaneously in the same model:

$$\begin{aligned} E[Y|X,\ \text{PBDEs 28, 47, 99, 100, 153, 154, } C] \\ = \alpha_0'' + \alpha_1'' X + \alpha_2''\text{PBDE 28} + \alpha_3''\text{PBDE 47} \\ + \alpha_4''\text{PBDE 99} + \alpha_5''\text{PBDE 100} \\ + \alpha_6''\text{PBDE 153} + \alpha_7''\text{PBDE 154} + \alpha_8'' C \end{aligned}$$

along with six separate regression models estimating each mediator as a function of the exposure:

$$E[\text{PBDE 28}|X,\ C] = \beta_{0\_28}'' + \beta_{1\_28}'' X + \beta_{2\_28}'' C$$

$$E[\text{PBDE 47}|X,\ C] = \beta_{0\_47}'' + \beta_{1\_47}'' X + \beta_{2\_47}'' C$$

$$E[\text{PBDE 99}|X,\ C] = \beta_{0\_99}'' + \beta_{1\_99}'' X + \beta_{2\_99}'' C$$

$$E[\text{PBDE 100}|X,\ C] = \beta_{0\_100}'' + \beta_{1\_100}'' X + \beta_{2\_100}'' C$$

$$E[\text{PBDE 153}|X,\ C] = \beta_{0\_153}'' + \beta_{1\_153}'' X + \beta_{2\_153}'' C$$

$$E[\text{PBDE 154}|X,\ C] = \beta_{0\_154}'' + \beta_{1\_154}'' X + \beta_{2\_154}'' C$$

The direct and indirect effects (specifically, the joint mediated effect through the set of mediators) were estimated using regression-based methods for multiple mediators (58).

In all the approaches, we estimated the following measures of the disparities in gestational age at delivery and PTB mediated by PBDEs, comparing each of the race and ethnicity groups to the non-Hispanic White group: the total effect (TE), the controlled direct effects (CDEs) while fixing the mediator(s) at various levels, the natural direct and indirect effects (NDE; NIE), and the overall percent mediated (PM) calculated as (NIE/TE) × 100%. All models used regression-based methods, and 95% CIs were obtained via the delta method (from closed-form parameter function estimation in single-mediator models) or bootstrapping (from direct counterfactual imputation estimation in multiple-mediator models). We further extended the models to allow for potential exposure–mediator or mediator–mediator interaction (29, 56, 59).

2.6.3 Secondary and sensitivity analysis

As secondary or sensitivity analyses, we evaluated the outcomes and mediator (WQS index) stratified by finer specifications of race and ethnicity including Hispanic origin or Asian background. We further conducted mediation analysis comparing selective subgroups to non-Hispanic White women. We also performed mediation analysis for PTB subcategories (very early/moderate PTB and late PTB). Furthermore, we evaluated mediation through the WQS index for the absolute risk difference (RD) of PTB using the g-formula approach (60).

Given that some of the proposed mediator-outcome confounders might be downstream factors of racism, hence potentially having an association with race and ethnicity, we conducted sensitivity analyses using the more generalized g-formula approach (23, 60–62), which allowed for a vector of the mediator-outcome confounders potentially affected by the exposure to be accounted for in the analysis.

We also performed the following analyses to evaluate the robustness of our main findings. First, we modeled the WQS index as a binary mediator (≥median vs. <median). Second, we evaluated potential non-linearity via categorizing the PBDEs into <LOQ and quartiles above LOQ, and the WQS index into quintiles, and we used these quantile measures as mediators. Given WQS regression's assumption of unidirectionality, we in addition explored the application of quantile g-computation (63), a flexible extension of WQS estimating the joint effects of a mixture while allowing for chemicals to act on both directions, although with the limitation of being subject to multicollinearity in the presence of highly correlated chemicals within a mixture (64). From the quantile g-computation results, we identified the PBDEs that contributed to the associations with shorter gestational age at delivery, and further created a weighted index of these chemicals as a mediator. Lastly, we conducted sensitivity analysis considering potential measurement errors of the mediator (65).

2.6.4 Statistical software

All causal mediation analyses were conducted using the CMAverse (v.0.1.0) package in R (https://bs1125.github.io/CMAverse/) (62). The WQS analyses were conducted using the gWQS (v.3.0.0) package in R (https://cran.r-project.org/web/packages/gWQS) (66).

3 Results

Among the 2008 women included in the study, 552 (27.5%) self-identified as non-Hispanic White, 504 (25.1%) self-identified as non-Hispanic Black, 568 (28.3%) self-identified as Hispanic, and 384 (19.1%) self-identified as Asian/Pacific Islander (Table 1). There were several differences in characteristics across these groups (Table 1). On average, compared with non-Hispanic White women, non-Hispanic Black women were younger, had higher BMI, lower education level, and less family income, and were more likely to be unmarried. Non-Hispanic Black women also had the highest plasma cotinine level and total and sedentary activity levels compared with other groups. Hispanic women had the highest mean BMI and plasma total lipid level, the lowest percentage of being nulliparous, and the highest percentages of attaining less than a college degree or being long-term immigrants. Asian/Pacific Islander women had the highest mean age, the lowest mean BMI, plasma cotinine level, and total activity level, as well as the highest percentage of being recent immigrants. Non-Hispanic Black women had shorter mean gestational ages at delivery (39.0 vs. 39.3 weeks) and higher risks of PTB (9.1% vs. 5.1%) compared with non-Hispanic White women. The outcomes among Hispanic or Asian/Pacific Islander women were similar to those of the non-Hispanic White women.

TABLE 1 Characteristics of the study population by race and ethnicity, NICHD Fetal Growth Study–Singleton Cohort (n = 2,008).

	Overall	Non-Hispanic White	Non-Hispanic Black	Hispanic	Asian/Pacific Islander
	(n = 2,008)	(n = 552)	(n = 504)	(n = 568)	(n = 384)
Age (years)	28.3 ± 5.4	30.3 ± 4.4	25.6 ± 5.5	27.1 ± 5.5	30.6 ± 4.5
Prepregnancy BMI (kg/m^2)	23.6 ± 3.0	23.3 ± 2.8	24.2 ± 3.1	24.4 ± 2.8	22.2 ± 2.6
Parity, n (%)					
0	979 (48.8)	299 (54.2)	253 (50.2)	223 (39.3)	204 (53.1)
1	689 (34.3)	184 (33.3)	157 (31.2)	204 (35.9)	144 (37.5)
2+	340 (16.9)	69 (12.5)	94 (18.7)	141 (24.8)	36 (9.4)
Education level					
Less than college degree	554 (27.6)	30 (5.4)	191 (37.9)	267 (47.0)	66 (17.2)
Some college or undergraduate	1,086 (54.1)	336 (60.9)	271 (53.8)	282 (49.6)	197 (51.3)
Graduate or postgraduate	368 (18.3)	186 (33.7)	42 (8.3)	19 (3.3)	121 (31.5)
Marital status[a], n (%)					
Married or living with partner	1,539 (76.6)	518 (93.8)	251 (49.8)	417 (73.4)	353 (91.9)
Not married	467 (23.3)	33 (6.0)	252 (50.0)	151 (26.6)	31 (8.1)
Family income during last year, n (%)					
Less than $30,000	470 (23.4)	21 (3.8)	205 (40.7)	196 (34.5)	48 (12.5)
$30,000–$49,999	288 (14.3)	40 (7.2)	90 (17.9)	125 (22.0)	33 (8.6)
$50,000–$99,999	451 (22.5)	166 (30.1)	86 (17.1)	95 (16.7)	104 (27.1)
$100,000 or more	523 (26.0)	305 (55.3)	57 (11.3)	54 (9.5)	107 (27.9)
Unknown	276 (13.7)	20 (3.6)	66 (13.1)	98 (17.3)	92 (24.0)
Plasma cotinine (ng/mL)[a]	1.1 ± 12.7	1.1 ± 13.2	2.7 ± 20.8	0.3 ± 4.4	0.0 ± 0.2
Plasma total lipids (non-fasting) (mg/dL)[a,b]	610.5 ± 98.7	613.3 ± 95.9	580.8 ± 99.0	628.3 ± 100.4	619.2 ± 91.2
Total activity (MET hours per week)[a]	323.1 ± 167.8	326.0 ± 147.8	354.8 ± 200.6	307.3 ± 158.9	300.3 ± 153.9
Sedentary activity (MET hours per week)[a]	26.1 ± 18.3	20.7 ± 12.2	37.1 ± 22.2	22.6 ± 17.0	24.4 ± 15.6
Acculturation[a], n (%)					
US-born	1,322 (65.8)	514 (93.1)	462 (91.7)	242 (42.6)	104 (27.1)
Recent immigrant (<10 years)	304 (15.1)	16 (2.9)	16 (3.2)	117 (20.6)	155 (40.4)
Long-term immigrant (≥10 years)	379 (18.9)	20 (3.6)	26 (5.2)	208 (36.6)	125 (32.6)
Gestational age at delivery (weeks)	39.2 ± 1.7	39.3 ± 1.5	39.0 ± 2.1	39.3 ± 1.5	39.3 ± 1.3
Preterm birth, n (%)	118 (5.9)	28 (5.1)	46 (9.1)	26 (4.6)	18 (4.7)

Means ± SD for continuous variables. N (%) for categorical variables.
[a]Numbers may not add up to total numbers owing to missing values. Variables with missing values (missing rate) included: marital status (0.1%), plasma cotinine (1.6%), plasma total lipids (1.1%), AHEI 2010 score (37.4%), total activity (0.2%), sedentary activity (0.2%), and acculturation (0.1%).
[b]Total lipids = total cholesterol × 2.27 + triglycerides + 62.3.

TABLE 2 Geometric means (95% confidence intervals) of lipid-adjusted PBDE concentrations, stratified by race and ethnicity and by preterm birth status.

Chemicals, ng/g lipid	Race and ethnicity				PTB status	
	Non-Hispanic White	Non-Hispanic Black	Hispanic	Asian/Pacific Islander	Preterm	Non-preterm
	(n = 552)	(n = 504)	(n = 568)	(n = 384)	(n = 118)	(n = 1,890)
PBDE 28	0.20 (0.18, 0.22)	0.29 (0.26, 0.33)	0.30 (0.26, 0.33)	0.25 (0.22, 0.29)	0.28 (0.22, 0.37)	0.25 (0.24, 0.27)
PBDE 47	4.48 (3.77, 5.33)	8.89 (7.49, 10.54)	5.53 (4.55, 6.72)	3.62 (2.88, 4.55)	6.10 (4.12, 9.03)	5.38 (4.87, 5.94)
PBDE 99	0.18 (0.13, 0.25)	0.52 (0.38, 0.73)	0.43 (0.32, 0.58)	0.24 (0.16, 0.34)	0.29 (0.14, 0.58)	0.32 (0.27, 0.38)
PBDE 100	0.55 (0.46, 0.67)	1.44 (1.19, 1.75)	1.01 (0.85, 1.21)	0.52 (0.41, 0.65)	0.84 (0.54, 1.30)	0.82 (0.74, 0.91)
PBDE 153	1.37 (1.16, 1.61)	1.90 (1.61, 2.25)	0.83 (0.73, 0.94)	0.83 (0.71, 0.98)	1.35 (0.95, 1.93)	1.16 (1.07, 1.26)
PBDE 154	0.05 (0.04, 0.07)	0.11 (0.08, 0.15)	0.07 (0.05, 0.09)	0.12 (0.09, 0.17)	0.07 (0.04, 0.14)	0.08 (0.07, 0.09)
∑PBDEs, pmol/g lipid[a]	27.8 (25.2, 30.8)	47.4 (42.8, 52.5)	32.7 (29.6, 36.1)	23.4 (20.6, 26.5)	36.6 (29.4, 45.6)	31.9 (30.2, 33.7)

Geometric means (95% CI) calculated using all machine-observed values including those below the LOQs, where zero and negative values were assigned the value of (lowest positive value)/2. PTB, preterm birth.
[a]∑PBDEs (in pmol/g lipid) refers to the molar sum of PBDEs, which was calculated by dividing each lipid-adjusted chemical concentration by its molecular weight and summing all detectable concentrations.

In Table 2, non-Hispanic Black women have higher GMs of all six PBDE congeners and ∑PBDEs than non-Hispanic White women. Across all groups, Hispanic and Asian/Pacific Islander women had the highest GMs of PBDE 28 and PBDE 154, respectively. When comparing those with vs. without PTB in the study population, four PBDEs (i.e., PBDE 28, 47, 100, and 153) and ∑PBDEs had higher GMs.

We used a WQS index to estimate the mixture effect of six PBDEs on gestational age at delivery (weights for each PBDE shown in Figure 2). The association of a 1-unit increase in the

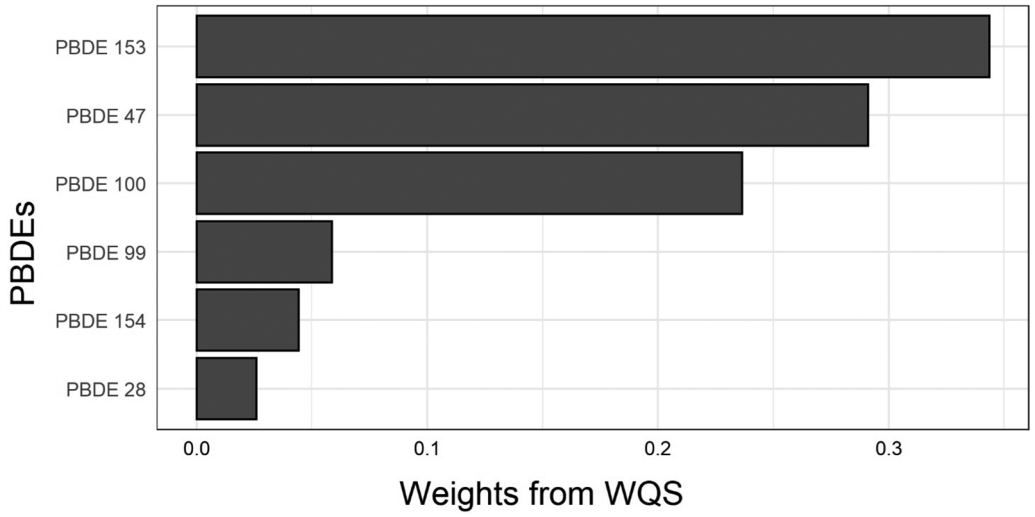

FIGURE 2
Weights for each PBDE congener from the weighted quantile sum index. WQS, weighted quantile sum.

WQS index with gestational age at delivery was β (95% CI) = −0.20 (−0.35, −0.05) weeks, adjusted for race and ethnicity and other covariates. Table 3 provides results from the mediation analysis, where the WQS index was considered a potential mediator for the racial and ethnic disparity of gestational age at delivery or PTB. Comparing non-Hispanic Black women with non-Hispanic White women, the covariate-adjusted difference in gestational age at delivery was β_{TE} (95% CI) = −0.30 (−0.54, −0.05) weeks. The CDEs (95% CIs) when fixing everyone's WQS index levels at the 25th, 50th, and 75th percentiles were −0.18 (−0.46, 0.10), −0.23 (−0.49, 0.02), and −0.32 (−0.57, −0.07) weeks, respectively. Overall, a suggestive NIE of β_{NIE} (95% CI) = −0.04 (−0.07, 0.00) weeks were mediated through the WQS index (proportion mediated = 11.8%). The odds ratio of PTB comparing non-Hispanic Black with non-Hispanic White women was OR_{TE} (95% CI) = 1.82 (1.00, 3.31), yet no statistically significant NIE was found. In addition, no statistically significant disparity was found when comparing Hispanic or Asian/Pacific Islander women with non-Hispanic White women.

The correlation coefficients between PBDEs are shown in Supplementary Figure S1. PBDE 28, 47, 99, and 100 were moderately to highly correlated, and PBDE 153 and 154 were weakly correlated. Using BKMR with hierarchical variable selection (based on the correlation structure, PBDE 28, 47, 99, and 100 were assigned as Group 1, and PBDE 153 and 154 were assigned as Group 2), we found that Group 2 was of relatively greater importance, and PBDE 153 was the most important chemical within Group 2 [reflected by the posterior inclusion probabilities (PIPs) shown in Supplementary Table S1] that was associated with shorter gestational age at delivery (Supplementary Figure S2). There were no qualitative interactions between the PBDEs (Supplementary Figure S3). Thus, for the single-mediator model, we included PBDE 153 as the mediator. Table 4 provides results from the mediation analysis, where only PBDE 153 was considered as a potential mediator. The CDEs (95% CIs) when fixing everyone's PBDE 153 levels at the 25th, 50th, and 75th percentiles were −0.18 (−0.45, 0.09), −0.18 (−0.45, 0.09), and −0.29 (−0.54, −0.05) weeks, respectively, yet with a non-significant NIE mediated via PBDE 153 (proportion mediated = 7.9%). No statistically significant NIE was found for the non-Hispanic Black vs. non-Hispanic White disparity in PTB.

Table 5 provides results when all six PBDEs were included simultaneously as multiple mediators. The CDEs (95% CIs) when fixing all PBDEs at the 25th, 50th, and 75th percentiles were −0.25 (−0.53, 0.02), −0.14 (−0.47, 0.17), and −0.27 (−0.61, −0.03) weeks, respectively, yet with a non-significant NIE jointly mediated via PBDE 28, 46, 99, 100, 153, and 154 (proportion mediated = 16.3%). No statistically significant NIE was found for the disparity in PTB. No exposure–mediator(s) or mediator–mediator interaction was found for any of the aforementioned analyses (p-values for interactions >0.05).

As secondary analysis, the outcomes stratified by further specified Hispanic origin or Asian background are provided in Supplementary Table S2. Several subgroups had shorter mean gestational ages at delivery than non-Hispanic White participants. Among them, those reporting Filipino background also had higher mean WQS index levels than non-Hispanic White women (Supplementary Figure S4). Mediation analysis results comparing Filipino to non-Hispanic White women are provided in Supplementary Table S3. The proportion mediated by WQS index for the shorter gestational age at delivery was 16% (95% CI: −11%, 61%) when comparing the $n = 45$ women with Filipino background with non-Hispanic White women.

The results from the sensitivity analyses to evaluate the robustness of our main results are shown in the Supplementary Materials. In summary, evaluating PTB in subcategories showed no significant findings (Supplementary Table S4), and

TABLE 3 Estimates of direct and indirect effects mediated through a weighted quantile sum exposure index of PBDEs for the associations of race and ethnicity with gestational age at delivery and preterm birth.

Race and ethnicity	Adjusted[a] β (95% CI[b]) for gestational age at delivery, weeks						
	Natural direct effect (β_{NDE})	Natural indirect effect (β_{NIE})	Controlled direct effects (CDEs), fixing the WQS index at the 25th percentile, median, and 75th percentile			Total effect (β_{TE})	Proportion mediated (PM), %
			$\beta_{CDE(25th)}$	$\beta_{CDE(median)}$	$\beta_{CDE(75th)}$		
Non-Hispanic White	REF	REF	REF	REF	REF	REF	REF
Non-Hispanic Black	−0.26 (−0.51, −0.01)	−0.04 (−0.07, 0.00)	−0.18 (−0.46, 0.10)	−0.23 (−0.49, 0.02)	−0.32 (−0.57, −0.07)	−0.30 (−0.54, −0.05)	11.8% (−3.8%, 27.5%)
Hispanic	0.07 (−0.18, 0.32)	−0.01 (−0.03, 0.01)	0.12 (−0.16, 0.40)	0.09 (−0.17, 0.34)	0.03 (−0.23, 0.29)	0.06 (−0.19, 0.31)	−20.7% (−123.7%, 82.2%)
Asian/Pacific Islander	−0.05 (−0.32, 0.21)	−0.01 (−0.03, 0.02)	−0.02 (−0.32, 0.28)	−0.04 (−0.31, 0.23)	−0.08 (−0.35, 0.20)	−0.06 (−0.32, 0.20)	13.1% (−50.6%, 76.7%)
	Adjusted[a] OR (95% CI[b]) for preterm birth						
	Natural direct effect (OR_{NDE})	Natural indirect effect (OR_{NIE})	Controlled direct effects (CDEs), fixing the WQS index at the 25th percentile, median, and 75th percentile			Total effect (OR_{TE})	Proportion mediated (PM), %
			$OR_{CDE(25th)}$	$OR_{CDE(median)}$	$OR_{CDE(75th)}$		
Non-Hispanic White	REF	REF	REF	REF	REF	REF	REF
Non-Hispanic Black	1.79 (0.98, 3.25)	1.02 (0.98, 1.06)	1.77 (0.89, 3.52)	1.78 (0.95, 3.32)	1.79 (0.98, 3.25)	1.82 (1.00, 3.31)	4.0% (−5.1%, 13.1%)
Hispanic	0.89 (0.45, 1.75)	1.01 (0.99, 1.03)	0.83 (0.38, 1.83)	0.85 (0.42, 1.73)	0.89 (0.45, 1.75)	0.90 (0.46, 1.77)	−7.4% (−60.1%, 45.2%)
Asian/Pacific Islander	0.97 (0.47, 2.01)	1.01 (0.98, 1.03)	0.81 (0.35, 1.87)	0.88 (0.41, 1.87)	0.96 (0.47, 1.99)	0.97 (0.47, 2.01)	−29.6% (−807.4%, 748.3%)

[a]Adjusted for maternal age (years), prepregnancy BMI (kg/m^2), parity (0, 1, 2+), education level (<college degree, some college/undergraduate, graduate/postgraduate), marital status (married or living with partner, not married), family income during last year (<$30,000, $30,000–$49,999, $50,000–$99,999, $100,000 or more, not reported), plasma cotinine level (ng/mL), plasma total lipids (ng/mL), total activity (MET hours per week), sedentary activity (MET hours per week), and acculturation (US born, recent immigrant, long-term immigrant). Observations with missing covariates were excluded from the adjusted models.
[b]Standard errors for calculating the 95% CIs obtained using the delta method, based on point estimates obtained using closed-form parameter function estimation.

evaluating the absolute risk of PTB on the risk difference scale showed similar findings (Supplementary Table S5). Using g-estimation yielded similar patterns of mediation (Supplementary Table S6). Modeling the WQS index as a binary mediator dichotomized at the median had very little impact on the indirect effect estimates (Supplementary Table S7). The associations between PBDE 153 or the WQS index and gestational age at delivery were linear (p-trend < 0.05, Supplementary Table S8), and modeling WQS or PBDE 153 as quantiles showed similar mediation effects (Supplementary Tables S9, S10). Using a weighted exposure index of 4 PBDEs (PBDE 28,99, 100, and 153) based on quantile g-computation analysis (selecting the PBDEs with weights toward an association with shortened gestational age at delivery, Supplementary Figure S5) yielded similar mediation patterns as the WQS index (Supplementary Table S11). Finally, Supplementary Figure S6 showed similar estimates across various magnitudes of potential mediator measurement error.

4 Discussion

In this multiracial/ethnic cohort of pregnant women in the United States, we demonstrated shorter gestational age at delivery, higher risk of PTB, and higher exposure levels to PBDEs among non-Hispanic Black than in non-Hispanic White women, and we evaluated potential mediation by PBDEs for the racial and ethnic disparities in gestational age at delivery and PTB utilizing several recently developed causal mediation approaches. In particular, we observed that a weighted index summarizing PBDEs as a mixture had a suggestive mediating role in the Black vs. White disparity in gestational age at delivery that accounted for 11.8% of the total disparity. No significant mediation was found for the disparity of PTB, or from evaluating other forms of PBDE mediators. We also revealed disparities in gestational age at delivery comparing the Filipino subgroup with non-Hispanic White women, although no significant mediation via PBDEs was found. While further validation using larger datasets are needed, our results point to the possibility of PBDE mixtures acting as mediators for the existing racial and ethnic disparities in gestational age at delivery.

Our observation of a higher risk of PTB and shorter mean gestational age at delivery among non-Hispanic Black women compared with non-Hispanic White women is consistent with previous reports (4, 9, 67). However, the PTB risks were lower than the general population since this study consisted of relatively healthy, non-obese individuals. We also observed higher average concentrations of PBDEs comparing non-Hispanic Black with

TABLE 4 Estimates of direct and indirect effects mediated through PBDE 153 concentrations for the associations of race and ethnicity with gestational age at delivery and preterm birth.

Race and ethnicity	Adjusted[a] β (95% CI[b]) for gestational age at delivery, weeks						
	Natural direct effect (β_{NDE})	Natural indirect effect (β_{NIE})	Controlled direct effects (CDEs), fixing PBDE 153 concentration at the 25th percentile, median, and 75th percentile			Total effect (β_{TE})	Proportion mediated (PM), %
			$\beta_{CDE(25th)}$	$\beta_{CDE(median)}$	$\beta_{CDE(75th)}$		
Non-Hispanic White	REF	REF	REF	REF	REF	REF	REF
Non-Hispanic Black	−0.27 (−0.52, −0.03)	−0.02 (−0.06, 0.01)	−0.18 (−0.45, 0.09)	−0.18 (−0.45, 0.09)	−0.29 (−0.54, −0.05)	−0.30 (−0.54, −0.05)	7.9% (−5.4%, 21.1%)
Hispanic	0.05 (−0.20, 0.30)	0.01 (−0.01, 0.03)	0.07 (−0.21, 0.34)	0.07 (−0.21, 0.34)	0.05 (−0.21, 0.30)	0.06 (−0.19, 0.31)	18.4% (−52.2%, 77.6%)
Asian/Pacific Islander	−0.07 (−0.33, 0.19)	0.01 (−0.01, 0.02)	−0.06 (−0.35, 0.23)	−0.06 (−0.35, 0.23)	−0.07 (−0.33, 0.19)	−0.06 (−0.32, 0.20)	−9.0% (−57.8%, 39.8%)
	Adjusted[a] OR (95% CI[b]) for preterm birth (cutoff: 37 weeks)						
	Natural direct effect (OR_{NDE})	Natural indirect effect (OR_{NIE})	Controlled direct effects (CDEs), fixing PBDE 153 concentration at the 25th percentile, median, and 75th percentile			Total effect (OR_{TE})	Proportion mediated (PM), %
			$OR_{CDE(25th)}$	$OR_{CDE(median)}$	$OR_{CDE(75th)}$		
Non-Hispanic White	REF	REF	REF	REF	REF	REF	REF
Non-Hispanic Black	1.81 (0.99, 3.32)	1.01 (0.98, 1.04)	1.92 (0.97, 3.79)	1.92 (0.97, 3.79)	1.81 (0.99, 3.31)	1.82 (1.00, 3.33)	1.3% (−5.0%, 7.6%)
Hispanic	0.89 (0.45, 1.78)	0.99 (0.94, 1.04)	0.91 (0.42, 1.97)	0.91 (0.42, 1.97)	0.89 (0.45, 1.78)	0.88 (0.45, 1.76)	7.3% (−50.4%, 64.9%)
Asian/Pacific Islander	0.98 (0.48, 2.03)	0.99 (0.97, 1.01)	0.90 (0.39, 2.07)	0.90 (0.39, 2.07)	0.98 (0.48, 2.03)	0.97 (0.47, 2.01)	33.9% (−911.4%, 979.2%)

[a]Adjusted for maternal age (years), prepregnancy BMI (kg/m^2), parity (0, 1, 2+), education level (<college degree, some college/undergraduate, graduate/postgraduate), marital status (married or living with partner, not married), family income during last year (<$30,000, $30,000–$49,999, $50,000–$99,999, $100,000, or more, not reported), plasma cotinine level (ng/mL), plasma total lipids (ng/mL), total activity (MET hours per week), sedentary activity (MET hours per week), and acculturation (US born, recent immigrant, long-term immigrant). Observations with missing covariates were excluded from the adjusted models.
[b]Standard errors for calculating the 95% CIs obtained using the delta method, based on point estimates obtained using closed-form parameter function estimation.

non-Hispanic White women, which aligned with previous studies that reported similar disparity patterns among certain PBDEs (e.g., 28, 47, 99, and 100) (36, 68). This disparity may be explained by differences in social and contextual factors contributing to sources of PBDE exposures, such as differences in residential neighborhoods (69), housing (e.g., indoor dust) (70), and furniture PBDE exposures (68). Furthermore, we observed higher mean levels of four PBDE congeners and ∑PBDEs in those who delivered preterm compared with non-preterm, suggesting that PBDEs, either individually or as mixtures, might be potential mediator(s) accounting for part of the disparities in PTB or gestational age at delivery. In our causal mediation analyses, we found that a weighted index of all PBDEs (i.e., the WQS index) accounted for 11.8% of the total Black vs. White disparity in gestational age at delivery. Particularly, we found that the CDEs were closer to the null when fixing everyone's WQS index at lower levels, suggesting the potential benefit in reducing the existing disparity in gestational age at delivery by intervening on PBDE levels in the entire population. Conversely, the proportion mediated by the WQS index for the Black vs. White disparity in PTB was only 4% (and non-significant), which could be explained either by lower statistical power owing to a limited number of events, or that the magnitude of mediation for gestational age at delivery might be relatively small to make a noticeable impact on the risk of PTB in this healthier population. Given this is the first study that evaluated the potential mediation role of PBDEs for this disparity, future studies of larger sample sizes or conducted among a higher-risk population might be needed to validate our findings. Past studies have revealed other mediators (such as socioeconomic and health factors, and access to healthcare) for the racial and ethnic disparity in PTB, but a large proportion of the disparity remained (9–11, 71–73). If PBDEs truly mediate part of the racial and ethnic disparity in length of gestation or PTB, then this class of chemicals might be an additional modifiable factor to help further alleviate this disparity.

Similarly to previous literature (5), we did not observe significant differences in gestational age at delivery or PTB comparing Hispanic or Asian/Pacific Islander women with non-Hispanic women. However, we did find a 38 per 1,000 births higher risk of PTB and 0.5-week shorter mean gestational age at delivery comparing a subgroup of Filipino women with non-Hispanic White women, which was consistent with previous studies showing that Filipino women had higher relative risk of PTB (compared with non-Hispanic White) than other Asian subgroups (74). Despite these Filipino women also having higher exposure levels to PBDEs, the results from mediation analysis were non-significant. This might be due to the small number of participants with various Asian backgrounds, although we could not rule out the possibility that there might be unmeasured confounding such as cultural, psychosocial, or early life factors that are driving this disparity,

TABLE 5 Estimates of direct and indirect effects mediated through concentrations of all six PBDE congeners (PBDE 28, 47, 99, 100, 153, and 154) for the associations of race and ethnicity with gestational age at delivery and preterm birth.

Race and ethnicity	Adjusted[a] β (95% CI[b]) for gestational age at delivery, weeks						
	Natural direct effect (β_{NDE})	Natural indirect effect (β_{NIE})	Controlled direct effects (CDEs), fixing all chemical concentrations at the 25th percentile, median, and 75th percentile			Total effect[c] (β_{TE})	Proportion mediated (PM), %
			$\beta_{CDE(25th)}$	$\beta_{CDE(median)}$	$\beta_{CDE(75th)}$		
Non-Hispanic White	REF	REF	REF	REF	REF	REF	REF
Non-Hispanic Black	−0.25 (−0.54, −0.02)	−0.05 (−0.16, 0.05)	−0.25 (−0.53, 0.02)	−0.14 (−0.47, 0.17)	−0.27 (−0.61, −0.03)	−0.29 (−0.57, −0.11)	16.3% (−16.2%, 81.1%)
Hispanic	0.05 (−0.19, 0.27)	0.01 (−0.05, 0.08)	0.20 (−0.07, 0.46)	0.23 (−0.02, 0.52)	−0.05 (−0.33, 0.21)	0.06 (−0.17, 0.26)	10.4% (−233.6%, 335.5%)
Asian/Pacific Islander	−0.04 (−0.29, 0.20)	−0.03 (−0.14, 0.05)	0.06 (−0.28, 0.36)	0.12 (−0.22, 0.43)	−0.13 (−0.43, 0.15)	−0.07 (−0.39, 0.18)	44.8% (−203.2%, 212.7%)
	Adjusted[a] OR (95% CI[b]) for preterm birth						
	Natural direct effect (OR_{NDE})	Natural indirect effect (OR_{NIE})	Controlled direct effects (CDEs), Fixing all chemical concentrations at the 25th percentile, median, and 75th percentile			Total effect[c] (OR_{TE})	Proportion mediated (PM), %
			$OR_{CDE(25th)}$	$OR_{CDE(median)}$	$OR_{CDE(75th)}$		
Non-Hispanic White	REF	REF	REF	REF	REF	REF	REF
Non-Hispanic Black	1.66 (0.93, 3.16)	1.04 (0.93, 1.15)	1.66 (0.93, 3.21)	1.66 (0.93, 3.20)	1.67 (0.93, 3.19)	1.73 (1.03, 3.04)	9.7% (−27.8%, 47.3%)
Hispanic	0.89 (0.51, 1.75)	1.01 (0.52, 1.74)	0.89 (0.51, 1.76)	0.89 (0.51, 1.76)	0.89 (0.51, 1.75)	0.90 (0.52, 1.74)	−8.7% (−150.4%, 170.8%)
Asian/Pacific Islander	0.97 (0.41, 1.93)	1.00 (0.92, 1.09)	0.97 (0.41, 1.95)	0.97 (0.41, 1.95)	0.97 (0.40, 1.94)	0.97 (0.41, 2.02)	4.8% (−100.2%, 103.3%)

[a]Adjusted for maternal age (years), pre-pregnancy BMI (kg/m^2), parity (0, 1, 2+), education level (<college degree, some college/undergraduate, graduate/postgraduate), marital status (married or living with partner, not married), family income during last year (<$30,000, $30,000–$49,999, $50,000–$99,999, $100,000, or more, not reported), plasma cotinine level (ng/ml), plasma total lipids (ng/mL), total activity (MET hours per week), sedentary activity (MET hours per week), and acculturation (US born, recent immigrant, long-term immigrant). Observations with missing covariates were excluded from the adjusted models.
[b]95% CIs obtained using the bootstrapping method, based on point estimates obtained using direct counterfactual imputation estimation.
[c]TE estimates slightly differ from Tables 3, 4 since causal imputation and bootstrap methods were used for models with multiple mediators.

especially when more than half of the Filipino women in this study were immigrants. Future studies with more specific focus on these racial/ethnic minority subgroups that collect acculturation-related variables are needed to further explore this mediation.

In this study, we compared three different approaches of incorporating PBDEs as potential mediators of racial and ethnic disparities in gestational age at delivery and PTB: reducing to a WQS index, selecting a single PBDE 153 congener according to prior knowledge and its relative importance from the hierarchical BKMR selection, and including six PBDE congeners as multiple mediators. Overall, the estimated proportion mediated via the single PBDE 153 congener was smaller than that via the WQS index. This is possibly owing to the limitation of selecting mediator(s) a priori based on the mediator-outcome association alone, which might leave out important mediator(s) weakly associated with the outcome that may also contribute to the indirect effect. The estimated proportion jointly mediated by multiple PBDEs was higher than the proportion mediated by the WQS index, but with much wider CIs due to potential overfitting or multicollinearity. Our example showed that the WQS approach carries the advantage of reducing the PBDEs to a single score to avoid overfitting or multicollinearity, while preserving the information from each congener, serving as a suitable approach to explore the overall contribution of a chemical mixture to a health disparity question (28).

We acknowledge several limitations of this study. First, this study consisted of women with low-risk of adverse health outcomes at baseline and without obesity, so our findings might not be fully generalizable to the overall US population. Second, unmeasured confounding was inevitable, such as other geographic, psychosocial, or lifestyle factors. Third, statistical power was limited when evaluating potential mediation within certain subgroups. Lastly, we were not able to directly measure historical or contemporary environmental racism or adverse environments in these data that are contributing to (or on the causal pathway for) the observed disparities where race and ethnicity act as a proxy for these complex processes (75). Further studies are needed to inform interventions on the policies and systems level.

This study has many unique strengths. First, this study utilized a prospective cohort design in a large, racially/ethnically diverse population with clinically validated outcomes and a comprehensive set of covariates. Second, we applied different statistical approaches to evaluate mediation(s) through individual as well as mixtures of PBDEs. Third, efforts were made to evaluate mediation for disparities in subcategories of PTB, or

among other under-studied racial and ethnic subgroups (e.g., based on Asian backgrounds). Lastly, we conducted various sensitivity analyses to validate the robustness of our findings.

5 Conclusions

In conclusion, in this multiracial/ethnic cohort of pregnant women in the United States, we found that non-Hispanic Black women had shorter gestational ages at delivery, higher risk of PTB, and higher exposures to PBDEs compared with non-Hispanic White women. Our mediation analysis provided suggestive evidence that the Black vs. White disparity in gestational age at delivery might be partially mediated by disparities in exposures to PBDEs. Lowering the PBDE exposures at the population level may help reduce this disparity.

Data availability statement

The datasets presented in this article are not readily available because of data usage and confidentiality agreements. Requests to access the data should be directed to the corresponding author, the senior author, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development Intramural Research Program. Requests to access the datasets should be directed to Tamarra James-Todd, tjtodd@hsph.harvard.edu.

Ethics statement

The studies involving humans were approved by Eunice Kennedy Shriver National Institute of Child Health and Human Development. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

ZW: Conceptualization, Formal Analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review and editing. CZ: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Resources, Supervision, Writing – review and editing. PW: Conceptualization, Investigation, Methodology, Supervision, Validation, Writing – review and editing. AB: Conceptualization, Investigation, Methodology, Supervision, Writing – review and editing. BW: Investigation, Methodology, Writing – review and editing. KK: Investigation, Methodology, Validation, Writing – review and editing. MB: Funding acquisition, Investigation, Methodology, Writing – review and editing. KH: Funding acquisition, Investigation, Methodology, Writing – review and editing. TJ-T: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review and editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/frph.2023.1285444/full#supplementary-material

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Food security status and cardiometabolic health among pregnant women in the United States

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Introduction: Pregnant women and their offspring are particularly vulnerable to food insecurity and its adverse effects during critical periods of fetal development. Racially/ethnically minoritized women in the United States (US) who are pregnant are additionally burdened by food insecurity, which may exacerbate cardiovascular health (CVH) disparities. Despite heightened social vulnerability, few studies have employed an intersectional framework, including race and gender, to assess the food insecurity and CVH relationship.

Methods: We used 2012–2018 and 2020 National Health Interview Survey data among US pregnant women aged 18–49 years old ($N = 1{,}999$) to assess the prevalence of food insecurity status by race/ethnicity and to investigate household food security status in relation to ideal CVH, using a modified ideal CVH (mICVH) metric. We categorized food security status as "very low/low", "marginal", or "high". To assess mICVH, a summary score of 7 clinical characteristics and health behaviors was dichotomized as yes [(7)] vs. no [<7]. Prevalence ratios (PRs) and 95% confidence intervals (CIs) of associations between food security status and mICVH were estimated using Poisson regression with robust variance. Models were adjusted for age, household income, educational attainment, geographic region, marital status, alcohol consumption, survey year, and race/ethnicity (in overall model).

Results: The mean age ± standard error was 29.0 ± 0.2 years. Among pregnant women, 12.7% reported "very low/low", 10.6% reported "marginal", and 76.7% reported "high" food security. "Very low/low" food security prevalence was higher among NH-Black (16.2%) and Hispanic/Latina (15.2%) pregnant women compared to NH-White (10.3%) and NH-Asian (3.2%) pregnant women. The mICVH prevalence was 11.6% overall and 14.5% for NH-White, 4.1% for NH-Black, 5.0% for Hispanic/Latina, and 26.7% for NH-Asian pregnant women. Among all pregnant women, "very low/low" and "marginal" vs. "high" food security status was associated with a lower prevalence of mICVH {[$PR_{very\ low/low}$ = 0.26 (95% CI: 0.08–0.75)]; [$PR_{marginal}$ = 0.47 (95% CI: 0.23 –0.96)]}.

Conclusion: Household food insecurity was higher among pregnant women in minoritized racial/ethnic groups and was associated with lower mICVH prevalence. Given the higher burden of food insecurity among minoritized racial/ethnic groups, food security may be an important intervention target to help address disparities in poor CVH among pregnant women.

KEYWORDS

food insecurity, ideal cardiovascular health, cardiovascular disease, health inequities, pregnant women, race factors, social determinants of health

Introduction

Food insecurity, defined as a lack of access to nutritious substances because of financial or resource constraints, is a major public health challenge that is associated with poor cardiovascular health (CVH) (1–3). Prior literature suggests that food insecurity is associated with cardiovascular disease (CVD) morbidity and mortality risk (2–6). Vulnerable groups are disproportionately impacted by food insecurity. For instance, pregnant women and their offspring are particularly vulnerable to food insecurity and its adverse effects during critical periods of fetal and child development (7, 8). Food insecurity during pregnancy can compromise fetal development (e.g., spina bifida due to inadequate dietary intake of folic acid) (7) as well as contribute to low birth weight (9) and preterm birth (8), all of which have been disproportionately observed among the offspring of NH-Black women (10–12). Pregnancy can also alter cardiovascular functioning (13), leading to poor CVH, which disproportionately burdens pregnant and postpartum women from minoritized racial/ethnic groups (14, 15). Additionally, women from racially/ethnically minoritized groups in the United States (US) are burdened by food insecurity (1, 16–19), which may consequently exacerbate existing CVH disparities among pregnant women (14, 15). Food insecurity is projected to worsen as climate change increasingly disrupts food systems, potentially reducing the accessibility and affordability of food available to vulnerable groups (20, 21). Food insecurity may also be facilitated by the neighborhood environment of pregnant women, ultimately influencing health behaviors. For instance, structurally racist practices, such as redlining, has symbiotically driven the disinvestment of communities while simultaneously giving rise to food deserts (areas lacking healthy food options) and food swamps (areas heavily concentrated with unhealthy food options), limiting access to nutrient dense food options for pregnant women (22–25). It is worth noting that the term food apartheid (inequitable food environments stremming from racist structures and practices) has been recommended to be used in place of "food deserts" (26, 27).

In 2022, the American Heart Association (AHA) introduced the *Life's Essential 8* as an updated public health strategy to quantify population-level ideal CVH and guide CVD risk mitigation (28). Consisting of modifiable health behavior and CVD risk factors, AHA's *Life's Essential 8* includes smoking status, body mass index (BMI), physical activity, diet, total cholesterol, blood pressure, fasting glucose, and sleep duration, which is a recently established risk factor for CVD (28, 29). Prior studies suggest that compared to men, women are more likely to be food insecure and have a lower prevalence of ideal CVH (1, 18, 19, 30, 31). Additionally, one US study reported that non-Hispanic (NH)-White adults were three times more likely to have ideal CVH compared to NH-Black and Hispanic/Latinx adults (32). Thus, pregnant women from minoritized racial/ethnic groups are more likely to have a lower ideal CVH prevalence compared to those who are NH-White, potentially increasing maternal morbidity risk.

Few studies have employed an intersectional framework—predicated on the idea that the interconnection of systems of power (e.g., race, ethnicity, gender, socioeconomic status) shape oppression and privilege (33)—while investigating the food insecurity and CVH relationship. Fewer were nationally-representative and included pregnant women from minoritized racial/ethnic groups, despite their heightened social vulnerability. Therefore, we investigated household food security status in relation to mICVH prevalence among pregnant women in the US. Since racial/ethnic disparities are observed among the general population for food insecurity (1, 16–19) and mICVH prevalence (32, 34), we hypothesized that "very low/low" and "marginal" food security prevalence as well as mICVH prevalence would be higher among pregnant women belonging to minoritized racial/ethnic groups compared to NH-White women. We also hypothesized that "very low"/'low' and "marginal" vs. "high" food security status is associated with lower mICVH prevalence among pregnant women.

Methods

Study population

We used 2012–2018 and 2020 National Health Interview Survey (NHIS) serial cross-sectional data, which uses three-stage cluster probability sampling to survey non-institutionalized individuals within US households. Further details on the NHIS study design and recruitment have been previously described (35). All NHIS participants provided written informed consent. Additionally, the National Institute of Environmental Health Sciences Institutional Review Board waived approval for the use of non-identifiable, publicly available NHIS data. The final response rate among sampled adults was 50.6% [range: 61.2% (2012)—45.2% (2020)]. Notably, lower average response rates in 2012 compared to 2020 are likely attributed to the shift from in-person to telephone-only household interviews conducted during the COVID-19 pandemic, resulting in lower-income households being underrepresented in the 2020 study sample (36).

Exposure assessment: Food security status

We defined household food security status as "very low/low", "marginal", or "high" using the validated US Department of Agriculture (USDA) Family Food Supplement scale. Our study included the 10-item Family Food Supplement, which was derived from the 18-item Food Security Survey Module (37). The 18-item Food Security Survey Module has been shown to have good reliability (Cronbach $\alpha = 0.81$ for households with children and 0.74 for all households) (38). Participants were asked about food availability and consumption in the past 30 days. For example, questions included "How often (often true; sometimes true; never true; or don't know) did the following happen in the past 30 days": "We couldn't afford to eat balanced meals; We worried whether our food would run out before we got money to buy more; We couldn't' afford to eat balanced meal". Participants were also asked whether or not (yes or no) any of

the followed occurred during the past 30 days: "Did any of your family not eat for a whole day because there wasn't enough money for food?"; Did you ever cut the size of meals or skip meals because there wasn't enough money for food?"; Did you ever eat less than you felt you should because there wasn't enough money for food?". A complete list of the questions is summarized in Supplementary Table S2. If participants responded to an item affirmatively as "yes", "often true", or "sometimes true", responses were counted as 1 and otherwise as 0 (37). Responses were then summed (0–10) and categorized as "very low/low" (3–10), "marginal" (1–2), and "high" (0) food security (37).

Outcome assessment: Ideal cardiovascular health

Modeled after the AHA's *Life's Essential 8*, we developed a modified version of the ideal CVH metric—mICVH—since diet data is unavailable in NHIS (28). A summary score of 7 self-reported clinical characteristics and health behaviors were dichotomized (yes [(7)] or no [<7]) using the following indicators, which were assigned a value of 1 if present and a value of 0 if absent: (1) smoking status (never smoked/quit smoking >12 months prior to study enrollment); (2) recommended body mass index (≥18.5 kg/m^2–<25 kg/m^2); (3) meet physical activity guidelines for Americans [≥150–300 min/week moderate exercise or ≥75–150 min/week vigorous exercise (39)]; (4) recommended sleep duration (7–9 h per night); and no prior diagnosis of (5) dyslipidemia, (6) hypertension, or 7) prediabetes/diabetes. Therefore, if participants indicated "yes" for each indicator, they were considered to have mICVH.

Potential confounders

We considered potential sociodemographic and lifestyle confounders *a priori* based on prior literature. Sociodemographic confounders included: age (18–30 or 31–49 years); annual household income (<$35,000, $35,000–$74,999, ≥$75,000); marital status (married/cohabitating, single/no live-in partner, or divorced/separated/widowed); educational attainment (<high school, high school graduate, some college, or ≥college); geographical region of residence (Northeast, Midwest, South, or West); and survey year. Alcohol consumption [current (heavy), current (≤moderate), former, or lifetime abstainer] was considered as a lifestyle confounder.

Potential modifiers

Race/ethnicity (NH-Asian, Hispanic/Latinx, NH-Black or NH-White) was investigated as a potential effect modifier based on prior literature revealing lower food insecurity and high cardiovascular disease prevalence among women from minoritized racial/ethnic groups (1, 17, 19). In the NHIS, participants self-identify race and ethnicity using standard categories defined by the post 1997 Executive Office of the President, Office of Management and Budget (40). Pregnant women identifying as races and ethnicities other than NH-White, NH-Black, Hispanic/Latina, and NH-Asian [e.g., American Indian/Alaska Native, Native Hawaiian/Pacific Islander, multiracial] were described as "NH-Other" due to small sample sizes and heterogeneity if groups were combined.

Statistical analyses

Among women ≥18 years of age who participated in the 2012-2018 and 2020 NHIS (n = 140,817), we excluded women ≥50 years of age (n = 74,313) and those who did not identify as a pregnant (n = 64,441). Further, women were excluded if they were missing data on food security status, mICVH metrics [fasting glucose, blood pressure, cholesterol, dietary patterns, physical activity, body mass index (BMI) and smoking status], pregnancy status, as well as the following confounders: age, sex/gender, or race/ethnicity (n = 124). After applying these exclusion criteria, the final analytic sample was 1,999 participants.

Data were weighted to obtain nationally representative estimates. We reported mean ± standard error for age, along with weighted percentages (to account for the complex survey design) for sociodemographic, lifestyle, health behavior, and clinical factors in the overall population and by household food security status. Weighted Poisson regression models with robust variance were used to estimate prevalence ratios (PRs) and 95% confidence intervals (CIs) of associations between food security status category and mICVH overall and by race and ethnicity. We report unadjusted and adjusted models for age, annual household income, educational attainment, geographic region, marital status, alcohol consumption, survey year, and race/ethnicity (in overall model). In models, "high" food security status was used as the reference group to compare "low/very low" and "marginal" food security status. We investigated potential effect modification/differences in associations between food security status and mICVH by including a multiplicative interaction term (race/ethnicity*food security status) in the overall model and performed a Wald test of the interaction term. A two-sided alpha level of 0.05 was used to determine statistical significance in all analyses. All analyses were conducted using survey procedures in Stata version 15.1 (StataCorp, LLC, College Station, TX).

Results

Study population characteristics

Among the 1,999 included participants, the mean age ± standard error was 29.0 ± 0.2 years (Table 1). Food security status prevalence was 12% for "very low/low", 9.0% for "marginal", and 79% for "high". "Very low/low" food security prevalence was higher among pregnant women identifying as

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TABLE 1 Sociodemographic characteristics among pregnant adults aged 18–49 years old by food security status, National Health Interview Survey, 2012–2018, 2020, (*N*=1,999).

Characteristics[a]	Food security status			
	Very Low/Low *n* = 254 (12.0%)[a]	Marginal *n* = 212 (9.0%)[a]	High *n* = 1,533 (79.0%)[a]	Overall *n* = 1,999 (100%)
Sociodemographic				
Age, mean ±SE (years)	27.5 ±.51	27.8 ±.57	29.3 ±.18	29.0 ±.16
18–30	72.0	72.5	59.5	62.2
31–49	28.0	27.5	40.5	37.8
Race/ethnicity				
Hispanic/Latinx	22.8	24.4	16.5	17.9
NH-Asian	1.3	4.9	5.5	4.9
NH-Black	21.2	23.8	14.0	15.7
NH-Other	4.2	4.8	1.9	2.5
NH-White	50.5	42.1	62.2	59.0
Educational Attainment[b]				
< High School	18.5	13.0	6.9	8.8
High School graduate	38.6	38.6	20.4	24.1
Some College	32.9	36.0	29.6	30.6
≥ College	10.0	12.4	43.1	36.5
Annual household income[b]				
<$35,000	70.7	51.9	25.4	33.1
$35–$74,999	19.8	39.6	30.2	29.8
≥$75,000	9.4	8.5	44.5	37.1
Unemployed/not in labor force[b]	60.9	57.7	34.7	39.9
Marital status[b]				
Married/living with partner/ cohabitating	52.6	68.6	80.5	76.1
Divorced/widowed	16.9	5.1	4.6	6.1
Single/no live-in partner	30.5	26.3	14.8	17.8
Region of residence				
Northeast	15.5	19.7	15.5	15.9
Midwest	23.1	16.6	22.5	22.0
South	45.2	39.0	39.9	40.5
West	16.2	24.8	22.1	21.6

SE, standard error; NH, non-Hispanic.
[a]Note all estimates are weighted for the survey's complex sampling design. Percentage may not sum to 100 due to missing values or rounding.
[b]Participants were missing information for educational attainment, annual household income, and marital status

NH-Black (16.2%), and Hispanic/Latina (15.2%) compared to both NH-White (10.3%) and NH-Asian (3.2%) pregnant women (Table 2). The mICVH prevalence was 11.6% overall and 14.5% for NH-White, 4.1% for NH-Black, 5.0% for Hispanic/Latina, 26.7% for NH-Asian pregnant women, and 6.1% for pregnant women identifying as races and ethnicities other than NH-White, NH-Black, Hispanic/Latina, or NH-Asian (Supplementary Figure S1). Pregnant women with "very low/low" food security had the highest prevalence of <high school educational attainment (18.5%) as well as annual household income <$35,000 (70.7%), were the least likely to be married/living with a partner/cohabitating (52.6%), and largely resided in the Southern region of the US (45.2%) (Table 1). Further, pregnant women with "very low/low food security" had the highest prevalence of current smoking (22.2%), current alcohol consumption (≥1 drink in the past year: 52.8%), and the lowest prevalence of excellent/very good/good health status (87.7%) as well as mICVH (1.6%) (Table 3).

Food security status and Ideal cardiovascular health

Among pregnant women with "high" food security status, mICVH prevalence was 14%, overall, was highest among pregnant women who identified as NH-Asian (29.8%), and was lowest among NH-Black (4.7%) pregnant women (Table 2). Among all pregnant women, "very low/low" vs. "high" food security status was associated with a 76% lower prevalence of mICVH [PR = 0.24 (95% CI: 0.08–0.75)]. "Marginal" vs. "high" food security status was associated with a 53% lower prevalence of mICVH [PR = 0.47 (95% CI: 0.23–0.96). Although effect measure modification was present (p-interaction < 0.001), stratified results were inestimable for some racial and ethnic groups due to small sample sizes. Among NH-White pregnant women, "very low/low" vs. "high" food security status was associated with a lower mICVH prevalence [PR = 0.26 (95% CI: 0.07–0.98)]. Small sample sizes

TABLE 2 Prevalence ratios of modified ideal cardiovascular health among pregnant adults who reported experiencing very/low and marginal food security compared to high food security overall, and by race and ethnicity[a], National Health Interview Survey, 2012–2018, 2020, (N = 1,999).

	Food security status, %	mICVH, %	Prevalence ratio (95% confidence interval)[b]	
			Crude	Adjusted
Overall (N = 1,999)		11.6		
High	79.0	14.0	Referent	Referent
Marginal	9.0	3.9	**0.28 (0.14, 0.56)**	**0.47 (0.23, 0.96)**
Very low/low	12.0	1.6	**0.11 (0.04, 0.32)**	**0.24 (0.08, 0.75)**
Hispanic Latinx (n = 437)		5.0		
High	72.5	6.2	Referent	Referent
Marginal	12.2	3.3	0.54 (0.14, 2.06)	0.41 (0.10, 1.67)
Very low/low	15.2	0.8	0.13 (0.02, 0.97)	NE
NH-Asian (n = 121)		26.7		
High	87.8	29.8	Referent	Referent
Marginal	9.0	6.0	NE	NE
Very low/low	3.2	0.0	NE	NE
NH-Black/ African American (n = 278)		4.1		
High	70.2	4.7	Referent	Referent
Marginal	13.6	3.6	0.77 (0.14, 4.09)	3.77 (0.43, 33.1)
Very low/low	16.2	1.9	0.40 (0.05, 3.33)	0.14 (0.01, 1.38)
NH-White (n = 1,103)		14.5		
High	83.3	16.9	Referent	Referent
Marginal	6.4	4.3	**0.25 (0.08, 0.80)**	0.34 (0.10, 1.08)
Very low/low	10.3	2.0	**0.12 (0.03, 0.48)**	**0.26 (0.07, 0.98)**

mICVH, modified ideal cardiovascular health; NH, non-Hispanic; NE, not able to estimate.

Bolded values indicate statistical significance at a two-sided p-value <0.05.

Models are adjusted for age (18–30 years, 31–49 years), annual household income (<$35,000, $35,000–$74,999, ≥$75,000), marital status (married/cohabitating, single/no live-in partner, divorced/separated/widowed), educational attainment (<high school, high school graduate, some college, ≥college), region of residence (Northeast, Midwest, South, West), alcohol consumption [current (heavy), current (≤moderate), former, lifetime abstainer], and survey year. Models in the total/overall sample are additionally adjusted for race and ethnicity (Hispanic/Latinx, NH-Asian, NH-Black/African American, NH-White).

All estimates are weighted for the complex survey design. Bolded values indicate statistical significance at a two-sided p-value < 0.05.

[a]There was a significant Wald test for interaction between race/ethnicity and food security status on modified ideal CVH (p < 0.001). Stratified results were inestimable for some race and ethnic groups due to small sample sizes.

[b]Modified ideal cardiovascular health includes never smoking/quit >12 months prior to interview, BMI 18.5 – < 25 kg/m^2, meeting physical activity guidelines, sleep duration of 7–9 h, and no dyslipidemia, hypertension, or prediabetes/type 2 diabetes.

precluded our ability to compare associations between food security status and mICVH for each race/ethnicity included in our study sample.

Discussion

In this nationally representative study among a racially/ethnically diverse sample of pregnant women, we investigated food security status in relation to mICVH prevalence. We observed racial/ethnic inequities in food insecurity with "very low/low" food security prevalence being higher among Hispanic/Latinx, NH-Black, and NH-Other pregnant women compared to NH-White and NH-Asian pregnant women. We found, in adjusted models, that "very low/low" vs. "high" food security status was associated with a lower prevalence of mICVH, which aligned with our hypothesis. Similarly, "marginal" vs. "high" food security status was also associated with a lower prevalence of mICVH. Estimates for pregnant women from minoritized racial/ethnic groups had wide confidence intervals or could not be estimated due to small sample sizes. However, despite limited power to detect associations by each race/ethnicity included in our study, there was a suggestion that associations between "very low/low" and "marginal" vs. "high" food security status and lower mICVH prevalence would be the strongest for pregnant women from minoritized racial/ethnic groups. It is worth noting that the relative difference between "very low/low", "marginal", and "high" food security status is small among NH-Asian pregnant women. Public health impact is likely the largest among pregnant women from minoritized racial/ethnic groups, compared NH-White pregnant women, due to the high burden of low food security and mICVH prevalence, even if the relative associations are the same (41). Food security may be an important intervention target for addressing CVH disparities among pregnant women.

Our findings are consistent with prior studies reporting that food insecurity and low mICVH prevalence among women from minoritized racial/ethnic groups was higher compared to as NH-White women (1, 18, 19, 28, 30–32, 42). Given the importance of nutrition in shaping maternal and fetal outcomes, food insecurity threatens to widen disparities among women from racially/ethnically minoritized groups. For instance, the offspring of NH-Black women experience the greatest burden of low birth weight as well as preterm births, which can be exacerbated by inadequate dietary intake due to food insecurity (7–12). The results of this study also indicate that mICVH prevalence, an independent predictor of CVD risk (43), was the lowest among pregnant women from minoritized racial/ethnic groups (except NH-Asian pregnant women). Disparities in mICVH prevalence, combined with inequities in health conditions experiences during pregnancy [e.g., preeclampsia (44, 45), gestational diabetes (46)], may further exacerbate disparities in CVD risk among pregnant women from minoritized racial/ethnic groups. Without public health interventions implemented to mitigate such inequities in maternal nutrition (e.g., addressing food insecurity), racial/ethnic disparities in poor birth outcomes will persist.

Although understudied, investigating social determinants, shaped by structural inequities, may help researchers better understand mechanisms driving racial/ethnic disparities in poor maternal health outcomes. For instance, access to quality healthcare during prenatal and postpartum periods is crucial for ensuring that the

TABLE 3 Health behavior and clinical characteristics among pregnant adults aged 18–49 years old by food security status, National Health Interview Survey, 2012–2018, 2020, (*N* = 1,999).

Characteristics[a]	Food security status			
	Very low/Low *n* = 254 (12.0%)[a]	Marginal *n* = 212 (9.0%)[a]	High *n* = 1,533 (79.0%)[a]	Overall *n* = 1,999 (100%)
Health behaviors				
Smoking status				
Never/quit >12 months prior	67.4	84.0	86.4	83.9
Former/quit ≤12 months ago	10.5	7.2	6.6	7.1
Current	22.2	8.9	7.1	9.0
Alcohol consumption[b]				
Lifetime abstinence (<12 drinks in life)	28.3	32.0	22.5	24.0
Former (no drinks past year)	18.9	20.1	18.1	18.4
Current (≥1 drink past year)	52.8	48.0	59.4	57.6
Leisure-time physical activity (PA)				
Never/unable	53.1	43.2	31.5	35.2
Does not meet PA guidelines	18.3	23.6	26.9	25.6
Meets PA guidelines[c]	28.6	33.2	41.6	39.3
Usual sleep duration				
Very short sleep (<6 h)	13.4	10.2	5.4	6.8
Short sleep (<7 h)	36.0	31.6	20.0	23.0
Recommended (7–9 h)	58.5	59.7	74.3	71.1
Long sleep (>9 h)	5.5	8.7	5.7	5.9
Clinical Characteristics				
Health status				
Excellent/very good/good	87.7	93.5	97.0	95.6
Fair/poor	12.3	6.5	3.0	4.4
Body Mass Index (BMI)				
Underweight (<18.5 km/m^2)	5.2	3.0	1.2	1.8
Recommended (18.5–<25 kg/m^2)	28.6	26.9	42.3	39.3
Overweight (25–29.9 kg/m^2)	22.1	21.7	27.6	26.4
Obesity (>30 kg/m^2)	44.1	48.4	29.0	32.5
Dyslipidemia[d]	5.2	2.2	2.1	2.5
Hypertension[e]	9.7	11.9	7.9	8.4
Diabetes/prediabetes[f]	7.6	5.5	3.5	4.2
Modified ideal cardiovascular health[g]	1.6	3.9	14.0	11.6

SE, standard error; NH, non-Hispanic.
[a]Note all estimates are weighted for the survey's complex sampling design. Percentage may not sum to 100 due to missing values or rounding.
[b]Participants were missing information for alcohol consumption.
[c]Meets PA guidelines defined as ≥150 min/week of moderate intensity or ≥75 min/week of vigorous intensity or ≥150 min/week of moderate and vigorous intensity.
[d]Dyslipidemia defined as currently taking prescribed medicine to lower cholesterol high cholesterol in the 12 months prior to interview.
[e]Hypertension defined as ever told on two or more different visits that you have hypertension or high blood pressure or currently taking prescribed medicine to lower blood pressure.
[f]Prediabetes defined as ever told by a doctor had prediabetic condition, prediabetes, or borderline diabetes. Type 2 diabetes defined as ever told by a doctor or health professional that you have diabetes or sugar diabetes and being told you have type 2 diabetes.
[g]Ideal cardiovascular health includes never smoking/quit >12 months prior to interview, BMI 18.5–<25 kg/m^2, meeting physical activity guidelines, sleep duration of 7–9 h, and no dyslipidemia, hypertension, or prediabetes/type 2 diabetes.

mother and her offspring are healthy. In fact, prenatal and postpartum healthcare settings may help to identify and address food insecurity during pregnancy (47). Further, some healthcare-based interventions (e.g., using a produce prescription program, providing produce vouchers, group prenatal care) (48–51) have been used to target food insecurity and improve cardiometabolic health (52) during pregnancy (48–53). While economic disadvantage may affect utilization of prenatal health care, some literature suggests that racialized pregnancy stigma experienced by women from minoritized racial/ethnic groups in the US can also result in poorer quality of health care during pregnancy and postpartum (54, 55). Other structural inequities contributing to neighborhood environments also contribute to food insecurity. For instance, pregnant women residing in food deserts and/or food swamps experiencing food insecurity may engage deleterious health behaviors (e.g., consuming more affordable, processed foods to prevent hunger), despite the existence of federal nutrition assistance programs such as the Supplemental Nutrition Assistance Program (SNAP) and the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC)—which provides

supplemental food, breastfeeding and nutrition education, as well as health care and social service referrals to economically disadvantaged women (and their children ≤5 years) during prenatal and postnatal periods (56). Processed food consumption among pregnant women can exacerbate the risk for health conditions such preeclampsia (44, 45) and gestational diabetes (46), for which stark racial/ethnic inequities exist among NH-Black compared NH-White women (44–46). Considering that such inequities exist, irrespective of socioeconomic status, the social vulnerability of women from minoritized racial/ethnic groups experiencing food insecurity during pregnancy is particularly heightened. Thus, multilevel public health interventions addressing social determinants are necessary to help alleviate racial/ethnic disparities. While we were not able to produce estimates for every racial/ethnic group after stratifying by race/ethnicity due to limited sample size, the burden of food insecurity and mICVH among pregnant women from minoritized racial/ethnic groups persisted, despite similar relative associations, which warrants further investigation (41).

There are study limitations to note. First, the data from the NHIS employed a cross-sectional study design, which precludes our ability to assess causal associations. Next, due to the unavailability of data on diet in the NHIS dataset, AHA's ideal CVH metric (which includes diet) could not be used for the present study, potentially underestimating associations between food security status and mICVH among pregnant women in our results. Additionally, all data, including data on individual components of the mICVH metric were self-reported, potentially resulting in misclassification. Pregnant women belonging to historically underrepresented populations identifying as racial/ethnic groups outside of Hispanic/Latinx, NH-Black or NH-White were categorized as NH-Other, precluding our ability to make inferences across separate racial/ethnic groups. It is important for future research to disaggregate heterogenous racial/ethnic groups considering that there is evidence of differences by national origin/heritage that are overlooked when racial and ethnic groups are aggregated into broad categories. Next, alcohol consumption during pregnancy could be considered as a potential mediator that impacted our results. However, in our *post-hoc* comparison of results with and without alcohol as a confounder in our models, results were largely unchanged. Additionally, the 2020 survey year had a lower average response rate compared to previous years, likely due to the COVID-19 pandemic, introducing potential nonresponse bias among lower-income households (which would likely underestimate the magnitude of inequities in associations between food insecurity and mICVH) that cannot be eliminated (36). Further, household food security status may not capture food insecurity among the individual, also potentially producing underestimations in associations reported in our study. Also, small sample sizes among racial/ethnic groups resulted in limited power to detect associations within racial/ethnic groups. Although data were unavailable, it is worth noting that different federal nutrition assistance programs (e.g., SNAP, WIC) may moderate associations between food security status and mICVH, with WIC being particularly pertinent as it offers additional programs (e.g., breastfeeding and nutrition education, as well as health care and social service referrals to economically disadvantaged women and their children ≤5 years) catered to prenatal and postnatal care that may improve overall health (56, 57). For instance, the additional programs offered by WIC (but not SNAP) may promote both food security and mICVH (56, 57).

Our study has noteworthy strengths that contribute to the scientific literature. For example, we used a large and racially/ethnically diverse, nationally representative sample of pregnant women in the US, including individuals from historically unrepresented groups. We also included sleep (a recently established CVD risk factor) as an mICVH metric in our study to investigate associations between food insecurity and mICVH among pregnant women. Further, household food security data was collected using the USDA Family Food Supplement scale, which has been previously validated (58). Given the increased vulnerability to food insecurity among pregnant women, future studies with large samples of pregnant women (particularly those from minoritized racial/ethnic groups) investigating contributors to food insecurity and ideal CVH disparities are needed.

Given the essential role of diet for women during pregnancy, assessing household food security status in relation to mICVH during pregnancy is important. Using a modified ideal CVH metric—mICVH—inclusive of sleep, "very low/low" and "marginal" vs. "high" food security status were found to be associated with lower mICVH prevalence among pregnant women. Disparities in food insecurity prevalence and mICVH were also observed among pregnant women belonging to minoritized racial/ethnic groups, except NH-Asian adults (possibly due to racial/ethnic inequities in earnings when comparing NH-Asian and NH-White adults to NH-Black and Hispanic/Latinx adults in the US) (59). Although we were unable to estimate associations between food security status and mICVH for pregnant women by each race/ethnicity, the high burden of low food security as well as non-ideal CVH along with the association between low food security and lower prevalence of mICVH suggest racial/ethnic disparities in relationships between food insecurity and ideal CVH among pregnant women in the US (41). Considering the racial/ethnic disparities in food insecurity and mICVH, replication among diverse populations with large sample sizes is warranted. Our results may inform future studies including eventual interventions that help address food insecurity in hopes of improving CVH and addressing disparities among pregnant women.

Data availability statement

The datasets analyzed during the current study are from the National Health Interview Survey, which is publicly available, and was retrieved from https://www.cdc.gov/nchs/nhis/index.htm.

Ethics statement

The National Institute of Environmental Health Sciences Institutional Review Board waived approval for the use of non-identifiable, publicly available NHIS data. The studies were

conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in the NHIS.

Author contributions

JM: Investigation, Writing – original draft, Writing – review & editing. SG: Investigation, Methodology, Writing – review & editing. CP: Formal analysis, Investigation, Visualization, Writing – review & editing. WJ: Data curation, Formal analysis, Investigation, Visualization, Writing – review & editing. CJ: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Writing – review & editing.

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Conflict of interest

CP and WJ were employed by Social & Scientific Systems, Inc.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fgwh.2023.1286142/full#supplementary-material

SUPPLEMENTARY FIGURE 1
Food Security Status among Pregnant Women by Race/Ethnicity, National Health Interview Survey, 2012-2018, 2020, (N=1,999). Note all estimates are weighted for the survey's complex sampling design. Percentage may not sum to 100 due to missing values or rounding. Racial/ethnic groups for 'NH-Other' include women identifying as: American Indian/Alaska Native, Native Hawaiian/Pacific Islander, or multiracial.

SUPPLEMENTARY FIGURE 2
Modified Ideal Cardiovascular Health Prevalence among Pregnant Women by Food Security Status and Race/Ethnicity, National Health Interview Survey, 2012-2018, 2020, (N=1,999). Note all estimates are weighted for the survey's complex sampling design. Percentage may not sum to 100 due to missing values or rounding. Racial/ethnic groups for 'NH-Other' include women identifying as: American Indian/Alaska Native, Native Hawaiian/Pacific Islander, or multiracial.

SUPPLEMENTARY FIGURE 3
Modified Ideal Cardiovascular Health Prevalence among Pregnant Women by Race/Ethnicity, National Health Interview Survey, 2012-2018, 2020, (N=1,999). Abbreviations: mICVH=Modified ideal cardiovascular health. Note all estimates are weighted for the survey's complex sampling design. Percentage may not sum to 100 due to missing values or rounding. Racial/ethnic groups for 'NH-Other' include women identifying as: American Indian/Alaska Native, Native Hawaiian/Pacific Islander, or multiracial.

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The hair tales of women of color in Northern Manhattan: a qualitative analysis

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Introduction: Exposure to endocrine disrupting chemicals (EDCs), such as phthalates, can negatively impact maternal and child health, contributing to impaired fetal growth, preterm birth, and pregnancy complications, as well as increased downstream risks of cardiometabolic disease and breast cancer. Notably, women of color (WOC) are the largest consumers of personal care products, which are a common source of EDC exposure.
Methods: The Let's Reclaim Our Ancestral Roots (Let's R.O.A.R) Pilot Study developed an educational intervention delivered during pregnancy to promote reduced use of phthalate-containing hair care products (HCPs). This mixed-methods study included: (1) a quantitative analysis and (2) a qualitative analysis of the educational sessions and the semi-structured focus groups to evaluate the factors that influenced the hair care practices and product choices of WOC at various stages of life, including their current pregnancy (hereafter referred to as the hair journey). During the sessions, participants learned about EDCs (with a focus on phthalates), the unequal burden of exposure for WOC, adverse implications of exposure, and exposure reduction strategies. Focus group sessions provided insight into participants' hair journeys from childhood to the current pregnancy and explored factors during their hair product selection process. All sessions were transcribed and imported into NVivo Version 12 for coding and thematic analysis.
Results: A total of 46 individuals were enrolled in the study, and 31 participated in an educational session. This current work synthesizes the qualitative analysis of this study. We identified two important life stages (before and after gaining agency over hair care practices and product choices) and three dominant themes related to HCP use: (1) products that impacted the hair journey, which involved all mentions of hair products, (2) factors that influenced the hair journey, which included individuals or entities that shaped participants' hair experiences, and (3) the relationship between hair and sense of self, where sense of self was defined as the alignment of one's inner and outer beauty.
Conclusion: The themes intersected and impacted the participants' hair journey. Cultural integration was a sub-theme that overlapped within the dominant themes and participants discussed the effect of traditions on their hair experiences.

KEYWORDS

endocrine disrupting compounds, hair, hair care products, pregnancy, product use, phthalates, exposure reduction, maternal exposure

1 Introduction

Endocrine disrupting chemicals (EDCs) are a group of compounds that mimic and disrupt different pathways in the endocrine system (1). EDC exposure *in utero* is associated with an increased risk of pre-term birth, obesity, and neurodevelopmental disorders for the fetus and an increased risk of chronic diseases and breast cancer for the mother (2, 3). Fetal EDC exposure has been more specifically linked to: cognitive deficits (4), obesogenic fetal programming (5), and negative impacts on testis development and future male fertility (6). Therefore, EDC exposure during pregnancy is a critical period during which EDC exposure will impact both fetus and mother. For many, personal care product use is a source of EDC exposure, as individuals often begin use of personal care products early in life and exposure often continues daily over the life course (7). Among the common EDCs found in personal care products, phthalates are often added to hair care products (HCPs) for a variety of enhancing purposes, including providing scent to products (8, 9). Phthalates are anti-androgenic (10, 11) and have been shown to interfere with hormone regulation as they can interact with both estrogen- and androgenic-related biological pathways (3, 8, 9). Exposure during critical windows of susceptibility for breast cancer includes windows of life where the breast tissue undergoes rapid changes (prenatal, pubertal, pregnancy, lactating and menopause transition). Exposures during the pregnancy window also have intergenerational effects on mother and fetus (2–6); therefore, interventions designed for reducing exposure during this time are potentially impactful.

EDC exposure during pregnancy may be particularly harmful for WOC due to their increased exposure to EDC-containing products, as compared to their counterparts (12–14). Phthalate metabolites have been found to be significantly higher among women of color (WOC) (3). This finding is unsurprising as WOC, especially Black women, are among the most frequent consumers of personal care products including HCPs which is in part due to varying hair textures among WOC (15, 16). In pregnant women, greater personal care product use is associated with higher concentrations of urinary phthalate metabolites and urinary metabolite concentrations vary by the type of personal care product (17–21). While there are studies analyzing EDC exposure concentrations in pregnant women, as well as studies that have analyzed their attitudes and intention to modify their use of personal care products during their pregnancy (22), very few studies focus on pregnant WOC.

Environmental exposure interventions have been established as an important method to promote better health outcomes, yet few studies consider HCP use and behaviors over the life course. These interventions promote environmental health literacy where environmental exposure literacy is combined with health literacy to inspire individuals to make informed decisions, take steps to reduce health risks, and work to protect the environment (23). Studies have highlighted and connected the issues of environmental justice and beauty product chemical exposures among WOC (24, 25); therefore, focusing on WOC, especially pregnant WOC, may have an impact on both mother and child, impacting multiple generations. Consequently, we designed an educational intervention study to reduce phthalate exposures during the pregnancy/postpartum window and increase environmental health literacy, with the long-term goal to improve fetal and maternal health.

The conceptualization and study design of the Let's Reclaim Our Ancestral Roots (Let's R.O.A.R) pilot study were realized through trusted partnerships with community leaders which included WE ACT for Environmental Justice and a breast cancer advocate and champion. WE ACT originated as a Harlem-based organization in 1988, created to tackle local environmental racism, but has grown to tackle environmental justice on a national level. The breast cancer advocate (DAHW), with leadership roles within organizations like the Young Survival Coalition which addresses the unique needs of young adults affected by breast cancer, served as the study's community scientist. The overall objective of the Let's R.O.A.R pilot study was to understand and determine if an educational intervention during pregnancy could decrease the use of phthalate-containing HCPs among pregnant WOC. We performed a quantitative analysis for this pilot study, which will be published separately. However, we were equally interested in performing a qualitative assessment to understand the impact this intervention would have on the behavior of our participants. Therefore, we explored the hair journey of WOC. We defined the hair journey as the relationship WOC have had with their hair starting with long lasting and impactful memories, their hair care journey over time, and overall sentiments regarding their hair. Within this journey we defined agency as the moment that WOC gain freedom or control of the decisions regarding their hair. Here, we report the qualitative phase of the study and participants' insights into their hair journey, including hair product use and perceptions regarding EDCs.

2 Materials and methods

2.1 Participants

We recruited pregnant WOC in the Northern Manhattan region in 2021 who were on average 31.37 ± 3.30 weeks pregnant. We consented a total of 46 study participants, 4 were recruited virtually through Instagram and 44 from an Obstetrics & Gynecology (OB/GYN) clinic. Our research staff contacted individuals who expressed interest in the study to assess their eligibility. Participants were eligible for the study if they: (1) were at least 18 years of age, (2) residents of Northern Manhattan or other New York City boroughs, (3) self-identified as a WOC, (4) were in their second or early third trimester of their pregnancy, and (5) had a smartphone and/or computer for zoom sessions. Forty-six individuals were eligible, consented, and enrolled in the study. Our study population was multicultural and racially and ethnically diverse. Fifty-two percent of women were born outside the United States (U.S.) and 78% identified as Hispanic, Latina, or of Spanish origin. Among those of Hispanic ethnicity ($n = 36$), 36% identified as Hispanic Black, 39% as Hispanic other, 8% as

Hispanic White, 9% self-reported as additional race origins, and 8% refused to report on race. Ten participants identified as Black and not of Hispanic, Latina, or of Spanish origin ($n = 10$). Of the 46 individuals, 31 participated in an English or Spanish educational intervention discussing the adverse implications of using phthalate-containing HCPs, as well as a focus group session.

2.2 Educational intervention sessions and focus groups

Our team facilitated ten 1-hour educational intervention sessions that were delivered via Zoom and attendance varied between 1 and 5 participants. The first part of the educational session included introductions followed by a member of our team prompting the attendees to share a brief background of their HCP use. We wanted to learn what participants could recall about their earliest experiences with their hair, including when and what products were being used in their hair during the period before they were able to make decisions regarding their hair journey. We asked the participants the following questions: (1) How far along are you in your pregnancy? (2) What is the earliest age you remember having someone putting product in your hair? (3) At what age did you take agency over your hair care routine? Then participants tuned into the educational video and PowerPoint. Following these presentations, participants participated in a brief question and answer segment and debriefing from the project coordinators.

Our study was modeled after a few key theoretical frameworks. Finn and O'Fallon's Environmental Health Literacy framework proposes that providing knowledge or information to individuals about their environmental exposures will empower them and inspire them to make more health-conscious decisions with regards to how they interact with the environment and the potential exposures (23). We also incorporated Marshall Ganz's Public Narrative: Self, Us, Now framework which suggests grounding the audience to be sure they are engaged, using methods such as storytelling, listening, and reflecting (26). The study sessions were designed to provide knowledge and engage the participants to have awareness and inspire action. Additional frameworks and concepts included discrete decision-making and consumer theory (27, 28) to understand their journey with their hair and what motivates their behaviors and product choices.

We conducted three 1-hour focus group sessions which were designed to gather feedback on the behavioral intervention, to discover an individual's hair journey from childhood to pregnancy, and to probe the major factors that have an effect on their current product selection process. Initially, the focus group sessions were delivered as stand-alone sessions no more than eight days after the educational intervention portion. However, given our observations that the participants were challenged by attending two separate sessions, the semi-structured focus group guide was incorporated into the end of the educational intervention sessions for seven of the ten total sessions. Given that all focus groups followed educational sessions, we do not expect the timing of the focus group to have influenced participants' responses. The questions posed included: (1) How has your self-care routine changed from before pregnancy to now? (2) What factors do you consider when selecting hair care products? (3) How does your hair influence how you perceive yourself?

All participants were compensated for meeting the various milestones throughout the study, including for attending the educational intervention session.

2.3 Data processing and management

We transcribed all English ($n = 7$) and Spanish ($n = 3$) educational intervention sessions and three stand-alone focus group sessions. A native Spanish speaker reviewed the Spanish session transcripts and translations for accuracy and to ensure cultural nuances were addressed and reflected appropriately. We uploaded all transcripts into NVivo Version 12 to manage and analyze the data through thematic analysis and coding.

2.4 Qualitative data analysis

We used thematic coding to analyze the transcriptions (29). The researchers (CLV, LCH, and JAM) compiled a list of common elements identified during the review of five of the ten educational session transcripts to create an initial codebook of parent codes (the overarching and most representative elements), child codes (corresponding themes that stemmed from a parent code), definitions of each code, and examples of text for each code. To ensure the clarity of the origin of each code, codes that were developed based on the responses from questions the research team posed in the educational and focus group segments regarding hair journey, products, and sense of self were labeled as the "Deductive" codes. Codes that emerged while reviewing the transcripts were labeled as "Inductive" codes. Three of the ten educational sessions were accompanied by separate focus group sessions until the research team decided to incorporate the focus group segment within the remaining seven educational sessions. Independently, CLV coded the stand-alone focus group transcripts ($n = 3$) and the remaining educational transcripts ($n = 5$). CLV identified additional parent and child codes that arose inductively and modified the codebook accordingly, which was discussed with LCH and JAM before being incorporated into the codebook. We used five of the ten sessions to create the initial codebook and assess saturation. Saturation was reached after coding nine of the transcripts. The final codebook contained 9 parent codes (over-arching themes) and 33 child codes (each of which corresponded to a parent code).

To identify the potential themes, one researcher (CLV) manually performed concept mapping to demonstrate the relationships between the parent codes based on the coding results. Additionally, we used the data analysis tools available through NVivo, including the hierarchical clustering analysis to repeat and validate the relationships produced manually. Together, these analyses produced graphical representations of

the most coded parent codes and mapped their relationships with one another. Based on the clustering of the parent codes, the potential dominant themes were identified and discussed among the team (CLV, LCH, and JAM).

3 Results

3.1 Women of color and their hair journey throughout the life course

We characterized hair care practices over the life course to frame our analysis, including: (1) the phase *before* gaining agency to make choices with regards to hair care and styling practices, (2) the phase *after* gaining agency, and (3) the *current* phase during their pregnancy. Our study revealed that the WOC who were participants in our study had very keen memories of their earliest encounters with hair products (i.e., before agency) and they were able to describe a range of factors that they take into consideration when choosing hair care products now (i.e., after agency).

There were three dominant themes, which collectively impacted the participants' hair journey, before and after gaining agency: (1) products that impacted the hair journey, (2) factors that influenced the hair journey, and (3) the relationship between hair and sense of self (Figure 1). Cultural integration emerged as a sub-theme that impacted the three dominant themes.

3.2 Before agency

3.2.1 Products and their impact on the hair journey

Before agency, participants did not necessarily make choices or provide input on what HCPs might be used in their hair. The purchasing of HCPs was often the responsibility of caregivers and/or guardians. Many participants recalled specific products used in their hair before they had agency. Participants were able to think back to specific ages hair product use began, product types, and even sensory-related memories such as the smell of specific products that were being used in their hair. A few participants could not recall a time in their life when products were *not* used in their hair. One participant, U.S.-born 33-year-old, stated:

> *"I have been using hair products since I was probably just out of infancy, as long as my hair was long enough, there was product in it."*

Cultural integration was a prominent sub-theme that could not be ignored, as it impacted the participants' hair journeys before agency. Living outside of their family's country of origin, many participants' hair journey relied on culturally traditional practices. There were numerous examples of how culture determined the types of products used in their hair before they gained agency. One said:

> *"I'm actually Indian. So, we are really big on like coconut oil and this other oil that's called Amla oil and that's supposed to be really good for our hair… That was put on my hair when I was young. So, that's something that our parents all gave us when we were young, but it's like completely natural."*

Participants recalled the importance of homemade products for hair care during early periods of their life. Homemade hair masks were especially popular among the women from non-U.S. backgrounds, including culinary ingredients, such as avocado,

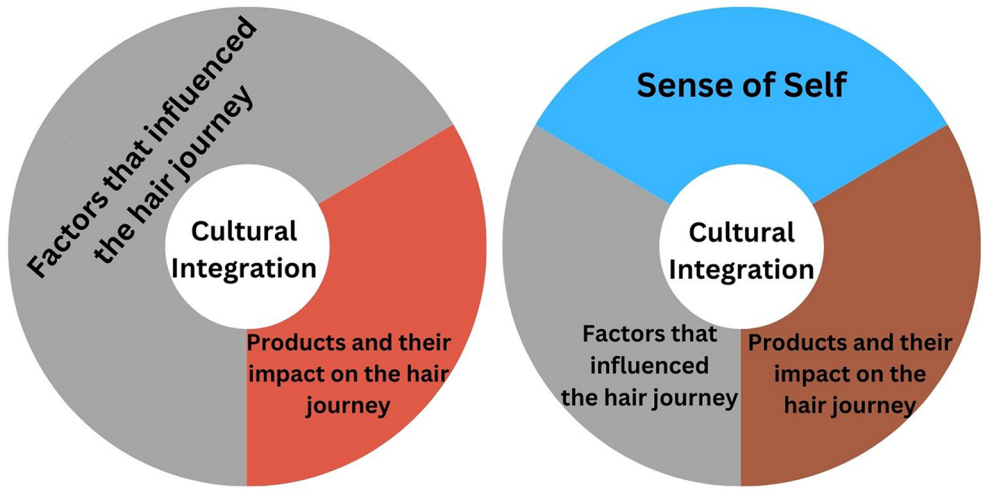

FIGURE 1
Identifying the dominant themes. Three dominant themes that impacted the hair journey of our participants were identified as: products and their impact on the hair journey, factors that influenced the hair journey, and the relationship between hair and sense of self. Cultural integration was an overlapping subtheme for all dominant themes.

mayo, and butter. A U.S.-born Dominican 22-year-old recalled her mother's homemade hair masks:

> *"My mom, she is Dominican, so like I grew up like her, always like doing like avocado hair mask and stuff like that. Like, she made her own stuff when she felt like my hair was dry."*

Participants also recalled their caregivers struggling to style and maintain the participant's hair. During the period before agency, their caregivers often considered the participant's hair texture or hair type as a factor for choosing the products they would use in their hair. Participants were aware of the differences in their hair texture in comparison to their caregivers or other individuals in their household. One participant stressed that her mother's hair was different from her hair because her mother was white. She recalled her mother considering their difference in hair textures when purchasing products:

> *"I never told her what to get me, but we have like completely opposite [or] different hair like her hair is thin and straight and then my hair is really curly and thick. So, I think she would get stuff specifically for me, because it was completely different."*

Another multiracial participant recalled her Mediterranean father unintentionally highlighting her hair because of his frequent application of baby oil to her hair.

> *"I was raised in a mixed household, and he was a single dad at the moment, and he didn't know what to do with my curly hair… he would soak it in baby oil, and it probably got highlights because it was being fried."*

3.2.2 Factors that influenced the hair journey

Before agency, caregivers influenced HCP use and practices. Many women reflected on the lack of agency they had when they were younger regarding their hair and that the decisions being made concerning their hair were the responsibility of their primary caregivers, which were predominantly mothers. One recalled:

> *"I remember my mom putting in products on my hair since I was a little baby…I remember being little, like two, three, and going to like Easter Sunday and like her putting Lottabody in my hair."*

Most of our participants alluded to their caregivers' decision-making being impacted by external factors ranging from ethnic culture, salon culture, and/or special events. For example, Dominican participants recalled their mothers or other family members as salon owners and/or frequenters of salons. For many Dominican participants, Dominican salons appeared to be integral to the Dominican hair experience.

> *"With like my family that my aunts or my mother, you know, since I am Dominican, having a hair salon is like, you know, there is always a family member with one. So, my aunt had a hair salon… So, I never did my own hair. They had someone usually like wash my hair and do the rollers."*

With close and trusted family members as salon owners, many participants were brought into salon culture early in life. Moreover, caregivers trusted the salon professionals with the participants' hair care and maintenance. Beauticians at the salon were permitted to make reversible and irreversible decisions from the use of temporary hair styling products to the use of permanent hair relaxers. One participant remembered:

> *"When I was about 10 someone [at] the salon actually relaxed my hair because she said that my hair was too thick, and she couldn't handle it and I was 10. So, I am not going to argue with an adult. And my grandma was there. She said okay. So, I was relaxing my hair for about five years just because that is how it started. Like I wasn't really, I didn't really have a choice."*

It was evident that most participants did not have agency over the decisions being made to their hair; therefore, their caregivers primarily regulated their hair journey early in life.

3.3 After agency

Study participants recalled the moments they gained agency over their hair care from purchasing their hair product, to deciding on a new style, or coloring their hair for the first time. For most participants, they gained agency during their pre-teen or early teenage years. During this period after agency, the themes of products that impacted the hair journey, factors that influenced the hair journey, and cultural integration remained key, but the participant's relationship between hair and sense of self became an equally important theme (Figure 1).

3.3.1 Products and their impact on the hair journey

After agency, participants chose what products to use but trusted various sources to guide their product choices. A few of our participants admitted that while they had agency and were now the decision-makers regarding their hair care practices, they did not experience having to do their own hair until the COVID-19 pandemic, as they often frequented salons which were temporarily shut during this time. A 22-year-old participant stated that:

> *"I used to go to the salon a lot. So, I don't think that is me taking care of my hair. I started going to the salon, like on my own when I was like 14, 15. And then recently, like during quarantine, I started taking like real good care of my like natural hair, like on my own, like picking my own products and stuff. So, I want to say when I was 20, I took agency over my hair completely."*

Participants who were born outside of the U.S., or whose guardians were born outside of the U.S., mentioned being sent

products from their countries of origin, from shea butter to certain shampoos. This was especially common among Dominican and African participants, establishing an intersection between product choice and one's culture. Even after agency, we found that for a few of our non-U.S. born participants, culture shaped their choices regarding their hair, especially when it came to product choices. It was evident that these participants held onto effective and trustworthy practices of their cultures and/or countries of origin, including integrating products from "back home" into their haircare regimen. A 33-year-old Liberian participant reported using "donut grease" or Shea Butter on her children's hair which she gets from family members when they return from traveling "back home." A 30-year-old Dominican participant said:

> *"I remember when I used to live in Dominican Republic…what we usually do there [is] like natural products, like made of carrots, avocado and things like that. And at the moment those are the type of products that I try to use. My mother sends them to me from Dominican Republic."*

3.3.2 Factors that influenced the hair journey

Family members and salon professionals remained key influencers for many of our participants after gaining agency. For some of our participants, the opinions of family members remained valuable. Many women continued in salon culture, entrusting their haircare to professional stylists and medical providers. During one focus group session, when asked if most of the products used in their hair currently or in the past were first introduced at a salon, the participants replied in the affirmative. In fact, purchasing products recommended by professionals was not unusual for some of our participants, especially those who described different hair-related conditions. One of our Dominican participants, 29 years old, mentioned:

> *"But if a dermatologist would tell me, no matter the price, this is going to work for your hair loss or this is going to work for the type of hair, I will get it. I will get it."*

After gaining agency, influencers also included friends and social media. Product advertisement in the past largely consisted of radio and television commercials, which likely impressed the caregivers of our participants during the before agency stage. Today however, social media has become one of the primary and most powerful sources for product advertisement. One participant mentioned:

> *"Now with social media, it plays a big role in our daily lives. So, it's like, you can see somebody that has natural curly hair or kinky hair, so okay, maybe I should give it a try. I'm a perfect example. I saw Tracee Ellis Ross's and I was like, I might as well go to Ulta to check up on it."*

One of our African participants reported struggling with terrible dandruff and recalled purchasing a line of products she heard about from an African social media influencer who also struggled with dandruff. The participant reached out to the influencer:

> *"She used to have dandruff a lot. And this product was very helpful, so that's how I contacted her. And then she gave me the lady's number and then I talked to the lady. So, that's how I went along, paid for it, 80 dollars for the whole set."*

A few women reported learning about potential risks of long-term exposure to personal care products with harmful chemicals through media platforms. A 31-year-old Dominican participant recalled her daughter watching a Tik-Tok video about harmful chemical exposures in hair products. It inspired her and her daughter to investigate a mobile phone application that provided information on chemical exposures in hair products. She recalled:

> *"I was noticing lots of hair when she would take a shower and wash her hair and it would be hair everywhere or she would be clogging our pipes all the time. So, then I started looking into it and I noticed that the product that we were using was really high in like dirty chemicals. Like it was on the Think Dirty app, it was coming out red."*

3.3.3 The relationship between hair and sense of self

Establishing the relationship between hair and sense of self appears to begin during the period after gaining agency (Figure 2). Once the participants had agency over their hair journey, we noticed discussions of being able to better align their inner and outer beauty. The participants began to make clear connections between how they felt about their hair (their outer beauty) and how they felt about themselves (inner beauty and self-esteem) with regards to when they were responsible for choices regarding their hair. Participants expressed that doing their hair has always helped brighten their moods, cheered them up, or made them feel beautiful. These discussions were not observed during discussions regarding the "before agency" period. It was evident that the relationship to their hair and their sense of self began forming at the time they began to have agency and remained important throughout their life.

Familial influences stretched beyond choosing products that impacted the hair journey, to also influencing participants' relationship between hair and sense of self, and how they felt their inner beauty and outer beauty aligned. Despite their control over their hair journey, participants remarked that they had family members who would criticize how they styled their hair, or when they made major changes to their hair. One 33-year-old U.S.-born Dominican participant stated that:

> *"I've learned how to manipulate my curls so that you can still wear it natural, and it still looks like presentable…you only feel pretty, attractive or good when your hair was pretty straight and that took a toll on me… I learned how to diffuse properly and how to properly do it so that I can feel confident in my own curls my own way… But now I'm grateful that I took some time to learn and try, because it can be scary,*

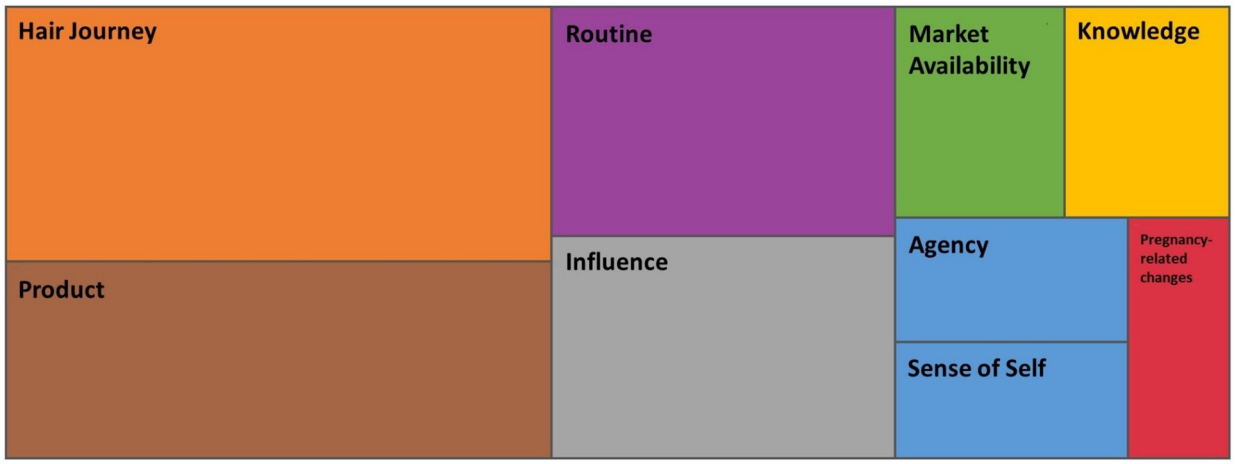

FIGURE 2
NVivo hierarchy tree clustering. Hierarchy tree map chart developed using NVivo coding software. Each box, represents a parent code, and the size of the box, represents the most frequently coded parent codes. The positions of the parent codes relative to the surrounding parent codes demonstrate potential relationships with the surrounding codes.

> *especially I'm Dominican as well and it can be scary going out into our world where everyone sees the girl with [an] image of perfection. Even family members, they'll be like, oh, do your hair, you look like a bruja, that's like a witch or whatever it is."*

Social pressures, including beauty standards, were identified as additionally having an effect on our participants after they had agency over their hair choices. A 33-year-old U.S.-born Hispanic participant stated:

> *"I should be able to feel good in my natural state, you know, and I shouldn't have to keep transforming myself just to fit in. So, it was a hard realization, but I had to break away from that because I know that I can't be chained to the beauty industry and I can't be a chain to the salon, you know, just to feel good about myself."*

There was also a clear connection between cultural integration and the relationship of one's hair journey and their sense of self that was present after gaining agency. A participant of Mexican and Indigenous descent shared:

> *"Yeah, really, I feel ugly like it's a matter how short I've cut it and I just wanted powerful, feminine and I don't know how to I guess express or let them know. So I prefer having my long hair, straight long black and I come from an indigenous background and we don't normally cut our hair…I learned more about my father's [Indigenous] side … there's a whole community out there who find strength in their hair… and it made me feel like, I don't know, welcomed, belonging. So, I've read more and got into more of spirituality of the idea of hair and strength and what it meant to the indigenous community and that's what I hope to pass down to my children so they can understand how hair is and what it means."*

3.3.4 Pregnancy

Participants did not view pregnancy as a distinct window with regards to hair care practices. Most of our participants did not acknowledge pregnancy as an important period until they were prompted during the focus group portions of the study. Only then did these participants describe changes they had made to their hair care and styling decisions during their pregnancy.

Many participants noted that while pregnancy may have caused changes to their hair, comfortability, and mood, their routines changed more due to the COVID-19 pandemic than pregnancy. Yet, a considerable number of our participants reported prioritizing care of their hair in some form, especially in attempts to empower their sense of self. One participant mentioned:

> *"If I'm feeling off and I do my hair, that will change my entire mood in a matter of a couple of hours. The health of my hair, prior to pregnancy, throughout pregnancy, it's extremely important. For me, to be able to do my hair and feel beautiful that's everything. That's [the] number one thing."*

A few women reported learning about potential risks of long-term exposure to personal care products with harmful chemicals through media platforms prior to attending our educational intervention. However, during the end-of-session participant feedback, many participants reported gaining knowledge about the potential health risks from personal care product exposures. Many were especially appreciative of gaining this knowledge during their pregnancy, as they reported considering the new information with regards to choosing personal care products for

their babies. The empowerment these participants expressed gaining with the provided knowledge was a major goal of this pilot study.

4 Discussion

Pregnancy is a window of susceptibility for women's health and lowering chemical burden could have positive impacts on the health outcomes of both mother and baby. Through focus groups and educational sessions with WOC we explored whether pregnancy would be a key phase that contributed to participants' hair journey, especially regarding their hair product choices. We spoke to WOC during their pregnancies, and few mentioned making major changes to their hair routine during this time. Many gained agency over their hair practices much earlier in their lives. Thus, there is a need to identify the most appropriate timing to effect change while considering the intersection between biological windows of susceptibility and the most culturally salient windows.

The Let's R.O.A.R pilot study followed Finn and O'Fallon's health literacy framework and Marshall Ganz's Public Narrative: Self, Us, Now framework (23, 26). The health literacy framework objectives promote the acquisition, comprehension, application, evaluation, and use of knowledge in terms of environmental health literacy to improve health outcomes for individuals and their communities (23). The public narrative framework engages the audience by incorporating methods such as storytelling, listening and reflecting (26). Let's R.O.A.R aimed to understand the awareness and perceptions of HCP use on psychosocial adjustment, health, and risk behaviors of pregnant WOC, and normative beliefs of hair and their identity. Therefore, we provided an educational intervention and obtained urinary data, but it was also equally important to allow WOC psychosocial space for conversations regarding their hair experiences during such a pivotal point of their lives, like their pregnancy.

The French PREVED Intervention Study educated pregnant women on methods for identifying and choosing alternatives to food pollutants, environmental pollutants, and personal care products (30). The group sought to measure and compare urinary metabolite concentrations among the participants who received the intervention, as well as quantify various psychosocial dimensions (i.e., gauging their self-esteem, risk perception, and their expectations of a healthy baby). Like the Let's R.O.A.R study, the PREVED study focused on evaluating psychosocial changes of pregnant participants, including self-esteem, risk perception, and the level of concern for EDC exposures. However, the PREVED study was not racially diverse and may not capture the psychosocial dimensions experienced by WOC living within the American standard of beauty. While there are other racially diverse environmental exposure intervention study models for pregnant women, they do not include psychosocial or qualitative assessments (31, 32). The Let's R.O.A.R study aimed to promote social and cultural awareness of EDCs and reduction of EDC exposure during critical windows of susceptibility. The Let's R.O.A.R pilot study aims to synergize the importance of a quantifiable intervention with psychosocial dimensions that offer an open space for shared stories and bonding with the intention of empowering pregnant WOC movement towards action.

The relationship between hair and sense of self arose as a particularly important theme during the period after participants gained agency over their hair journey. The transitionary period for when participants recalled first gaining agency remained a vivid memory where participants came into their agency for various reasons. A few mentioned that it became more convenient for them to start doing their own hair as their caretaker(s) was no longer available. Other participants revealed that their transition into agency over their hair journey occurred in pre-adolescent or early adolescent ages. Given puberty through adolescence is a crucial window of susceptibility to environmental exposures, learning of EDC exposures and health prior to gaining agency could be effective in changing behavior as evidenced in the *HERMOSA* intervention study. In the *HERMOSA* study, measurement of urinary metabolite exposures in young Latina girls pre- and post-intervention demonstrated that EDC exposure was reduced upon education and being provided alternative, cleaner personal care products (33). A caveat to this period is that full agency may not be achievable presenting challenges in the routine implementation of healthier options.

Corroborating others (34, 35), we also observed that a sense of self was connected to women's hair care styling practices as it was where inner beauty matched outer beauty. Many of our participants reported considering hair products based on function and ability to manipulate their hair, i.e., defining curls. The fixation of HCPs on hair manipulation can likely be traced back to the fixation of society on labeling hair as "good hair" (straighter/longer/finer) vs. "bad hair" (tightly coiled/kinky/coarse), which has had negative psychosocial consequences on WOC, especially Black women (24, 36, 37). The marketing of products to promote beauty and certain societal beauty standards, rather than bodily health, may be a structural barrier to having the ability to make the healthier choice, further contributing to environmental beauty injustice. Ideas of beauty and structural barriers should be considered when designing interventions; otherwise, education is not enough if it makes unrealistic expectations of individuals when they are facing upstream forces. Moreover, ideas of beauty and structural barriers must also be considered in context to the target population.

Participants also expressed narratives regarding family as a major influential factor in the hair journey. Prior to gaining agency, most participants admitted to not having much of a say in their hair journey, such as the products being used, and decisions being made. Participants fully trusted and/or depended on the authoritative individuals in their life, which often included family. After gaining agency, some of our participants described family influences continuing to impact their hair journey, whether it was internalizing comments their family would make regarding their hair, referrals from family members to use certain products, or salon referrals. Our findings further validate prior studies that demonstrate the existence of a strong relationship between familial and caregiver influence and a Black woman's hair journey (38, 39).

Our participants expressed narratives that were unique to intersectional identities such as the multiracial narrative. For some of our participants, their multiracial and/or multiethnic identities, were an important aspect of their hair stories. One poignant story was told by a participant of Mexican and Indigenous heritage who described her childhood surrounded by her Mexican family members. She often felt pressured to style and cut her hair similarly to that of those around her. However, as she got older and learned more about her Indigenous roots and Indigenous hair practices, she became inspired to retain her length and felt a sense of strength as she continued to grow her hair. Studies discuss the shift in multiracial individuals' identities, including their physical appearances over time (40); this participant's story and that of other participants of multiple races and/or ethnicities further illustrates what Pauker, Lukate and Foster referred to as the malleability of the multiracial identity and how the intersectional identities of those of multiple races and/or ethnicities are experienced within one's self and outward (34, 40). In our study, this is where we saw strong connections between cultural integration, sense of self, and the overall hair journey.

The cultural integration subtheme was especially prominent amongst our Dominican participants with respect to salon culture. The Dominican beauty salon industry in New York City is well documented and our Washington Heights/Inwood area is known to have a Dominican salon on nearly every block, practically serving as a "cultural staple" for Dominican neighborhoods in New York City (41). Candalerio argues that the beauty shop helps shape the connection between culture and identity. We found this to be true, as our participants discussed their first Dominican salon visit as a rite of passage. Some even recalled the age they were first able to go to the salon without their guardian. The salon was where they first experienced the transformation of their hair to their culture's more acceptable standards of beauty. For one of our participants, the salon was where she experienced her first negative feeling towards her hair as the stylists gave her a hair relaxer to make her hair more manageable. Many Black and mixed-race women grapple with their sense of self and their relationship to their hair and beauty. This is due to historical and present-day societal pressures, where lighter skin and straighter hair has been established as close to whiteness, thus closer to beauty, femininity, and acceptability (34). In 2018, Mitchell and colleagues' multiracial and multiethnic qualitative analysis found that most individuals judge their "typicality" (how similar they perceive themselves to be to their ethnic-racial group) and their "atypicality" (differences compared to their ethnic-racial group) based on a number of factors including hair, skin color, and facial features (42). Mitchell specifically suggested that their Latinx participants judged themselves as atypical amongst other Latinx individuals due to their appearance, which was usually a result of adopted stereotypes such as being Latinx with darker skin and "black hair" (42).

Our findings reflect a specific place and time. Participant demographics represent the demographics of Northern Manhattan and the surrounding boroughs, with 78% of Hispanic, Latina, or Spanish descent, of which 44% of our participants identified as Dominican. We conducted this study during the COVID-19 pandemic, which forced us to move to a virtual engagement. While the virtual setting may have limited meaningful engagement with some participants, it also made the study more accessible for some participants, particularly those who were in the final trimester of their pregnancy and reported being uncomfortable or feeling sick. Future studies could purposefully sample across various age groups, abilities, gender identities, and pregnancy trimesters to delve into more specific questions pertinent to subgroups.

Our qualitative study impressed credibility as investigator triangulation was used during the coding process by involving several researchers as research team members. These individuals were involved in addressing the organizational aspects of the study and the process of data analysis. While data was coded by one researcher, the initial working codebook and the themes were analyzed and established by three different researchers. Analysis also included the generation of a manual concept map followed by a comparison with the NVivo cluster analysis. When the interpretations of the researchers differed, the discrepancies were thoroughly discussed until the most suitable interpretation and best representation of the meaning of the data was established.

Our study is not without limitations. With the racial and ethnic makeup of our participants, it is important to note the origin, race and ethnicities of the individuals who collected and analyzed the data during this study. It is important to note that all three of the researchers who led the data analysis (CLV, LCH and JAM) are not Hispanic migrants or of Hispanic origin, unlike the majority of our participants. However, the researchers would identify themselves as culturally aware and experienced with working with communities of Hispanic origin due to their engagement with these communities through their research work, community outreach, and their community partnerships. The educational intervention and focus group facilitators were women of color, two African American women and one native Spanish-speaking Hispanic woman. One of the facilitators is a cis-gender Southern Black woman with 4C textured natural hair (JAM). Another facilitator is a Puerto-Rican native Spanish speaker with wavy hair, mostly worn straightened (AR). A third facilitator is an African American woman and cancer survivor whom, after losing her hair during her cancer treatment, continues to-date to shear her hair, donning a bald head (DAHW). Thus, while blind spots exist, hair commonalities and differences between the participants and facilitators may have encouraged respondents to either, be more open or be more reserved, in sharing their hair journey.

We found that products that impacted the hair journey, factors that influenced the hair journey, and the relationship between hair and sense of self were important contributing factors to the hair journeys of the WOC in our study. These themes were interconnected in that the factors that influenced the hair journey often informed decisions and/or inspired what products participants purchased or how participants styled their hair (Figure 3). These factors had lasting impacts on participants' sense

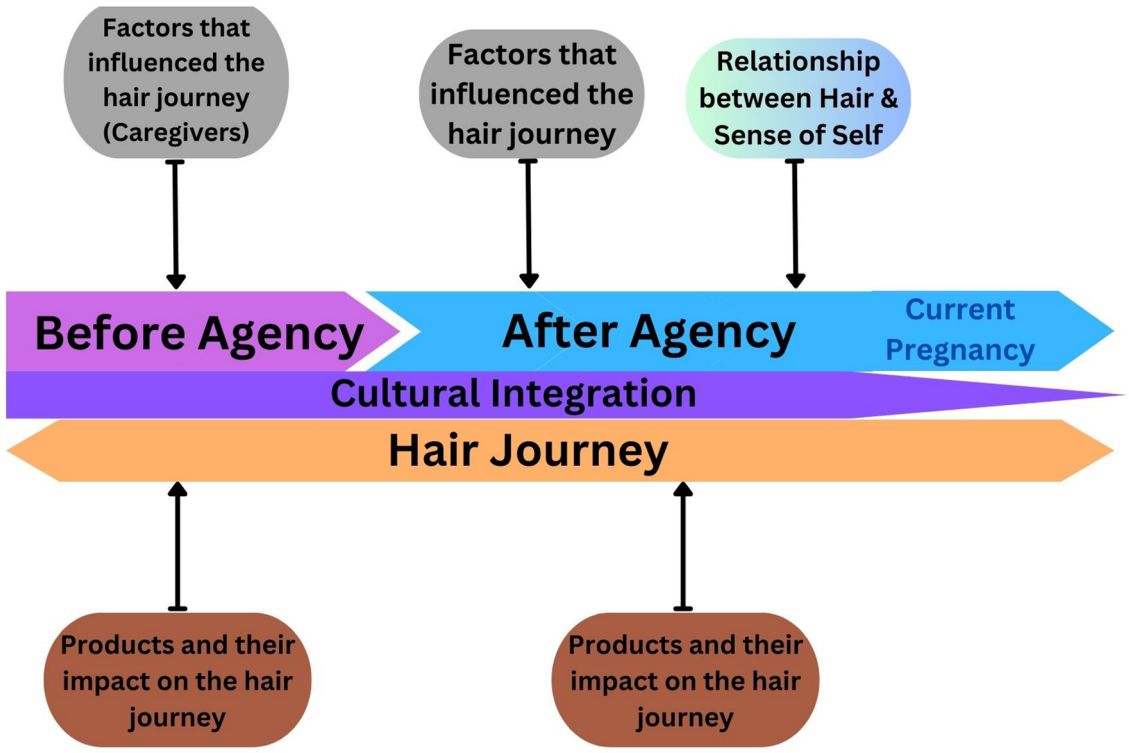

FIGURE 3
Illustrative study schematic. There were two major stages in the hair journey: "before agency" (pink) and "after agency" (blue), with the current pregnancy of the participants falling under "after agency." Products and their impact on the hair journey (brown) and factors that influenced the hair journey (grey) were major factors during both stages of the hair journey; however, "sense of self" began during the period "after agency." Cultural integration (purple) remained an overlapping subtheme throughout the entire hair journey (orange double arrow).

of self and/or their relationship to their hair. This coincided with previously published studies where participants reported receiving negative remarks about their hair or wearing their hair in its natural state from their maternal figures and/or other female family members (43, 44). Cultural integration was evident with regards to the products purchased and/or used, and how participants styled their hair to better connect with their heritage and strengthen their sense of self. These factors were crucial in the telling of hair stories and experiences throughout these WOCs' lives. Through speaking with WOC during pregnancy, it was apparent that there is an opportunity and need to include qualitative psychosocial dimensions to inform culturally salient and inclusive interventional studies. However, our study also provided further insight that qualitative psychosocial dimensions can further our understanding on the commonalities and the unique factors that influence oneness with inner and outer beauty for WOC living in a society where mainstream beauty standards are not inclusive.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors after all publications using the raw data or publications being supported by the raw data have been published, without undue reservation.

Ethics statement

The studies involving humans were approved by the Internal Review Board at Columbia University. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their informed consent electronically to participate in this study.

Author contributions

CLV: Data curation, Formal Analysis, Investigation, Project administration, Resources, Software, Visualization, Writing – original draft, Writing – review & editing, Validation. LCH: Investigation, Methodology, Resources, Software, Supervision, Writing – review & editing, Formal Analysis. FT: Investigation, Methodology, Writing – review & editing, Project administration. EB: Methodology, Writing – review & editing, Resources. AAML: Resources, Writing – review & editing. KP: Writing – review & editing. DAHW: Writing – review & editing, Conceptualization, Methodology. MM: Writing – review & editing, Resources. BM:

Writing – review & editing, Resources. PS: Writing – review & editing, Resources. MBT: Resources, Writing – review & editing, Methodology. JAM: Conceptualization, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The Maternal and Infant Environmental Health Riskscape study of perinatal disparities in greater Houston: rationale, study design and participant profiles

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Introduction: The Maternal and Infant Environmental Health Riskscape (MIEHR) Center was established to address the interplay among chemical and non-chemical stressors in the biological, physical, social, and built environments that disproportionately impact perinatal health among Black pregnant people in a large and diverse urban area with documented disparities in the U.S.

Methods: The MIEHR cohort is recruiting non-Hispanic Black and non-Hispanic white pregnant people who deliver their infants at major obstetric hospitals in Houston, Texas. At enrollment, all participants are asked to provide urine samples for chemical [metals, cotinine, and polycyclic aromatic hydrocarbons (PAHs)] analyses and blood samples. A subset of the cohort is asked to provide oral and vaginal swabs, and fecal samples. Questionnaire and electronic health record data gather information about residential address history during pregnancy, pregnancy history and prenatal care, sociodemographic and lifestyle factors, experiences of discrimination and stress, and sources of social support. Using information on where a participant lived during their pregnancy, features of their neighborhood environment are characterized. We provide summaries of key individual- and neighborhood-level features of the entire cohort, as well as for Black and white participants separately.

Results: Between April 2021 and February 2023, 1,244 pregnant people were recruited. Nearly all participants provided urine samples and slightly less than half provided blood samples. PAH exposure patterns as assessed on 47% of participants thus far showed varying levels depending on metabolite as compared to previous studies. Additionally, analyses suggest differences between Black and white pregnant people in experiences of discrimination, stress, and levels of social support, as well as in neighborhood characteristics.

Discussion: Our findings to date highlight racial differences in experiences of discrimination, stress, and levels of support, as well as neighborhood characteristics. Recruitment of the cohort is ongoing and additional neighborhood metrics are being constructed. Biospecimens will be analyzed for metals and PAH metabolites (urine samples), miRNAs (plasma samples) and the microbiome (oral swabs). Once enrollment ends, formal assessments are planned to elucidate individual- and neighborhood-level features in the environmental riskscape that contribute to Black-White disparities in perinatal health.

KEYWORDS

MIEHR, environment, health disparities, maternal health, preterm birth, neighborhood, stress

Introduction

Despite major breakthroughs in medical care, health inequities persist among U.S. populations and are especially consequential for pregnant people and their children. As compared with other racial and ethnic groups, Black pregnant people suffer the highest risks of poor pregnancy outcomes in the nation. Essentially unchanged from the period 2007 to 2016 (1), pregnancy-related mortality in 2020 was almost 3 times higher among Black as compared to white pregnant people (2). There are also disparities in the prevalence of preterm birth, which is a primary cause of perinatal death and a risk factor for adverse health outcomes for an infant throughout the life course (3), with a prevalence of 14.4% and 9.1% among Black and non-Hispanic white populations, respectively (4). Similar to national trends, racial inequities in health outcomes are strikingly evident in Harris County, Texas (5), the third most populous county in the nation and home to Houston, a city with an immensely diverse population and more families living below the poverty line than the rest of Texas or the nation (6). Pointedly, Houston and Harris County both earned an "F" in the March of Dimes 2022 Report Card for preterm birth (7).

Though not well-understood, racial disparities in perinatal health are likely related to factors other than genetics, behavior, access to health care or individual-level socioeconomic status (8–12). Indeed, the American College of Obstetricians and Gynecologists (ACOG) recognizes the importance of structural racism (i.e., macro-level conditions that limit opportunities, resources, and well-being of less privileged groups) on influencing maternal and infant health outcomes (13). Because of redlining and other exclusionary practices of financial lenders, Black communities have been historically burdened by housing discrimination and neighborhood segregation (14), leading to limited investments in communities of color including grocery stores, schools and health care facilities, and a higher concentration of industries and hazardous wastes sites nearby (15). The siting of key sources of pollution located within or near Black neighborhoods results in another form of structural racism, i.e., environmental injustice, with residents in these communities experiencing a disproportionate burden of environmental exposures to contaminants in the air they breathe, water they drink, and where their children play (16–19).

Owing to critical gaps in our understanding of Black-White disparities in perinatal health, we established the Maternal and Infant Environmental Health Riskscape (MIEHR) Center, an NIH P50 Center of Excellence on Environmental Health Disparities Research, with an overall goal to evaluate the impact of multiple stressors on adverse maternal and infant outcomes in the greater Houston area. Premised on an environmental riskscape framework (20), we are examining chemical and non-chemical stressors in the biological, physical, social, and built environments that contribute to racial disparities in perinatal health, either directly or in combination with each other. Moreover, the study location provides a nexus for research on the impact of the environment on perinatal health disparities as Houston is the most diverse city in the nation (21) and is unfortunately also plagued by income disparities, with far greater of proportions of Hispanic (22%) and Black (20%) residents who live in poverty as compared with non-Hispanic white residents (5%) (22). In this paper, we describe the protocols being used in recruitment of the MIEHR cohort and provide exposure profiles for the cohort (and separately for Black and white participants) enrolled through February 28, 2023.

Methods

Recruitment

The MIEHR cohort has a goal of recruiting ~1,200 non-Hispanic Black and non-Hispanic white maternal-infant dyads from three large academic OB/GYN hospitals in the Texas Medical Center (TMC) in Houston, Texas (see Figure 1). Enrollment began in April 2021 at Memorial Hermann Hospital followed by enrollment at Ben Taub Hospital in July 2021 and at Texas Children's Pavilion for Women in June 2022. Eligibility criteria include the following: resident of the 8-county greater Houston area (Brazoria, Chambers, Fort Bend, Galveston, Harris, Liberty, Montgomery, or Waller County); 18 years of age or older; non-Hispanic Black/African American or non-Hispanic White, by self-identification; singleton delivery with no identified congenital anomaly; cognitively aware enough to participate in the study (i.e., able to provide informed consent); and English-speaker. The study protocol has been reviewed and approved by

the IRBs at Baylor College of Medicine and The University of Texas Health Science Center at Houston under a reliance agreement.

Potential participants are initially identified using unified electronic health record (EHR) systems at each hospital enabling ready access, identification, and patient scheduling and tracking. Each weekday, trained obstetrics research coordinators review records of potential pregnant people who have been admitted for labor and delivery during the previous 24-hr period (or 72-hr period for Monday mornings) as well as antepartum and postpartum lists of patients. Potentially eligible participants are approached by research coordinators at a time when it does not interfere with their clinical care to verbally confirm eligibility. Potential participants who are interested and eligible (meeting inclusion and exclusion criteria) are assigned a study identifier and written informed consent is obtained.

Questionnaire administration

Once consented, research coordinators administer a questionnaire electronically in REDCap, which is HIPAA–compliant and secure. The questionnaire seeks information about the following: maternal and paternal sociodemographics; residential history during pregnancy; pregnancy history and prenatal care; tobacco, alcohol, and other substance use during pregnancy; antibiotic and probiotic use during pregnancy; and maternal family health history. We also ask participants whether they are willing to be recontacted for participation in additional research activities for which they or their child may be eligible in the future and if yes, to provide their contact information. Data are also abstracted from EHRs including: maternal height and pre-pregnancy weight, insurance status, vaccination history during pregnancy, comorbidities and chronic diagnoses, prior pregnancy history, obstetric complications and diagnoses related to the index pregnancy, date of last menstrual period, dates of all ultrasounds received and associated fetal biometry (estimated fetal weight, head circumference, biparietal diameter, abdominal circumference), date of delivery, type of delivery (e.g., vaginal, cesarean), infant sex, infant anthropometry (head circumference, weight, length), and infant Apgar scores.

Biological sample collection

All participants are provided the opportunity to provide urine and blood biospecimens. A subset of pregnant people at Ben Taub Hospital and Texas Children's Pavilion for Women are asked to also provide oral and vaginal swabs and fecal samples, as well as consent to collect oral and fecal/meconium from their infants. Blood samples are collected in 10 ml EDTA lavender top tubes, preferably during routine blood draws, and are immediately (within one hour) transported in coolers with frozen gel packs to the laboratory for processing. Spot urine samples are collected in sterile 100 ml urine specimen containers and stored with fecal samples and oral and vaginal swabs (if collected) in a cooler with a gel pack until they are transported to the laboratory on the same day that they are collected. Whole blood, plasma and urine samples are aliquoted in 1.5 ml sterile cryovials. All samples are stored at −80°C. Maternal oral swabs will undergo 16S ribosomal RNA (16S rRNA) and whole genome sequencing (WGS), microRNAs (miRNAs) will be profiled in plasma, and metals and monohydroxylated polycyclic aromatic hydrocarbons (OH-PAHs) metabolites will be measured in urine samples (see below). All other biological samples are being banked for use and analyses in future studies.

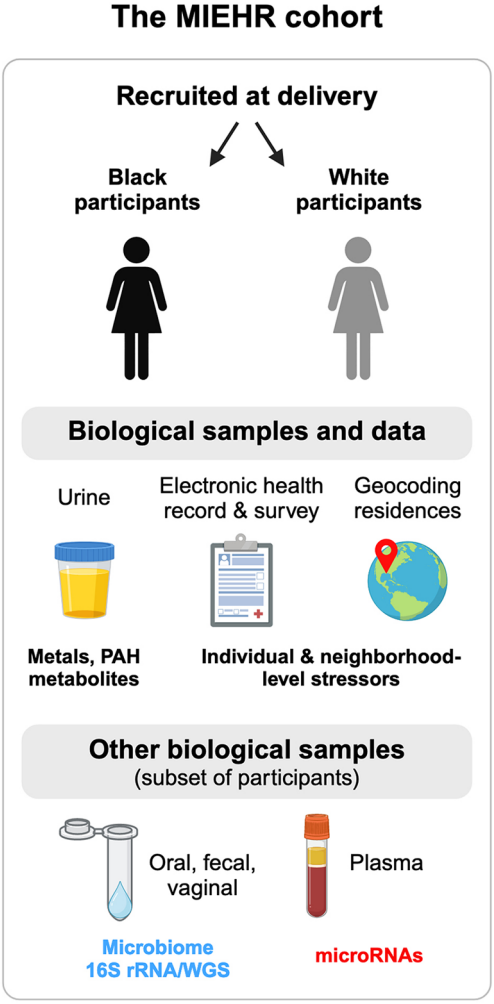

FIGURE 1
Overview of the MIEHR cohort recruited at major obstetric hospitals in Houston, Texas (April 2021-onwards) and the research projects underway. This image was created with BioRender.com.

Individual-level exposures to non-chemical stressors (discrimination, stress and social support)

As part of the questionnaire, we administered Krieger's Experiences of Discrimination (EOD) scale, a validated nine-item measure about lifetime experiences of unfair treatment in different settings that has demonstrated high internal consistency

and test-retest reliability (23). Specifically, pregnant people are asked how many times they have ever experienced discrimination in the following situations: at school; getting a job; at work; getting housing; getting medical care; getting service in a store/restaurant; getting credit, bank loans or a mortgage; on the street or in a public setting; from the police or in the courts. Responses on the EOD are coded as 0 ("never"), 1 ("once"), 2.5 ("2–3 times"), and 5 ("4 or more times") and summed to compute situation and frequency scores that range from 0 to 9 and 0 to 45, respectively, where higher scores indicate greater experiences of discrimination (23). We also ask questions assessing participant's perceptions of stress in their lives and during their pregnancy (not stressful, average stress, very stressful), as well as the level of support from the father of their babies and from families and friends (none, a little, a good amount, and an excellent amount). Lastly, because the greater Houston area is prone to weather-related and industrial disasters (24) and stressful life events have the potential to increase risks of adverse birth outcomes (25), we ask about experiences related to Hurricane Harvey (that resulted in catastrophic flooding in the Houston area in August of 2017 and thereafter), as well as the COVID-19 pandemic.

Individual-level exposures to chemical stressors

Cotinine, a marker of tobacco smoke exposure and the following OH-PAH metabolites are being assessed in maternal urine samples: 1-hydroxynaphthalene (1-NAP), 2- hydroxynaphthalene (2-NAP), 2- hydroxyphenanthrene (2-PHE), 3-hydroxyphenanthrene (3-PHE), 4-hydroxyphenanthrene (4-PHE), combined 1/9-hydroxyphenanthrene (1/9-PHE), combined 2/3/9- hydroxyfluorene (2/3/9-FLUO), 1-hydroxypyrene (1-PYR), 3-hydroxybenzo[c] phenanthrene (3-BCP), 1-hydroxychrysene (1-CHRY), 6-hydroxychrysene (6-CHRY), and 1-hydroxybenz[a]anthracene (1-BAA). Extraction of PAH metabolites from urine was performed by liquid-liquid extraction followed by liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis (26). Briefly, urine samples were spiked with an isotopically labeled internal standard mixture and mixed with 1 ml of 0.5 M ammonium acetate buffer containing 200 units/ml of β-glucuronidase/sulfatase enzyme (MP Biomedicals, LLC, Solon, OH, USA). The urine samples were incubated overnight (~16 h) at 37°C. Urine samples were then diluted by the addition of 2 ml of water followed by extraction using a mixture of 80% pentane: 20% toluene (v/v). PAH metabolites were chromatographically separated using a Waters Acquity I-Class UPLC system (Waters Corporation; Milford, MA, USA) connected with an Acquity UPLC BEH C18 column (50 × 2.1 mm, 1.7 µm, Waters; Milford, MA, USA). Identification and quantification of PAH metabolites was performed on an ABSCIEX 5,500 triple quadrupole mass spectrometer (Applied Biosystems; Foster City, CA, USA). Quality assurance protocols include analysis of two Standard Reference Materials (SRM 3,672, SRM 3,673) containing certified values for several PAH metabolites. HPLC grade water was used for sample/procedural blanks. We replaced urinary concentrations of PAHs below the limit of detection (LOD) with values of the LOD divided by $\sqrt{2}$ (27). To account for urine dilution, creatine concentrations were also measured, and urinary OH-PAH metabolite concentrations were adjusted for creatinine concentrations. Urinary concentrations of 40 metals are also being measured (Lithium, Beryllium, Vanadium, Chromium, Manganese, Cobalt, Nickel, Copper, Zinc, Arsenic, Selenium, Rubidium, Strontium, Molybdenum, Cadmium, Tin, Antimony, Tellurium, Cesium, Barium, Tungsten, Thallium, Lead, Uranium; in addition to 16 rare-earth metals) and will be reported on in the future.

Neighborhood-level exposures to non-chemical and chemical stressors

Participants' residential addresses at delivery and during pregnancy are geocoded using ArcGIS Pro (version 3.1, Esri, Redlands, CA). We are developing several area-level measures and linking them with a mother's residential history to inform specific aspects of their social, built, and physical neighborhood environments. A few of these measures are discussed in more detail below.

Proximity to point sources of pollution

Given that disparities in residential proximity to industrial facilities based on race/ethnicity and socioeconomic position have been documented (28), we are constructing metrics that will allow us to evaluate exposure risks associated with living near point sources of air pollution. To date, we have accessed location information on all national and state Superfund sites in the 8-county study area ($n = 46$) (29) and computed residential distance (based on address at delivery) to the nearest site for MIEHR study participants. Future work will construct similar metrics related to proximity to major roadways and other point or area sources of pollution.

Tree canopy coverage

We computed the percentage of tree canopy surrounding a participant's residence using data from the National Land Cover Database (NLCD) tree canopy dataset for 2021 that provides the proportion of tree canopy within 30×30 m^2 gridded cells. Using ArcGIS Pro's Zonal Statistics as Table Tool, we averaged the percentages of tree canopy of all cells in which the centroid of the cell was contained within a 300 m buffer of a mother's residence.

Socioeconomic deprivation

We used U.S. Census American Community Survey (ACS) five-year (2016–2020) estimates of socioeconomic and demographic variables to construct Area Deprivation Index (ADI) for all census tracts in the study area. ADI is a composite measure of neighborhood socioeconomic disadvantage that incorporates information on education, employment, income, poverty, household, and housing characteristics (30). We applied the R "Sociome" package to construct estimates that includes 15 original ACS variables for constructing ADI (the number of households

without a telephone and the number of occupied housing units without complete plumbing were excluded from the computation) (31). Higher ADI scores indicate greater neighborhood deprivation.

Social vulnerability

We downloaded data for the social vulnerability index (SVI) from the Centers for Disease Control and Prevention (CDC)/ Agency for Toxic Substances and Disease Registry (ATSDR). The SVI is a census tract-level composite metric comprised of 15 neighborhood characteristics in four domains (socioeconomic factors, household composition and disability, minority status and language, and housing type and transportation) and identifies communities at risk for public health emergencies related to natural and anthropogenic disasters (32). Higher SVI values indicate higher risk.

Racialized economic segregation

As proposed by Krieger et al. (33), we constructed the Index of Concentration at the Extremes (ICE) combined for race and income for all census tracts in our 8-county study area, using data from the U.S. Census ACS. ICE is a spatial measure of racialized economic segregation and here, we contrasted census-tract level differences between the proportions of high-income (>$100,000) non-Hispanic white persons and low-income (<$25,000) non-Hispanic Black persons. ICE has values ranging from −1 (areas of extreme economic and racial privilege) to 1 (areas of extreme economic and racial privilege).

Food access

We downloaded census-tract level indicators of food access for the 8-county study area from the USDA Food Access Research Atlas for 2019, including proportion of housing units that are without a vehicle and beyond ½ mile from a supermarket (34).

Statistical analyses

We sought to characterize individual and neighborhood characteristics among pregnant people who enrolled in the MIEHR cohort. We calculated descriptive statistics for individual-level sociodemographic, behavioral, and health history information collected from questionnaires or abstracted from EHRs; data are presented both overall and by race. We also summarized the responses to the EOD scale and questions about sources of stress and social support by race. We computed summary statistics including the mean and standard deviation, selected percentiles, and detection frequency for urinary concentrations of selected OH-PAHs with at least 50% of values above the LOD (i.e., 1-NAP, 2-NAP, 2-PHEN, 3-PHEN, 2/3/9-FLUO and 1-PYR), as well as cotinine. Spearman rank correlation analysis was conducted between cotinine and OH-PAHs. Over the 8-county study area, we categorized values of ADI, ICE, and SVI into quintiles whereas we classified food access by tertiles because of a highly skewed distribution. We linked the census tract of a pregnant person's residence at delivery to the appropriate quantile of each metric and evaluated the percentile breakdown of neighborhood features for the study population together and stratified by race. Statistical or spatial analyses were performed in SAS (version 9.4) or ArcGIS (version 3.1.2).

Results

As of February 28, 2023, 1,244 pregnant people were enrolled in the MIEHR cohort: 926 (74.4%) at Memorial Hermann Hospital, 211 (17.0%) at Texas Children's Pavilion for Women and 107 (8.6%) at Ben Taub Hospital. In total, nearly 80% of participants agreed to be re-contacted. Almost all participants ($n = 1{,}241$, 99.8%) provided urine samples and 595 (49.8%) provided blood samples. We also compared pregnant people who provided blood samples to the total cohort and there were little differences in the sociodemographic characteristics between these two groups. Among participants who were offered the opportunity to provide additional biological samples ($n = 318$), most (93.1%) provided oral swabs whereas relatively few provided vaginal swabs (24.2%) or fecal (15.1%) samples.

Table 1 presents a sociodemographic breakdown of the MIEHR cohort. Fifty-six percent of pregnant people were between the ages of 25–34 when they delivered their infants; most (61.1%) were non-Hispanic Black. Similar proportions of pregnant people report an annual household income of less than $35,000 (35.5%) or $75,000 or more (38.5%). Most pregnant people did not smoke (96%) or use alcohol (87.3%) during their pregnancy. There are notable differences in the sociodemographic profiles of Black and white pregnant people in the MIEHR cohort: 33.2% of Black pregnant people were less than 25 years of age when they delivered their infants as compared to 8.3% of white pregnant people; almost two-thirds (63.4%) of Black pregnant people were single as compared to 10.1% of white pregnant people; there was a five-fold difference in the percentage of Black pregnant people with household incomes lower than $35,000 as compared to white pregnant people; and a greater proportion of Black pregnant people as compared to white pregnant people initiated prenatal care at or after 13 weeks (21.1% vs. 6.8%). Regarding lifestyle factors, while the prevalence was low in both groups, there was almost a 3-fold increase in the proportion of white pregnant people as compared to Black pregnant people who reported using alcohol during their pregnancy (20.7% vs. 7.6%, respectively). As shown in Figure 2, the MIEHR cohort comes from a large, dispersed, geographic area in greater Houston. Over three-fourths of pregnant people (76.7%) did not move during their pregnancy. Among pregnant people who lived at more than one address while pregnant, 266 (21.4%) reported one move, 17 (1.4%) reported two moves, and 3 (0.2%) reported three moves.

Individual-level exposures: non-chemical stressors (discrimination, stress and social support)

Table 2 reports on experiences of lifetime discrimination reported by pregnant people in different settings. In total, 83.9% of white participants reported no experiences of lifetime

TABLE 1 Sociodemographic characteristics of MIEHR study participants, greater Houston area, April 2021—February 2023, *N* = 1,244.

Sociodemographic Characteristics	Total	Black	White
	N = 1,244	*N* = 760	*N* = 484
	n (%)	*n* (%)	*n* (%)
Recruitment site			
Ben Taub Hospital	107 (8.6)	83 (10.9)	24 (5.0)
Texas Children's Pavilion for Women	211 (17.0)	82 (10.8)	129 (26.7)
Memorial Hermann Hospital	926 (74.4)	595 (78.3)	331 (68.4)
Age (years)			
<25	292 (23.5)	252 (33.2)	40 (8.3)
25–29	346 (27.8)	224 (29.5)	122 (25.2)
30–34	347 (27.9)	170 (22.4)	177 (36.6)
≥35	259 (20.8)	114 (15.0)	145 (30.0)
Preterm birth			
Pre-term	259 (20.8)	178 (23.4)	81 (16.7)
Full term	985 (79.2)	582 (76.6)	403 (83.3)
Nativity			
U.S.-born	1,137 (91.4)	692 (91.1)	445 (91.9)
Foreign-born	107 (8.6)	68 (8.9)	39 (8.1)
Employment			
Yes	749 (60.2)	386 (50.8)	363 (75.0)
Not employed	495 (39.8)	374 (49.2)	121 (25.0)
Highest educational attainment			
≤High school degree	408 (32.8)	351 (46.2)	57 (11.8)
College degree or higher	836 (67.2)	409 (53.8)	427 (88.2)
Marital status			
Single, never married	531 (42.7)	482 (63.4)	49 (10.1)
Married/Living with partner	696 (55.9)	265 (34.9)	431 (89.0)
Separated/widowed/divorced	17 (1.4)	13 (1.7)	4 (0.8)
Income			
Less than $ 34,999	441 (35.5)	398 (52.4)	43 (8.9)
$ 35,000–$ 74,999	254 (20.4)	194 (25.5)	60 (12.4)
$ 75,000 and above	479 (38.5)	105 (13.8)	374 (77.3)
Don't know	52 (4.2)	48 (6.3)	4 (0.8)
Prefer not to answer	18 (1.4)	15 (2.0)	3 (0.6)
Smoked cigarettes during pregnancy			
Never smoker	939 (75.5)	616 (81.1)	323 (66.7)
No	255 (20.5)	109 (14.3)	146 (30.2)
Yes	50 (4.0)	35 (4.6)	15 (3.1)
Exposure to secondhand cigarette smoke in the home or car during pregnancy			
No	1,015 (81.6)	581 (76.4)	434 (89.7)
Yes	228 (18.3)	179 (23.6)	49 (10.1)
Missing	1 (0.1)	0 (0.0)	1 (0.2)
Consumed alcohol during pregnancy			
Never drinker	202 (16.2)	181 (23.8)	21 (4.3)
No	883 (71.0)	521 (68.6)	362 (74.8)
Yes	158 (12.7)	58 (7.6)	100 (20.7)
Missing	1 (0.1)	0 (0.0)	1 (0.2)
Initiation of prenatal care			
No prenatal care	12 (1.0)	10 (1.3)	2 (0.4)
<13 weeks	998 (80.2)	553 (72.8)	445 (91.9)
≥13 weeks	193 (15.5)	160 (21.1)	33 (6.8)
Don't know	40 (3.2)	36 (4.7)	4 (0.8)
Prefer not to answer	1 (0.1)	1 (0.1)	0 (0.0)

discrimination as compared to 47.4% of Black participants. The most common situations for Black participants reported experiencing discrimination were when they were getting services in a store or restaurant (32.5%), on the street or in a public setting (31.7%) or at work (30.5%). The summary scores for frequency of experiencing discrimination were 5.8 (SD = 8.7) and 0.9 (SD = 2.8) among Black and white participants, respectively. Table 3 summarizes stress experiences following the arrival of Hurricane Harvey in August 2017 and during the COVID-19 pandemic. A larger proportion of Black pregnant people (38.0%) than white pregnant people (16.9%) reported being impacted by Hurricane Harvey and had higher levels of stress in all contexts (i.e., new or worsened respiratory conditions; new or worsened anxiety; new or worsened depression; displaced from home; experienced extensive property loss or damage; or experienced new or worsened financial hardship). While more white than Black participants report that they or a family member tested positive for SARS-CoV-2, a greater proportion of Black participants reported that they (or a family member) were hospitalized. The financial impact of the COVID-19 pandemic in terms of employment (reductions in wages, hour worked or job loss) was greater among white participants (64.3%) as compared to Black participants (49.9%) whereas more Black than white participants had difficulty with getting food (15.3 vs. 7.9%), housing (13.3 vs. 2.7%) or transportation (11.6 vs. 2.9%).

In contrast to experiences following Hurricane Harvey or during the COVID-19 pandemic, higher proportions of Black as compared to white pregnant people reported "not stressful" when asked about the amount of stress during their pregnancy (30.4% vs. 11.0%) whereas the proportions of participants reporting "very stressful" were similar between the groups (see Table 4). Also shown in Table 4 are summaries of responses about assistance and support from the father or family members and friends. Whereas 83.5% of white participants reported receiving an "excellent amount" of support from the father, only 57.5% of Black participants reported this same level of support. There were also differences by race for participants receiving low levels of social support with 17.5% of Black participants reporting "a little" or "none", as compared to 5.4% of white participants. In contrast, there were modest differences by race in the amount of assistance and support from family members and friends.

Individual-level exposures: chemical stressors

Urinary concentrations of OH-PAH metabolites (μg/g creatinine) for 579 study participants showed that at least 50% of the values were above the LOD for 1-NAP (100%), 2-NAP (100%), 2/3/9-FLUO (83.8%), 1/9-PHEN (74.1%), 2-PHEN (58.2%), and 1-PYR (57.2%). The 50th (25th and 75th) percentiles for these PAH metabolites were 0.634 (0.384,1.107) (1-NAP), 5.844 (3.136, 10.595) (2-NAP), 0.032 (0.020, 0.053) (2-PHEN), 0.040 (0.023, 0.072) (1/9-PHEN), 0.070 (0.044, 0.127) (2/3/9-FLUO) and 0.036 (0.022, 0.062) (1-PYR) μg/g creatinine (Figure 3). Because PAHs are constituents of cigarette smoke, a heat map of the Spearman rank correlation coefficients for these OH-PAHs as well as cotinine was performed as shown in Supplementary Figure S1. Pair-wise correlations ranged from 0.085 to 0.690 and most ($n = 14$; 66.7%) of the correlation coefficients were 0.5 or lower. The highest correlations

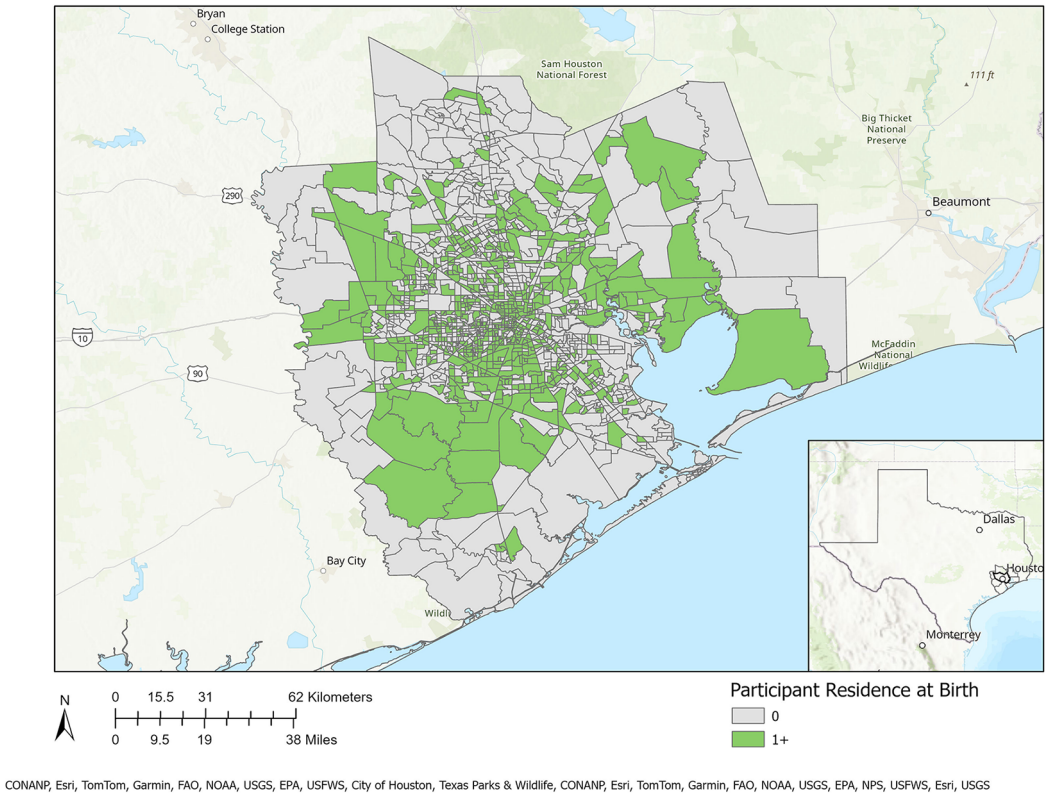

FIGURE 2
Residential locations of MIEHR cohort participants recruited through February 2023 in the greater Houston (8-county) study area (census tracts with residential locations of at least one study participant are shaded in green).

were observed between 2-PHEN and 1-PYY (0.69), 2-PHEN and 2/3/9-FLUOR (0.67), 1/9-PHEN and 2/3/9-FLUOR (0.66), 2-PHEN and 1/9-PHEN (0.65), 1/9-PHEN and 1-PYR (0.63), 2/3/9-FLUOR and 1-PYY (0.57) and 1-NAP and 2-NAP (0.54).

Neighborhood-level exposures: Non-chemical stressors (tree canopy, socioeconomic deprivation, social vulnerability, residential segregation, food access)

In total, the median proportion of tree canopy cover within 300 m of participant's residence at delivery was 9%; 95% of participants were classified as having less than 23% tree canopy cover near their homes. There were little differences in this metric of residential greenness by race—the 25th, 50th, and 75th percentiles of tree canopy cover were 4.8, 9.4, and 15.4% for white participants and 4.8, 9.0 and 13.3% for Black participants. Figure 4 displays the spatial distribution of census tract-level ADI, SVI, ICE and Food Access for the 8-county study area. As shown in Table 5, substantially larger proportions of Black participants as compared to white participants lived in neighborhoods with: (1) high levels of socioeconomic disadvantage (upper two quintiles for ADI: 64.5% vs. 17.5%, respectively), (2) greater risk for public health emergencies (upper two quintiles for SVI: 59.8% vs. 19.6%, respectively), (3) higher levels of racialized economic segregation (lower two quintiles of ICE: 73.8% vs. 19.7%, respectively) and (4) the lowest levels of food access (upper tertile of food access: 49.7% vs. 16.7%, respectively).

TABLE 2 Experiences of discrimination of MIEHR study participants, greater Houston area, April 2021—February 2023.

Experiences of discrimination[a]	Black	White
	N = 760	*N* = 484
Number	*n* (%)	*n* (%)
0	360 (47.4)	406 (83.9)
1–2	163 (21.4)	57 (11.8)
3+	236 (31.1)	19 (3.9)
Missing	1 (0.1)	2 (0.4)
Summary score	mean ± SD	
Situations (possible range: 0–9)	1.8 ± 2.4	0.3 ± 0.6
Frequency (possible range: 0–45)	5.8 ± 8.7	0.9 ± 2.8

[a]In 9 scenarios.

Neighborhood-level exposures: chemical stressors (proximity to superfund sites)

The median value from a participant's residence to the closest Superfund site was 3.62 miles, with the residences of Black

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TABLE 3 Stress events during hurricane harvey (August 2017) and the COVID-19 pandemic, MIEHR study participants, greater Houston area, April 2021—February 2023.

Stress events	Black	White
	N = 760	*N* = 484
	n (%)	*n* (%)
Impacted by Hurricane Harvey		
No	470 (61.8)	400 (82.6)
Yes	289 (38.0)	82 (16.9)
Don't know	1 (0.1)	1 (0.2)
Missing	0 (0.0)	1 (0.2)
Tested positive for COVID-19		
No	501 (65.9)	232 (47.9)
Yes	257 (33.8)	251 (51.9)
Don't know	1 (0.1)	0 (0.0)
Missing	1 (0.1)	1 (0.2)
Hospitalized for COVID-19		
No	231 (89.9)	244 (97.2)
Yes	26 (10.1)	7 (2.8)
Someone in the household tested positive for COVID-19		
No	543 (71.4)	232 (47.9)
Yes	216 (28.4)	250 (51.7)
Don't know	0 (0.0)	1 (0.2)
Missing	1 (0.1)	1 (0.2)
Someone in the household hospitalized for COVID-19		
No	195 (90.3)	241 (96.4)
Yes	21 (9.7)	9 (3.6)
Reduction in reduced wages, work hours or lost job during the pandemic		
No	378 (49.7)	172 (35.5)
Yes	379 (49.9)	311 (64.3)
Don't know	2 (0.3)	0 (0.0)
Missing	1 (0.1)	1 (0.2)
Difficulty with childcare access during the pandemic		
No	628 (82.6)	397 (82.0)
Yes	128 (16.8)	86 (17.8)
Don't know	3 (0.4)	0 (0.0)
Missing	1 (0.1)	1 (0.2)
Difficulty getting food during the pandemic		
No	643 (84.6)	443 (91.5)
Yes	116 (15.3)	38 (7.9)
Don't know	0 (0.0)	2 (0.4)
Missing	1 (0.1)	1 (0.2)
Difficulty with housing during the pandemic		
No	657 (86.4)	469 (96.9)
Yes	101 (13.3)	13 (2.7)
Don't know	0 (0.0)	1 (0.2)
Prefer not to answer	1 (0.1)	0 (0.0)
Missing	1 (0.1)	1 (0.2)
Difficulty with transportation during the pandemic		
No	670 (88.2)	467 (96.5)
Yes	88 (11.6)	14 (2.9)
Don't know	0 (0.0)	2 (0.4)
Prefer not to answer	1 (0.1)	0 (0.0)
Missing	1 (0.1)	1 (0.2)
Difficulty getting medication, accessing healthcare, or paying for medical expenses during the pandemic		
No	670 (88.2)	456 (94.2)
Yes	89 (11.7)	25 (5.2)
Don't know	0 (0.0)	2 (0.4)
Missing	1 (0.1)	1 (0.2)

TABLE 4 Stress and support during pregnancy, by race, of MIEHR study participants, greater Houston area, April 2021—February 2023.

	Black	White
	N = 760	*N* = 484
	n (%)	*n* (%)
Description of the amount of stress during pregnancy		
Not stressful	231 (30.4)	53 (11.0)
Average stress	335 (44.1)	294 (60.7)
Very stressful	193 (25.4)	136 (28.1)
Don't know	0 (0.0)	0 (0.0)
Prefer not to answer	0 (0.0)	0 (0.0)
Missing	1 (0.1)	1 (0.2)
The amount of assistance and support received during pregnancy from the baby's father		
None	77 (10.1)	16 (3.3)
A little	56 (7.4)	10 (2.1)
A good amount	182 (23.9)	49 (10.1)
An excellent amount	437 (57.5)	404 (83.5)
Don't know	1 (0.1)	1 (0.2)
Prefer not to answer	6 (0.8)	3 (0.6)
Missing	1 (0.1)	1 (0.2)
The amount of assistance and support received during pregnancy from family members or friends		
None	42 (5.5)	7 (1.4)
A little	51 (6.7)	25 (5.2)
A good amount	209 (27.5)	119 (24.6)
An excellent amount	456 (60.0)	331 (68.4)
Don't know	1 (0.1)	0 (0.0)
Prefer not to answer	0 (0.0)	1 (0.2)
Missing	1 (0.1)	1 (0.2)

participants slightly closer to a site (3.40 miles) as compared to residences of white participants (3.90 miles). The interquartile range of residential distances to the nearest Superfund site was 3.61 miles for all participants, and 3.38 and 4.05 miles for Black and white participants, respectively.

Discussion

Black pregnant people suffer the highest risks of poor pregnancy outcomes in the nation and the reasons for this disparity are poorly understood. Hence, we established the MIEHR cohort in a large and diverse urban area in the U.S. to unravel factors that help to explain Black-White disparities in preterm birth and other perinatal outcomes. Our focus is on examining effects of chemical and non-chemical stressors in the biological, physical, social, and built environments, i.e., the environmental riskscape, which contribute to racial disparities in maternal and child health. Extensive data is being collected in the MIEHR cohort through administration of questionnaires and EHR abstraction, along with collection of biological samples for chemical, miRNA, and microbiome assessments. Beyond individual-level factors, features of a pregnant person's neighborhood environment are also being characterized. Initial analysis of individual- and neighborhood-level factors among the 1,244 pregnant people enrolled in MIEHR through the end of February 2023 suggests

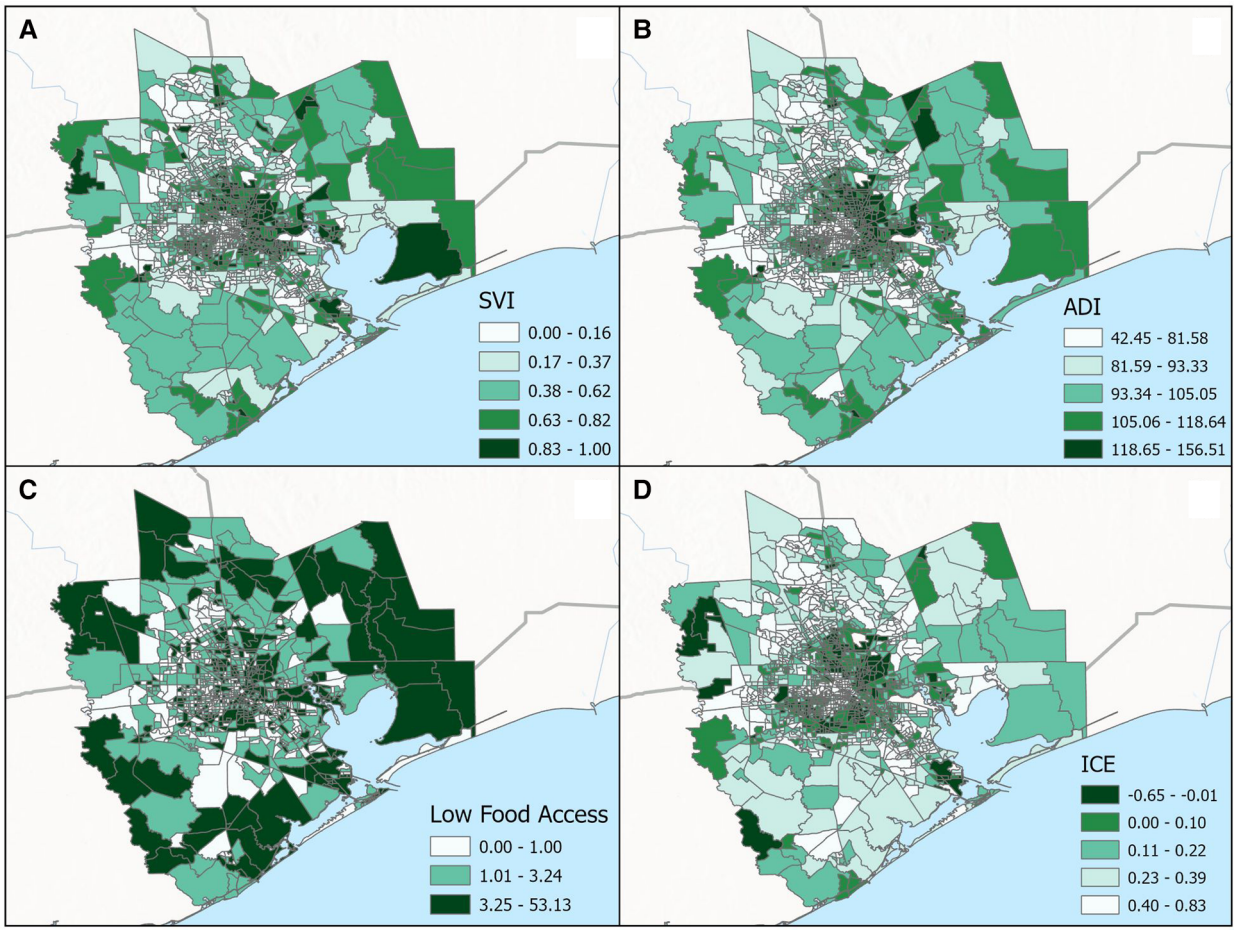

FIGURE 3
Categorical breakdown across census tracts for the (**A**) social vulnerability index (SVI), (**B**) area deprivation index (ADI), (**C**) low food access and (**D**) index of concentration at the extremes (ICE) for the greater Houston (8-county) study area.

differences between Black and white pregnant people in experiences of discrimination, stress, and levels of support, as well as in characteristics of their neighborhoods.

An earlier meta-analysis of the epidemiologic evidence reported significant albeit relatively small impacts of individual-level sources of psychosocial stress on adverse birth outcomes (35). Stress during pregnancy is associated with increased concentrations of catecholamines (36) and activation of the hypothalamic-pituitary-adrenal (HPA) axis that triggers a cascade of events culminating in the release of cortisol (35, 37), which crosses the placenta and may adversely impact fetal development and parturition (37). Our findings regarding racial differences in stress levels depended on whether questions were specific to events (like Hurricane Harvey or the pandemic) or were general in nature. In the aftermath of specific disasters, Black participants reported experiencing higher levels of stress than white participants, while reports of general stress were lower among Black as compared with white participants. Findings from the literature have been mixed. In one study and contrary to our findings, perceived stress levels, as assessed using Cohen's Perceived Stress Scale (PSS-14 $\geq$ 30), were greater among Black (24.7%) than white (7.7%) pregnant participants from Philadelphia, PA (38). On the other hand in a study using the Pregnancy Risk Assessment Monitoring System (PRAMS) data from 2012 to 2013, the prevalence of traumatic stressors were higher among white participants as compared to Black participants whereas there were little differences for either financial or relationship stressors (39).

A recent review points to a greater role for stressors like racial discrimination on increased risks for adverse birth outcomes (40). Consistent with prior findings that individuals of color have greater opportunity to experience stressful conditions due to the intersection of race and gender (41), Black pregnant people in the MIEHR cohort experienced greater discrimination as compared to their white counterparts. Our findings are similar to results from an earlier investigation of 112 pregnant people who were recruited in Chicago, Illinois that used the same scale as we applied in our study (42), as well as in a recently published cross-sectional analysis of 198 women that relied on a different tool (the Schedule of Racist Events measure) to assess discrimination (43).

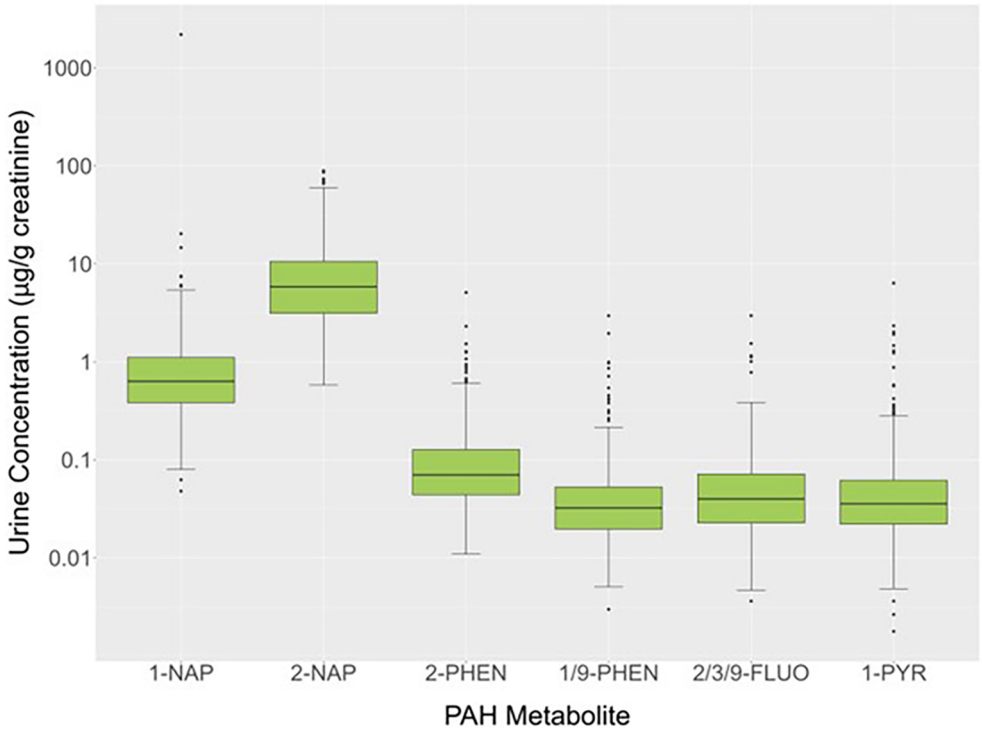

FIGURE 4
Box plots of OH-PAHS for a subset of the MIEHR cohort (n = 579).

TABLE 5 Neighborhood features of MIEHR study participants, greater Houston area, April 2021—February 2023.

Neighborhood feature	Total	Black	White
	N = 1,244	N = 760	N = 484
	n (%)	n (%)	n (%)
Area deprivation index (ADI)			
Q1 (42.5–75.64)	155 (12.5)	24 (3.2)	131 (27.1)
Q2 (75.65–89.98)	251 (20.2)	95 (12.5)	156 (32.2)
Q3 (89.99–104.96)	263 (21.1)	151 (19.9)	112 (23.1)
Q4 (104.97–121.56)	327 (26.3)	263 (34.6)	64 (13.2)
Q5 (121.57–156.51)	248 (19.9)	227 (29.9)	21 (4.3)
Social vulnerability index (SVI)			
Q1 (0–0.17)	240 (19.3)	53 (7.0)	187 (38.6)
Q2 (0.18–0.37)	224 (18.0)	102 (13.4)	122 (25.2)
Q3 (0.38–0.62)	231 (18.6)	151 (19.9)	80 (16.5)
Q4 (0.63–0.82)	257 (20.7)	199 (26.2)	58 (12.0)
Q5 (0.83–1.00)	292 (23.5)	255 (33.6)	37 (7.6)
Index of concentration at the extremes (ICE $_{(race + income)}$)			
Q1 (−0.65 - −0.01)	456 (36.7)	418 (55.0)	38 (7.9)
Q2 (0–0.10)	200 (16.1)	143 (18.8)	57 (11.8)
Q3 (0.11–0.22)	182 (14.6)	108 (14.2)	74 (15.3)
Q4 (0.23–0.39)	187 (15.0)	55 (7.2)	132 (27.3)
Q5 (0.40–0.83)	219 (17.6)	36 (4.7)	183 (37.8)
% Low food access to supermarkets			
Q1 (0–1.00)	416 (33.4)	167 (22.0)	249 (51.5)
Q2 (1.01–3.24)	369 (29.7)	215 (28.3)	154 (31.8)
Q3 (3.25–53.13)	459 (36.9)	378 (49.7)	81 (16.7)

Whereas there were modest differences in levels of support from family members and friends for Black and white pregnant people in our study, white pregnant people generally reported receiving higher levels of paternal support. The benefits of social support are hypothesized to operate through several pathways by reducing inflammation and biological aging. Population-based studies have reported Black-White differences in biological aging (44, 45), as well as inverse associations among Black (but not white) adults who participate in more social groups (44). A pilot study of 49 pregnant Black participants reported inverse associations between social support and pro-inflammatory cytokines (IL-2, IL-5, andIL-6) (46). While results from a systematic review and metanalysis suggest associations between low social support and increased risks for preterm birth, especially among participants with high stress levels (pooled OR of 1.52 (95% CI, 1.18, 1.97) (47), a consensus document from the March of Dimes concluded the evidence was insufficient regarding the role of social support in explaining Black-white disparities in preterm birth (48).

Neighborhoods represent shared physical characteristics, social and economic resources, and social interaction among residents (49, 50). Neighborhood socioeconomic disadvantage, which is a well-studied attribute of the neighborhood environment, has been consistently associated with adverse perinatal health even after controlling for individual-level factors (49, 51–53). Moreover, consistent with the hypothesis of a psychosocial pathway through which the residential environment adversely

impacts pregnant people (54), studies have found in non-pregnant populations that neighborhood conditions associated with disadvantage are conducive to stress (55) and are linked to increased cumulative biological risk, allostatic load and cortisol levels (56–59). In our study, we found substantially larger proportions of Black participants as compared to white participants lived in neighborhoods with high levels of socioeconomic disadvantage. Similarly, based on assessment of ICE and SVI, higher proportions of Black women lived in neighborhoods that were socially and racially isolated or at elevated risk for natural or industrial disasters, respectively. While the evidence for the impact of residential greenspace on perinatal health is mixed (60), we are also computing metrics of greenness surrounding homes that a participants lived in during their pregnancy, including at delivery. Not surprisingly in an urban area such as Greater Houston, on average, there was less than 10% of tree canopy near a participant's residence and we found little differences in residential greenness between Black and white participants.

Given inequalities in the spatial distribution of environmental hazards, disadvantaged communities experience a higher burden of exposure to chemical stressors as evidenced in studies conducted across the U.S (17, 61, 62)., as well as in large urban areas (63, 64) including Houston (65). Hence, our focus on factors in the environmental riskscape extends to such stressors, particularly exposures to metals and PAHs in the physical environment that can occur via multiple pathways (ingestion, inhalation, or skin contact). Oxidative stress is a common pathway for metal-induced physiologic perturbations and subsequent toxicities (66, 67) and has been implicated in PAH toxicity as well (68, 69). During pregnancy, oxidative stress may result in alterations in signaling pathways, protein modifications, activation of inflammatory pathways and DNA oxidation; all of which may impact vascular function at the maternal placental interface (70).

Comparison of measured urinary concentrations of OH-PAHs in the present investigation with those previously reported in other populations, either during pregnancy or around the time of delivery is limited given differences in adjustment for urine dilution; as such, our comparisons were restricted to studies where OH-PAH concentrations were adjusted for creatinine. Median 1-PYR concentrations in our study (0.036 μg/g creatinine) were similar to levels measured in investigations conducted on pregnant people in Brazil (0.030 μg/g creatinine) and Saudia Arabia (0.050 μg/g creatinine) whereas they were lower than previously reported in studies from the Czech Republic (0.120 μg/g creatinine) (71), Japan (0.124 μg/g creatinine) (72), Poland (0.35 μg/g creatinine) (73), Haojiang, China (0.570 μg/g creatinine) (74), Taiyuan, China (1.83 μg/g creatinine) (75) and Iran (6.5 μg/g creatinine) (76). For 1-NAP, levels measured in the MIEHR cohort (median = 0.630 μg/g creatinine) fell between those reported in other studies. Whereas lower values were reported for pregnant people living in the Czech Republic (0.40 μg/g creatinine) (71), 1-NAP values were considerably higher in investigations in Iran (4.6 μg/g creatinine) and Brazil (16.99 μg/g creatinine) (77). For 2-NAP, concentrations were higher in our study when compared to levels in pregnant people in South Korea (78) [arithmetic mean (AM) = 9.44 μg/g creatinine vs. 0.010 μg/g creatinine], Canada [geometric mean (GM) = 6.002 μg/g creatinine vs. 2.61 μg/g creatinine] (79), Brazil (median = 5.84 μg/g creatinine vs. 3.62 μg/g creatinine vs.) or Iran (median = 5.84 μg/g creatinine vs. 2.5 μg/g creatinine). In contrast, median levels of 2-PHEN of 0.032 μg/g creatinine in the MIEHR cohort were low relative to reports in the Czech Republic (71) (0.170 μg/g creatinine), China (80) (0.109 μg/g creatinine), or Poland (73) (0.430 μg/g creatinine). Overall, PAH exposure patterns varied in our cohort compared to pregnant people in other countries; also, where comparisons could be made, concentrations in our study were similar (2-NAP) or lower (1-NAP and 1-PYR) than those reported for NHANES for either females ages 3 and older or adults ages 20 and older (81).

Future directions

We continue to enroll pregnant people in the MIEHR cohort. Analyses of urinary metal concentrations are underway as are maternal oral microbiome testing and miRNA analyses in plasma samples. Work is also ongoing to characterize a participant's neighborhood environment more fully by developing metrics for proximity to major roadways and other major pollution sources. With complete cohort data, we will formally evaluate differences in exposure profiles between Black and white cohort members and associations between exposure to the mixture of metal and OH-PAH metabolites and perinatal health outcomes, as well as the potential modifying role of neighborhood stressors on these associations. We are also planning on developing disparity-aware classifiers to identify the most informative set of features that predict risk for preterm birth for Black and white women. Future studies will continue to follow up pregnant participants and their children to evaluate the impact of the environmental riskscape on their longer-term health and well-being.

Data availability statement

The datasets presented in this article are not readily available because de-identified data will be made available according to the restrictions as specified in the IRB protocol. Requests to access data should be directed to elaine.symanski@bcm.edu.

Ethics statement

The studies involving humans were approved by Baylor College of Medicine Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

ES: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing. KW: Conceptualization, Methodology, Supervision, Writing – review & editing. HM-F: Supervision, Writing – review & editing. KA: Supervision, Writing – review & editing. IM: Data curation, Formal Analysis, Writing – review & editing. JA: Data curation, Formal Analysis, Writing – review & editing. AC: Data curation, Visualization, Writing – review & editing. KK: Formal Analysis, Writing – review & editing. CW: Writing – review & editing. CC: Writing – review & editing. MS: Writing – review & editing. HS: Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The reviewer CH declared a past co-authorship with the author KK to the handling editor.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/frph.2024.1304717/full#supplementary-material

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Examining modification of the associations between air pollution and birth outcomes by neighborhood deprivation in a North Carolina birth cohort, 2011–2015

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Background: Evidence from studies of air pollutants and birth outcomes suggests an association, but uncertainties around geographical variability and modifying factors still remain. As neighborhood-level social characteristics are associated with birth outcomes, we assess whether neighborhood deprivation level is an effect measure modifier on the association between air pollution and birth outcomes in a North Carolina birth cohort.

Methods: Using birth certificate data, all North Carolina residential singleton live births from 1 January 2011 to 31 December 2015 with gestational ages of 20–44 weeks (n = 566,799) were examined for birth defect diagnoses and preterm birth. Exposures were daily average fine particulate matter ($PM_{2.5}$), daily 8-h maximum nitrogen dioxide (NO_2), and daily 8-h maximum ozone (O_3) modeled concentrations, and the modifier of interest was the neighborhood deprivation index (NDI). Linear binomial models were used to estimate the prevalence differences and 95% confidence intervals (CI) for the association between ambient air pollution and birth defect diagnoses. Modified Poisson regression models were used to estimate risk differences (RDs) and 95% CIs for air pollution and preterm birth. Models were stratified by the neighborhood deprivation index group (low, medium, or high) to assess potential modification by NDI.

Results: Approximately 3.1% of the study population had at least one birth defect and 8.18% were born preterm. For preterm birth, associations with $PM_{2.5}$ and O_3 did not follow a conclusive pattern and there was no evidence of modification by NDI. The associations between NO_2 and preterm birth were generally negative across exposure windows except for a positive association with NO_2 and preterm birth for high NDI [RD: 34.70 (95% CI 4.84–64.56)] for entire pregnancy exposure. There was no evidence of associations between pollutants examined and birth defects.

Conclusions: There may be differences in the association between NO_2 exposure and preterm birth by NDI but we did not observe any evidence of associations for birth defects. Our results support the public health protection afforded by reductions in air pollution, even in areas of neighborhood deprivation, but future research conducted in areas with higher levels of air pollution and evaluating the potential for modification by neighborhood deprivation level would be informative.

KEYWORDS

air pollution, birth outcomes, neighborhood deprivation, modification, preterm birth, birth defects

Introduction

Preterm birth (PTB) and birth defects are two of the leading causes of infant mortality in the United States (1–3). These adverse birth outcomes are also associated with high medical expenses, higher risk of medical conditions across the life course, and developmental disabilities (4–9). Across live born infants in the United States since 2010, about 10% (9.57–10.49) were preterm, defined as being born before 37 weeks of gestation (10); and about 3% had at least one birth defect diagnosed in their first year of life. Birth defects can range in severity with over 1,000 different types identified (11). There are several established risk factors for adverse birth outcomes, e.g., age of the birthing person and smoking for preterm birth (12–14), and heavy alcohol use, certain medications, and uncontrolled diabetes for birth defects (15–19). Researchers have also reported associations between environmental exposures, such as lack of greenspace, extreme heat, and air pollution, and adverse birth outcomes (20–31).

Over the past few decades, evidence has accumulated suggesting an association between air pollution and birth outcomes. A number of studies have identified a positive association between increases in exposure to air pollutants (i.e., NO_2, $PM_{2.5}$, O_3) and preterm birth (32–34), with some studies finding that exposure to O_3 specifically during the first two trimesters of pregnancy heightens the risk of preterm birth (32). While most studies have found positive associations between air pollution and preterm birth, a 2020 systematic review identified five (among 24 total studies on $PM_{2.5}$ and preterm birth) that did not find an association when measuring exposure across pregnancy or by trimester (35). However, evidence regarding the association between air pollution and birth defects is less consistent. Some studies have reported associations between NO_2 and congenital heart defects (36), but others have not (37), and findings between O_3 and $PM_{2.5}$ with birth defects are very inconsistent (32, 34). Given the heterogeneity reported across studies, there are uncertainties around the role of exposure timing, birthing parent characteristics, geographical variability, and other mediating or modifying factors in the relationship between air pollution and poor birth outcomes (38). In addition, there is limited knowledge on the mechanisms by which air pollution may affect birth outcomes (39, 40).

Given the well-documented sociodemographic disparities in both air pollution exposure, particularly with higher levels of pollution occurring in areas with a higher proportion of non-White residents (41–43), and racial disparities observed in birth defects and preterm birth (44–47), structural factors may potentially modify air pollutant–birth outcome associations. Research has also shown that neighborhood-level characteristics such as neighborhood deprivation are associated with poor birth outcomes (48–53). Environmental and social factors likely contribute to cumulatively impact birth outcomes, worsening disparities (54, 55). However, there is limited information on how air pollutants and neighborhood deprivation interact with one another to impact birth outcomes.

To address this gap, the goal of this study was to examine if the neighborhood deprivation level is an effect measure modifier on the association between air pollution and birth outcomes using data from all eligible births in North Carolina (NC).

Materials and methods

Study population

Birth certificate data for live births were provided by the NC Department of Health and Human Services' Division of Public Health linked with data from the Birth Defects Monitoring Program ($n = 588{,}135$). The population for this study included all live, singleton births with gestational age between 20 and 44 weeks delivered from 1 January 2011 to 31 December 2015 with residence at delivery in NC. These specific years were selected due to data availability and consistency of records as a result of changes made to the North Carolina birth cohort in 2010. After excluding multiple births ($n = 20{,}586$), deliveries outside of 20–44 weeks gestational age ($n = 642$), and missing residential address at time of delivery that precluded geocoding ($n = 8$), the final sample was 566,799 births. The residential address at time of delivery was geocoded to the corresponding census tract using ArcGIS (ESRI, version 10.8, Redlands, CA).

Birth outcomes

The outcomes of interest in this study were birth defects and preterm birth. Birth defects were identified from the North Carolina birth defect monitoring program (NCBDMP), which is

a surveillance system that uses medical records to identify all birth defects by type that are diagnosed in the first year of life in NC (56). We chose birth defects with previous evidence of associations with air pollutant exposures to examine in this analysis: these included pulmonary valve atresia/stenosis, tetralogy of Fallot, atrioventricular septal defects, and lower limb reduction defects; we also examined gastroschisis due to higher prevalence among non-White births (57–59).

PTB was defined as delivery at less than 37 weeks completed gestation based on clinical estimate of gestational age as reported on the birth certificate. All live, singleton births without any birth defects, gestational age between 20 and 44 weeks, and birth weight between 1,000 and 6,000 g were included in analyses of preterm birth.

Air pollution exposures

The air pollutants of interest in this study were daily average fine particulate matter ($PM_{2.5}$), daily 8-h maximum nitrogen dioxide (NO_2), and daily 8-h maximum ozone (O_3) concentrations. Daily census tract–level concentration estimates for daily average $PM_{2.5}$ and 8-h maximum for O_3 came from the EPA's Fused Community Multiscale Air Quality model surface using Downscaling (fCMAQ) model. The fCMAQ model links observed pollution data from EPA monitoring sites with deterministic chemistry and meteorology data from the Community Multiscale Air Quality model through a spatially and temporally varying coefficient model (60–62). These data are available for download at RSIG-related downloadable data files (https://www.epa.gov/hesc/rsig-related-downloadable-data-files). Daily 8-h maximum NO_2 concentration estimates were extracted from a hybrid ensemble model with 1 km^2 spatial resolution, which used multiple machine learning algorithms and predictor variables, including satellite data, meteorological variables, land-use variables, elevation, and chemical transport model predictions to estimate daily concentrations for NO_2 at 1 km^2 grid resolution (63). $PM_{2.5}$ and O_3 data were provided at the census tract level, and NO_2 data were aggregated to census tract level. Births were then linked to air pollutant concentrations by census tract of residential address at time of birth, and daily concentrations of $PM_{2.5}$, NO_2, and O_3 were averaged across each trimester. Trimester 1 was considered to go through week 12, and trimester 2 began at the start of week 13 and continued through week 26.

Modifier

A neighborhood deprivation index (NDI) was created using principal component analysis on 2010 census variables including housing, poverty, employment, occupation, and education at the census tract level (64). The NDI used here is a relative ranking of neighborhood deprivation for NC census tracts compared to one another; a higher index value is interpreted as having more deprivation. Neighborhood deprivation categories were determined by visually examining the distribution of NDI across all census tracts in NC and using a nearest centroid sorting clustering method to group census tracts into three NDI levels (low, medium, or high deprivation) (65). Individuals were assigned an NDI category based on census tract of the residential address at time of birth.

Covariates

Covariates of interest in this study were obtained from the birth certificate records and included birthing parent demographic characteristics of age at delivery, race/ethnicity (white, non-Hispanic, Black, non-Hispanic; Hispanic; Asian or Pacific Islander, non-Hispanic; American Indian, non-Hispanic; other), marital status (married or unmarried), Medicaid status at time of delivery (yes or no), education (<high school, high school, >high school), and month of conception (estimated using clinical estimate of gestational age and birth date). In the context of these analyses, race and ethnicity are used to represent potential stress from experiencing interpersonal and structural racism as well as residential segregation within the US and not as a biological construct (66).

Statistical analysis

As the objective of these analyses was to evaluate the potential for effect measure modification of air pollutant–birth outcome associations by neighborhood deprivation, unstratified and NDI-stratified (low, medium, and high) models were run. The presence of effect measure modification was evaluated qualitatively by examining the separation of stratified effect estimates from the unstratified effect estimate. Confounders of interest were determined using a directed acyclic graph (DAG, Supplementary Figure S1) (67).

Linear binomial regression models were used to estimate the prevalence differences (PDs) and 95% confidence intervals (CIs) for the association between ambient air pollution concentration and individual birth defect diagnoses for any birth defects and specific birth defect types. Any birth defect includes all diagnosed birth defect phenotypes and not just the specific phenotypes examined individually. The associations were estimated per 10,000 births for each individual air pollutant ($PM_{2.5}$, NO_2, and O_3). Exposure contrasts for each pollutant were approximately 10% increases with values: 1 $\mu g/m^3$ increase for $PM_{2.5}$, 4 ppb increase in O_3, and 7 ppb increase in NO_2. Exposures were assigned as the average daily pollutant concentration across the first trimester (weeks 1–12). Models for birth defects were adjusted for birthing parent age at delivery (centered at age 26 with a quadratic term), race/ethnicity (white, non-Hispanic as reference), and education (>high school as reference).

Modified Poisson regression models were used to estimate risk differences (RDs) and 95% CIs for air pollution and PTB. The associations were estimated per 10,000 births for each individual air pollutant ($PM_{2.5}$, NO_2, and O_3), with approximately 10% increases as reported above. Exposures were assigned as the

average daily pollutant concentration per each day, each gestational week, first and second trimester, and the entire pregnancy. We did not examine third trimester due to inconsistent exposure windows for PTBs. Models for PTB were adjusted for birthing parent race/ethnicity (white, non-Hispanic as reference), birthing parent age at delivery (centered at age 26 with a quadratic term), marital status (married as reference), Medicaid status (no as reference), education (>HS as reference), and month of conception (index variable as referent).

Linear binomial regression models were fit for birth defects rather than modified Poisson regression models due to low count numbers of specific defects but were checked across model types where possible and produced identical results.

Statistical analyses were performed using SAS (version 9.4; Cary, NC). All figures were created using R (version 4.1.0; Vienna, Austria; packages: ggplot2).

Sensitivity analyses

Due to the relatively low prevalence of birth defects in comparison to PTB, we were unable to adjust for the same number of covariates across models for birth defects and PTB. We conducted sensitivity analyses using linear binomial regression to estimate the PDs for the association between air pollution and birth defects stratified by NDI adjusting for marital status and month of conception in addition to the current adjustment set reported. Due to small cell counts, the convergence of these models was uncertain. For specific birth defects, (pulmonary valve atresia/stenosis, tetralogy of Fallot, atrioventricular septal defects, and lower limb reduction defects), sensitivity analyses were conducted using the exposure over weeks 3–8 only due to previous literature on sensitive windows for these outcomes (28, 36, 68). In addition, sensitivity analyses were conducted examining the interaction between NDI and air pollution, with both terms and an interaction term in the linear models. For interaction effects, we set an alpha level of 0.10.

IRB approval/human subjects research approval

This analysis was approved as minimal risk/existing data under the University of North Carolina (IRB) (09–0828). This study was also approved as observational research involving human subjects by the EPA's Human Subject's Research Review Official [HSRRO Project # F09-019CS].

Results

Descriptive information on this cohort and outcomes

Overall, there were 566,799 live births eligible for our study of birth defects from 2011 to 2015. Among those, 17,691 (3.1%) had at least one birth defect, 479 (0.08%) had pulmonary valve atresia or stenosis, 245 (0.04%) had tetralogy of Fallot, 299 (0.05%) had atrioventricular septal defects, and 80 (0.01%) had a lower limb reduction defect. Among the 566,512 birthing parent–infant pairs included in the analysis on PTB (which excluded those with any birth defects), there were 46,289 (8.17%) PTB cases. The majority of the full population (55.81%) identified as white, non-Hispanic, 23.67% identified as Black, non-Hispanic, 15.04% as Hispanic, 3.92% as Asian/Pacific Islander, non-Hispanic, 1.31% as American Indian, non-Hispanic, and 0.25% as another race. Among this population, the majority (60.0%) had more than a high school diploma, 22.50% completed high school, and another 17.19% completed less than high school. About 55.38% of the people who gave birth in this population were on Medicaid at the time of birth and 41.03% were unmarried. Demographic characteristics by outcome are presented in Table 1.

Exposure and modifier information

Across North Carolina from 2011 to 2015, average daily $PM_{2.5}$ exposure during trimester 1 ranged from 5.05 to 22.36 μg/m^3 with

TABLE 1 Descriptive information on cohort of births from 2011 to 2015 (*N* = 566,799).

Birthing person information	Total population	Among those with preterm birth	Among those with any birth defect
	N (%)	*N* (%)	*N* (%)
Race/ethnicity			
White, non-Hispanic	316,331 (55.81)	21,091 (94.70)	10,395 (58.76)
Black, non-Hispanic	134,148 (23.67)	13,384 (31.54)	4,004 (22.63)
Hispanic	85,262 (3.92)	5,798 (13.66)	2,510 (14.19)
Asian/Pacific Islander, non-Hispanic	22,239 (3.92)	1,411 (3.32)	478 (2.70)
American Indian, non-Hispanic	7,408 (1.31)	634 (1.49)	270 (1.53)
Other, non-Hispanic/unknown	1,411 (0.25)	120 (0.28)	34 (0.19)
Education level			
Less than high school	97,445 (17.19)	96,681 (17.18)	3,190 (18.07)
Completed high school	127,506 (22.50)	126,324 (22.45)	4,188 (23.73)
More than high school	340,073 (60.00)	337,861 (60.05)	10,274 (3.02)
Medicaid status	313,903 (55.38)	26,475 (62.39)	10,618 (60.02)
Unmarried	232,555 (41.03)	20,663 (48.69)	7,646 (43.23)
Outcomes of interest			
Preterm birth	42,438 (7.54)	—	—
Any Birth defect	17,691 (3.12)	—	—
Gastroschisis	213 (0.04)		
Pulmonary valve atresia/stenosis	479 (0.08)	—	—
Tetralogy of fallout	245 (0.04)	—	—
Atrioventricular septal defects	299 (0.05)	—	—
Limb reduction defects	80 (0.01)	—	—

an interquartile range (IQR) of 8.55–10.47 μg/m^3. The average daily O_3 exposure during trimester 1 ranged from 26.93 to 60.54 ppb with an IQR of 34.73–46.15 ppb. The daily average NO_2 exposure across trimester 1 ranged from 0.32 to 41.73 ppb with an IQR of 9.63–17.53 ppb. The exposures did not differ substantially across trimester or neighborhood deprivation level (Tables 2,3). Neighborhood deprivation levels across the state ranged from −2.00 to 4.39 (Supplementary Figure S2) and the IQR for NDI was −0.63 to 0.65. The low NDI group ranged from −2.000 to −0.323, the medium NDI group ranged from −0.324 to 0.986, and the highest NDI group ranged from 0.987 to 4.390. The magnitude of pollutant exposure did not differ across NDI levels (Tables 2,3).

Risk differences for preterm birth

Associations between $PM_{2.5}$ and PTB were generally negative among low and medium NDI strata across the entire pregnancy, but there were positive leaning associations for those residing in a high NDI; however, these generally had confidence intervals that overlapped with the null value of 1 (Figure 1 and Supplementary Table S1). Despite this, for the associations

TABLE 2 Descriptive statistics for exposure to PM2.5 (μg/m$_3$), O_3 (ppb), NO_2 (ppb) among preterm births stratified by NDI level.

	Min	25th pctl	Median	75th pctl	Max
Overall					
$PM_{2.5}$ (μg/m^3) during trimester 1	5.05	8.55	9.41	10.47	22.36
O_3 (ppb) during trimester 1	26.93	34.73	40.31	46.15	60.54
NO_2 (ppb) during trimester 1	0.32	9.63	13.28	17.53	41.73
NDI at birth	−2.00	−0.63	−0.02	0.65	4.39
Among low NDI cluster					
$PM_{2.5}$ (μg/m^3) during trimester 1	5.47	8.67	9.52	10.62	21.09
O_3 (ppb) during trimester 1	27.04	34.44	40.19	46.18	60.46
NO_2 (ppb) during trimester 1	0.32	10.61	14.26	18.28	41.73
NDI at birth	−2.00	−1.21	−0.84	−0.58	−0.32
Among medium NDI cluster					
$PM_{2.5}$ (μg/m^3) during trimester 1	5.05	8.42	9.26	10.31	22.36
O_3 (ppb) during trimester 1	26.93	35.06	40.44	46.11	60.36
NO_2 (ppb) during trimester 1	0.33	8.64	11.79	15.85	36.61
NDI at birth	−0.32	−0.07	0.20	0.53	0.99
Among high NDI cluster					
$PM_{2.5}$ (μg/m^3) during trimester 1	5.85	7.97	9.53	10.52	18.27
O_3 (ppb) during trimester 1	27.00	34.37	40.29	46.23	60.54
NO_2 (ppb) during trimester 1	1.11	11.15	15.52	19.74	34.82
NDI at birth	0.99	1.17	1.46	1.95	4.39

min, minimum; 25th pctl, 25th percentile; 75th pctl, 75th percentile; max, maximum.

TABLE 3 Descriptive statistics for exposure to PM2.5 (μg/m$_3$), O_3 (ppb), NO_2 (ppb) among preterm births stratified by NDI level.

Exposure or modifier	Min	25th pctl	Median	75th pctl	Max
Overall					
NDI	−2.00	−0.48	0.11	0.82	4.39
$PM_{2.5}$ (μg/m^3)					
Entire pregnancy	6.03	8.73	9.52	10.24	14.93
Trimester 1	5.07	8.54	9.39	10.43	19.83
Trimester 2	5.23	8.51	9.32	10.32	21.79
O_3 (ppb)					
Entire pregnancy	30.34	37.80	40.33	43.03	55.14
Trimester 1	27.34	34.79	40.45	46.08	60.23
Trimester 2	26.13	35.11	40.59	45.73	60.53
NO_2 (ppb)					
Entire pregnancy	1.00	9.84	13.14	17.24	33.42
Trimester 1	0.36	9.53	13.17	17.42	37.08
Trimester 2	0.78	9.44	12.92	17.24	39.89
Among low NDI cluster					
NDI	−2.00	−1.15	−0.80	−0.55	−0.32
$PM_{2.5}$ (μg/m^3)					
Entire pregnancy	6.17	8.85	9.69	10.38	13.21
Trimester 1	5.51	8.65	9.53	10.58	19.83
Trimester 2	5.23	8.61	9.44	10.48	20.11
O_3 (ppb)					
Entire pregnancy	30.34	37.67	40.27	43.06	55.14
Trimester 1	27.34	34.61	40.45	46.23	60.23
Trimester 2	26.13	34.86	40.54	45.90	60.53
NO_2 (ppb)					
Entire pregnancy	2.24	10.72	14.03	17.54	30.80
Trimester 1	0.42	10.39	14.01	17.99	36.27
Trimester 2	1.73	10.16	13.78	17.87	39.89
Among medium NDI cluster					
NDI	−0.32	−0.06	0.22	0.55	0.99
$PM_{2.5}$ (μg/m^3)					
Entire pregnancy	6.03	8.59	9.35	10.10	13.58
Trimester 1	5.07	8.42	9.25	10.27	19.39
Trimester 2	5.57	8.37	9.18	10.16	20.10
O_3 (ppb)					
Entire pregnancy	30.38	37.95	40.43	43.00	53.79
Trimester 1	27.42	35.04	40.50	45.95	60.23
Trimester 2	26.22	35.42	40.68	45.59	60.32
NO_2 (ppb)					
Entire pregnancy	1.00	9.00	11.69	15.42	32.50
Trimester 1	0.36	8.56	11.69	15.76	37.08
Trimester 2	0.78	8.57	11.55	15.54	37.37
Among high NDI cluster					
NDI	0.99	1.18	1.52	1.98	4.39
$PM_{2.5}$ (μg/m^3)					
Entire pregnancy	6.74	8.93	9.63	10.32	14.93
Trimester 1	6.09	8.67	9.53	10.50	17.65
Trimester 2	6.15	8.63	9.47	10.41	21.79
O_3 (ppb)					
Entire pregnancy	30.82	37.68	40.19	43.06	53.37
Trimester 1	27.40	34.47	40.33	46.10	59.90
Trimester 2	27.10	34.71	40.45	45.82	60.45
NO_2 (ppb)					
Entire pregnancy	1.69	11.75	15.89	19.15	33.42
Trimester 1	1.75	11.30	15.69	19.91	34.72
Trimester 2	1.64	11.08	15.25	19.59	33.86

min, minimum; 25th pctl, 25th percentile; 75th pctl, 75th percentile; max, maximum.

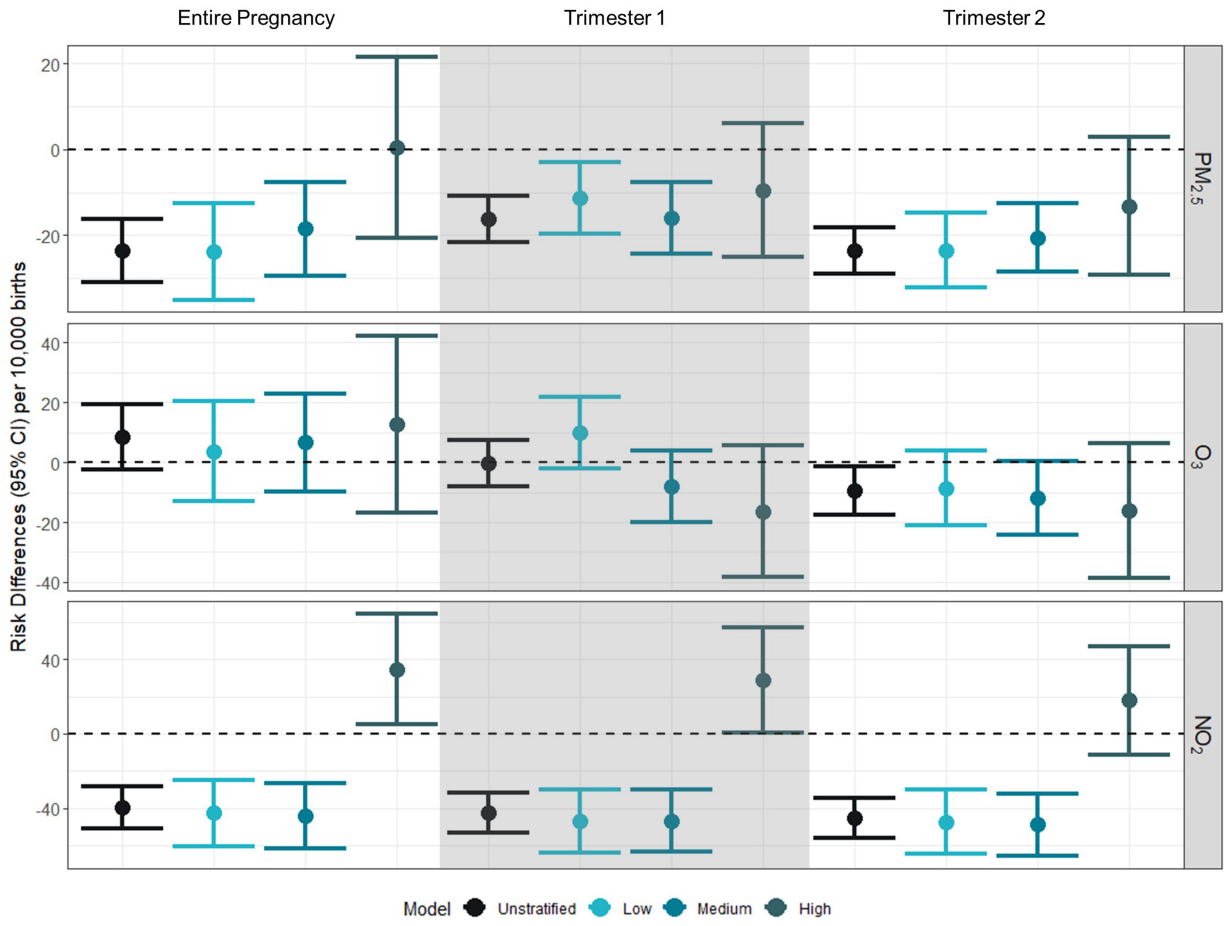

FIGURE 1
Risk differences (95% CI) for gestational exposure to $PM_{2.5}$, O_3, and NO_2 and preterm birth per 10,000 births. Risk differences represent the absolute increase in number of preterm births per 10,000 associated with a 10% increase in the exposure of interest ($PM_{2.5}$: 1 μg/m^3; O_3: 4 ppb; NO_2: 7 ppb). Unstratified models were adjusted for birthing parent race/ethnicity (white, non-Hispanic as reference), birthing parent age at delivery (centered at age 26 with a quadratic term), marital status (married as reference), Medicaid status (no as reference), education (>HS as reference), and month of conception (index variable as referent). Models were further stratified by NDI levels at low (−2 to −0.323), medium (−0.324 to 0.986), high (0.987–4.39).

between $PM_{2.5}$ and PTB, there was no statistical evidence of modification by NDI with confidence intervals overlapping.

Across time periods and NDI values, the relationship was generally insignificantly different from the null value of 1, across exposure windows. There was a negative association [RD: −9.32 (95% CI: −17.44 to −1.19)] between O_3 and PTB in the second trimester in the adjusted model. There was no evidence of modification by NDI.

We observed negative associations between NO_2 and preterm birth for the entire pregnancy for the adjusted model [RD: −39.53 (95% CI: −50.77 to −28.28)], low NDI [RD: −42.78 (95% CI: −60.80 to −24.76)], and medium NDI [RD: −44.24 (95% CI: −61.79 to −26.68)], but a positive association was observed between NO_2 and preterm birth for the entire pregnancy among those residing in a high NDI [RD: 34.70 (95% CI: 4.84–64.56)]. This pattern of association was similar for trimesters 1 and 2, with negative associations between NO_2 and preterm birth for the adjusted models, low NDI, and medium NDI, and a positive association between NO_2 and preterm birth for high NDI. When comparing across strata of the NDI, we see evidence of effect modification for NO_2 by NDI level across all exposure windows.

Prevalence differences for birth defects

In general, across all pollutants examined, no evidence of association was observed between pollutants and birth defect prevalence, and associations did not differ across NDI levels or trimesters (Figure 2 and Supplementary Table S2).

In the sensitivity analysis that additionally adjusted for month of conception and marital status, we observed associations that were not significantly different from the null value of 1 (Supplementary Table S3). When examining exposures across gestational weeks 3–8, only similar null associations were observed (Supplementary Table S4).

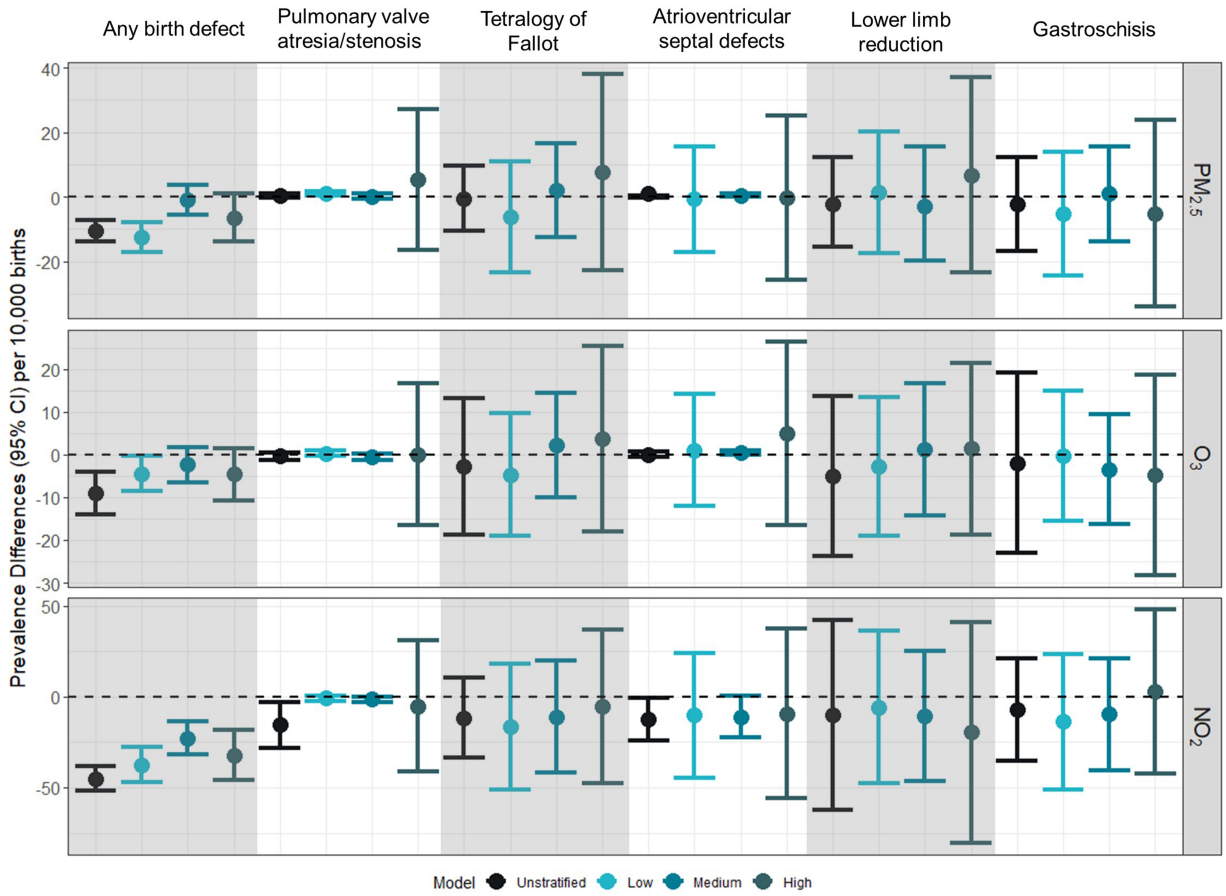

FIGURE 2
Prevalence difference (95% CI) for first trimester exposure to $PM_{2.5}$, O_3, and NO_2 and selected birth defects per 10,000 births. Prevalence differences represent the absolute increase in the number of preterm births per 10,000 associated with a 10% increase in the exposure of interest ($PM_{2.5}$: 1 μg/m^3; O_3: 4 ppb; NO_2: 7 ppb). Unstratified models were adjusted for birthing parent age at delivery (centered at age 26 with a quadratic term), race/ethnicity (white, non-Hispanic as reference), and education (>HS as reference). Models were further stratified by NDI levels at low (−2 to −0.323), medium (−0.324 to 0.986), high (0.987–4.39).

Results for sensitivity analyses examining the interaction between NDI and air pollution for PTB and birth defects are shown in Supplementary Tables S5 and S6, respectively.

Discussion

Summary of results

Overall, we did not observe any strong associations between $PM_{2.5}$, O_3 and NO_2 with prevalence of birth defects in this cohort of singleton live births in North Carolina from 2011 to 2015 and stratifying by neighborhood deprivation level did not substantially alter these associations. In terms of preterm birth, associations with $PM_{2.5}$ were generally negative. It is possible that areas with higher levels of $PM_{2.5}$ are also areas with higher access to resources and high-quality healthcare leading to negative associations between $PM_{2.5}$ and poor birth outcomes. Modest associations were observed between O_3 exposure during trimester 3 and preterm birth for those in neighborhoods considered to be at medium and high levels of neighborhood deprivation. In earlier trimesters, negative associations were generally observed between O_3 exposure and preterm birth. Across all trimesters, there was an increased risk of preterm birth associated with NO_2 exposure for those in highly deprived neighborhoods.

We evaluated air pollution exposures over trimesters of pregnancy. Previous studies have examined weeks and months of pregnancy as well (69, 70), though inconsistency in the exposure window associated with preterm birth is a noted uncertainty (32–34). For example, Krajewski et al. (70) reported an increased risk of PTB associated with $PM_{2.5}$ and O_3 exposure across gestational weeks and generally null effects for NO_2. Alman et al. (69) observed elevated odds of preterm birth with PM2.5 exposure in months 3 and 4 as well as weeks 9–12, while Wang et al. reported increased hazard ratios for weeks 20–28 for $PM_{2.5}$, 18–31 for NO_2, and 23–31 for O_3 (71). In general, the results of weekly, monthly, and trimester-specific average air pollutant exposure concentrations have yielded inconsistent associations with preterm birth, and no single exposure window has been identified as etiologically relevant.

We expected to see higher prevalence differences or risk differences for air pollution and birth outcomes for more deprived neighborhoods, but we only saw this for the association between NO_2 and preterm birth. Since the inception of the Clean Air Act and the National Ambient Air Quality Standards in the United States, criteria air pollutant levels have steadily decreased over time (72, 73). It is possible that the levels for the other pollutants in North Carolina from 2011 to 2015 do not vary enough across the state to observe an association or that they are generally lower due to air pollution controls that have been put in place and have reduced air pollution. It is also possible that other correlated exposures that may exist in high deprivation neighborhoods are interacting with air pollution to create a higher association between NO_2 and preterm birth such as noise pollution or limited green space. These other harmful exposures may be correlated with neighborhood deprivation due to environmental injustices in lower income neighborhoods.

Context with other literature

There are few studies examining if neighborhood deprivation level modifies the association between air pollution and birth outcomes. In general, some studies have identified links between heightened exposure to air pollution and some specific birth defects and preterm birth during critical periods of pregnancy (59, 74–76); however, these studies are in places with higher levels of ambient air pollution than observed in North Carolina for this study period. Our results are consistent with another study that reported mostly null non-significant associations between air pollution and birth defects in North Carolina. A study similar to ours in New York City reported inverse associations between NO_2 and birthweight in the most and least deprived neighborhoods indicating that the associations between NO_2, neighborhood deprivation, and birth outcomes may be complicated (77). In addition, only a few studies have observed associations between neighborhood deprivation and the prevalence of birth defects overall, but one showed an association between increased neighborhood deprivation and higher prevalence of gastroschisis (50, 78). Some studies report positive associations with air pollution and preterm birth, especially with NO_2 (79–81). Further research has identified that neighborhood deprivation is associated with increased preterm birth risk and one study demonstrated that neighborhood deprivation and urbanicity are associated with a higher risk, implying that there may be risks associated with the interaction between neighborhood deprivation and traffic-related air pollution (38, 64).

Potential strengths and limitations

There are some limitations that may affect these results and their generalizability. Air pollutant exposures and neighborhood deprivation were assigned to parent–infant dyads based on the census tract they resided in at the time of birth, which does not account for any movement during pregnancy prior to birth or general day-to-day movement in areas outside of the census tract in which individuals live. Movement may be differential by neighborhood deprivation if people residing in more deprived areas need to leave their neighborhoods more often to access resources during pregnancy. A limitation specific to our birth defects analysis is that we were limited in how many covariates we could adjust for and in our ability to examine interaction between co-exposure to high levels of NDI and air pollution due to small counts of more rare birth defects during the study period. In addition, owing to the use of birth certificate records, we do not have access to behavioral factors or conditions that might exacerbate risk of adverse outcomes. In addition, by using birth certificate records, we had to use proxy measures for some covariates, such as partner status is defined using marital status in the birth certificate data and people who are unmarried and live with their partner may be classified as unmarried. We used spatiotemporal models to predict air pollution concentrations averaged at the census tract level. While these models provide well-validated predictions for $PM_{2.5}$, O_3, and NO_2, they are not available for other criteria or hazardous air pollutants. In addition, we used modeled output at the census tract level for each of the three criteria pollutants examined even though there is known variability in the spatial heterogeneity of these three criteria pollutants.

Despite these limitations, there are several strengths of this study. By using this large North Carolina birth cohort, which includes all live births and registered birth defects identified through active case ascertainment, we were able to examine the associations for very rare birth defects. The use of modeled air pollution data allowed us to include all births for which the residence at delivery could be geocoded and linked with a census tract, including both urban and rural census tracts, regardless of the distance from a stationary monitor. The modeled air pollution data allowed us to predict daily concentrations and incorporated atmospheric conditions as part of the concentrations estimates.

In addition, we were able to examine possible critical periods for preterm birth by assigning exposures across trimesters. Previous work examined weekly exposure averages to the same pollutants but did not identify a consistent week or weeks of exposure thought to be critical for preterm birth. Thus, we chose to evaluate trimesters of exposure to facilitate comparison with results of other studies of air pollution or NDI and birth outcomes. The etiology for, and timing of, insults for the different birth defect phenotypes examined in our analyses varies. The critical window of exposure for congenital heart defects and limb defects includes gestational weeks 2–8, while the critical window of exposure for gastroschisis is later, gestational weeks 7–12. For ease of interpretation and to facilitate comparison of results with our analyses as well as with other published results, we used the first trimester as the exposure window of interest for all birth defect phenotypes.

Public health implications

Overall, our study found a notable association between NO_2 exposure and preterm birth, but we did not observe any strong associations for birth defects. This study examined modification

by NDI and not the joint effect of neighborhood deprivation and air pollution, so further research measuring the joint effect of the two coexisting exposures would address this gap in data. In addition, this study was done in North Carolina where air pollution concentrations are relatively low. In general, our results support the public health protection afforded by EPA's National Ambient Air Quality Standards, even in areas of neighborhood deprivation. Future research conducted in areas with higher air pollution levels and evaluating the potential for modification by neighborhood deprivation level will be informative.

Data availability statement

The data analyzed in this study are subject to the following licenses/restrictions: data used in this study contain personally identifiable information and are not available without authorization from the NC Department of Health and Human Services. Requests to access these datasets should be directed to https://schs.dph.ncdhhs.gov/contacts.htm.

Ethics statement

The studies involving humans were approved by University of North Carolina at Chapel Hill Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

KC: Formal Analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. AK: Formal Analysis, Methodology, Validation, Visualization, Writing – original draft. MJ: Data curation, Methodology, Writing – review & editing. TL: Data curation, Project administration, Writing – review & editing. LM: Methodology, Writing – review & editing. KR: Conceptualization, Methodology, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/frph.2024.1304749/full#supplementary-material

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State of the maternal healthcare continuum in Guinea, awaiting the next Demographic and Health Survey: the case of the five communes of Conakry in 2022

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Background: The continuum of maternal health care ensures consistency in the delivery of care from pregnancy to the postnatal period. It recommends a minimum of 4 antenatal visits, skilled birth attendance, and 42 days of postnatal care. This approach helps reduce maternal deaths. The aim of this study was to estimate the proportion of women who had completed the different stages of the continuum of maternal health care (four antenatal visits, given birth under the care of qualified personnel, and received postnatal care within 42 days of delivery).
Methods: This was a cross-sectional analytical study conducted in the five communes of Conakry, using a two-stage cluster sampling for data collection. Results were described using medians and percentages. The proportions of women in the continuum of care, and at the different stages of this continuum, have been weighted. Multivariate logistic regression was used to identify the factors associated with non-completion of the different stages of the maternal health care continuum among the women included in this study.
Results: We found that 26.9% of women had completed all stages of the maternal health care continuum, while 73.1% had not. While 56.7% received four antenatal visits, only 29.5% delivered under the care of a qualified healthcare professional. Key factors associated with discontinuity were not attending school (AOR 1.825: 1.594–2.089), unemployment (AOR 4.588: 3.983–5.285), having two or more living children (AOR 1.890: 1.016–1.296), and not receiving a free Long-Lasting Insecticidal Net at the first Antenatal Care.
Conclusion: Maternal care discontinuity is a major issue in Guinea. The country's Health Development Plan had set an expected level for maternal care which has not been met as of 2022. The completeness of care is influenced by various factors, including individual socio-demographic characteristics and factors related to the organization, availability, and quality of health services. To reduce maternal and child mortality rates, it is essential to improve interpersonal communication during antenatal care, ensure the availability of quality health services, and conduct a national study on maternal health service quality and maternal satisfaction. This will help establish a proper continuum of care for mothers and children.

KEYWORDS

continuum of maternal health care, associated factors, Conakry, Guinea, 2022

1 Introduction

Maternal mortality remains a significant global health issue. There were approximately 810 maternal deaths per day in 2017, with 94% of them occurring in low-income countries (1). Sub-Saharan Africa continues to be the region with the highest number of maternal deaths, accounting for 67% of all such deaths worldwide (2).In countries with limited resources, the maternal mortality rate is as high as 462 per 100,000 live births. By contrast, in high-income countries, this rate is only 11 per 100,000 live births, as per the statistics of 2017 (2). Complications during and after pregnancy are the leading cause of death for women. However, some of these complications may exist before pregnancy and worsen during it if not addressed within the framework of the women's care (3).

Severe bleeding (especially after childbirth), postpartum infections, high blood pressure during pregnancy (pre-eclampsia and eclampsia), and complications related to unsafe abortion are the leading causes of maternal deaths, accounting for 75% of all causes (4). Other infections (malaria, HIV, etc.) and chronic diseases (heart diseases, diabetes, etc.) account for the rest of the causes of maternal deaths (4).

It is known that many maternal deaths could be prevented if appropriate care were available and accessible for the health of the mother, newborn, and child (4, 5).These cares include quality family planning, skilled care during pregnancy, childbirth (6, 7), and after birth, as well as quality services after an abortion and the ability to have a safe abortion when allowed by law.

Efforts made to achieve the Millennium Development Goals (MDGs) have resulted in a significant reduction in maternal deaths. According to the United Nations report published in 2017 on the MDGs for 2015, maternal mortality has decreased by 45% worldwide since 1990, and the under-five mortality rate has been reduced by more than half (5). Despite significant progress, maternal healthcare coverage services remain unequal in low- and middle-income countries (6). Therefore, for implementing actions related to the Sustainable Development Goals (SDGs), improving maternal, neonatal, and child health is strongly recommended (7).

In recent decades, there has been an increased focus on implementing the continuum of care approach to improve the quality of maternal health services. The continuum of maternal health care ensures consistency in the delivery of care from pregnancy to the postnatal period. It recommends a minimum of 4 antenatal visits, skilled birth attendance, and 42 days of postnatal care. This approach helps reduce maternal, neonatal, and child mortality rates (8). The continuum of care is a public health intervention that is simple, cost-effective, and low-tech. Its aim is to address the health challenges of mothers, newborns, and children. It involves providing care throughout different stages of life, including adolescence, pregnancy, childbirth, the postnatal period, and childhood. The goal is to improve the health and survival of both mothers and children (9). A meta-analysis has shown that continuous care before and after pregnancy can reduce the risk of neonatal and perinatal mortality by 21% and 16%, respectively, leading to a good continuum of care that helps reduce the maternal mortality rate (10).

However, the proportion of women benefiting from a continuum of maternal health care is low in resource-limited countries, especially in sub-Saharan Africa. A study conducted in Ghana in 2015 showed that only 8% of women benefited from a good continuum of maternal care (11). Another study conducted in Ethiopia in 2020 revealed that only 12.1% of women had completed the continuum of maternal care (12).

In Guinea, progress has been made in recent years to improve maternal and newborn health indicators. However, further efforts are still needed to save the lives of mothers and children. According to the 2018 Demographic and Health Survey (DHS), 81% of women who had a live birth received antenatal visits care from a qualified provider. However, only 35% of women had attended at least 4 antenatal visits. Additionally, just 55% of births were assisted by qualified health personnel. Furthermore, only 49% of women had a postnatal examination within 48 h of birth (13).A secondary analysis based on 2018 Demographic and Health Survey data showed that only 20% of women benefit from a good continuum of maternal care in Guinea (14). It is worth noting that the latest study on the maternal care continuum in Guinea is one of the few studies available, but it relies on outdated data. For a health program to be effective, regular assessments are essential to identify hindrances and suggest corrective actions promptly, for a better outcome. The current study provides updated data on the continuum of maternal care in Conakry, Guinea. In this study, we did not compare our method to that of DHS. We simply wanted to show the importance of having approximate data on certain key health indicators between two DHS surveys, which often take a considerable amount of time to complete. This allows health actors to adjust intervention approaches promptly to prevent the worsening of a health issue due to delayed identification. This serves as a form of internal self-assessment, awaiting an external evaluation of the impact of health interventions, which is typically conducted through DHS surveys carried out every five years. It is not our intention to compare the DHS with our survey. We simply want to highlight the need to carry out small periodic surveys between two DHSs to assess progress towards national health objectives. This will enable the Ministry of Health to readjust operational interventions prior to the evaluations that are often carried out through the DHS. As we know, DHS surveys are carried out every five years. We believe that waiting five years to undertake certain corrective actions could compromise the achievement of health status results. In short, this survey must guide operational actions. The objective of this study was to estimate the proportion of women who had completed the various stages of the continuum of maternal health care, i.e., those who had completed the four antenatal visits, given birth under the care of qualified personnel, and received postnatal care within 42 days of delivery, during the 12 months preceding the survey in Conakry, as well as to identify the factors associated with non-completion of the various stages of the continuum of maternal care.

2 Materials and methods

2.1 Study design

This is a cross-sectional analytical study conducted based on prospectively collected data from women who gave birth in the 12 months preceding the survey.

2.2 Study setting

This study was carried out in the five communes of the city of Conakry (Dixinn, Kaloum, Matam, Matoto, and Ratoma). Conakry is the political capital of the Republic of Guinea, a West African country covering an area of 245,857 km^2. The country is divided into four natural regions (Lower Guinea, Middle Guinea, Upper Guinea, and Forested Guinea). Administratively, the country has 8 administrative regions, including the special area of Conakry. Each administrative region is divided into prefectures, corresponding to the health district in terms of health administration. In total, Guinea has 38 health districts, including 5 in Conakry and 33 in the interior of the country.

Based on projections from the National Institute of Statistics, Guinea's population in 2022 was estimated to be 13,261,638 with women accounting for 52% of the population. The annual population growth rate is 2.9%, while the synthetic fertility rate is 4.8 children per woman. Unfortunately, the literacy rate in Guinea remains low, with only 32.0% of individuals aged 15 and older considered literate. The socio-economic situation in Guinea is also characterized by persistent poverty, with 43.7% of the population living below the poverty threshold (15). In addition to the high maternal mortality rate and low healthcare coverage, the country is grappling with the emergence and re-emergence of epidemic diseases (16).

2.3 Study population

The research focused on women between the ages of 15 and 49 who had given birth within the 12 months prior to the survey. A total of 5,335 women were interviewed in March 2022 across five communes in the city of Conakry. The reason for selecting women who had given birth within the last 12 months preceding the survey was to minimize any potential errors in maternal recall.

2.4 Sampling and data collection

We conducted a study using a two-stage stratified sampling method based on the "World Health Organization" type. The city of Conakry consists of five communes, each of which was considered a stratum. In the first stage, we selected primary units or clusters in each commune. The technical team carried out this selection based on the list of neighborhoods in the communes from the third General Population and Housing Census (RGPH-3) of 2014 in Guinea. The census was updated in 2017 by the National Institute of Statistics and included 9,668 enumeration areas, 1,505,805 households, and 11,555,061 residents in 201 (17). The census district/sector was chosen as the primary unit. In each commune or stratum, 30 units were randomly selected, irrespective of the number of base units contained in the sampling frame of the various communes. The number of units was not identical in all communes. However, each commune had the necessary number of units in the sampling frame to be able to draw the 30 units envisaged by the survey.

The city of Conakry comprises 5 communes. Within each commune, we selected 30 units, amounting to a total of 150 primary units. The sampling frame for the primary units (clusters) used for this study was that established by the National Institute of Statistics after the third general population census (RGPH-3) of 2014 and updated in 2017. The sampling frame for the primary units was the exhaustive list of all enumeration areas in each commune. The selected primary units were also referred to as "clusters" during data collection. Households located within the perimeter of the selected primary unit were considered secondary units.

The process of household sampling was carried out in a randomized manner within the neighborhood. Upon entering the field, the data collection teams conducted a comprehensive reconnaissance of the cluster's environs to identify all boundaries and contours. The selection of households containing the survey targets was done in accordance with the method recommended by the WHO for coverage surveys in households and the investigator's guide developed for this purpose (18).

After the reconnaissance, the data collection agent positioned themselves at one of the corners and threw a pen. The pen's tip indicated the direction to follow. The agent counted two compounds and started data collection in the third compound. They then continued in this manner until they reached the quota of eligible women for the study. In each household, all eligible women were interviewed. To avoid overlaps, clusters belonging to the same neighborhood were assigned to the same agent.

Data were collected using a pre-tested questionnaire designed on the Kocollect application. The questionnaire was administered to target women by medical students in their final year of medical school, trained for this purpose. The language used during the administration was either French or the national language, depending on the understanding of the women. In order to ensure comprehension, the questionnaire was translated into Guinean national languages during the training of the investigators. The information collected for this study was based on self-declarations made by the women during interviews with the investigators.

2.5 Definition of study variables

- Dependent Variables

The outcome variable of this study was the continuum of care for maternal health services. The continuum of care is a composite indicator, which was constructed as a binary variable. This means that a woman was considered to have received continuum of care if she reported receiving services at the following three levels:

- At least four antenatal care visits for pregnancy monitoring.
- Delivery assisted by a qualified healthcare professional (doctor, nurse, midwife).
- Postnatal care for the mother and newborn within 42 days or six weeks after childbirth (19).

The continuum of care for women and mothers is considered incomplete if any of the three stages are missed. Continuous care during pregnancy is defined as completing antenatal visits, while continuous care during delivery is defined as delivering with the assistance of qualified personnel and having antenatal visits. Lastly, the completion of four antenatal care visits, delivery by qualified personnel, and postnatal care are considered continuous care at the postpartum level, which is also deemed a complete continuum of care (20).

- Independent Variables

Based on Owilli et al.'s continuum of care, the conceptual model consists of four main components: family and individual, socio-economic, child characteristics, and field (21). The family and individual factors include the mother's age, ethnic origin, religion, and obstetric history. Information on services received during antenatal and postnatal visits was also collected. The socio-economic factors include the mother's level of education and occupation (21).

2.6 Data analysis

The data analysis was conducted using IBM SPSS Statistics version 25. To summarize numerical variables, descriptive statistics were employed, presenting the data as medians with their corresponding interquartile ranges or means with their standard deviations. On the other hand, categorical variables were summarized by calculating proportions with their corresponding confidence intervals. The proportions of women on the continuum of care, as well as on the different stages of this continuum, have been weighted as follows.

Overall modeling was performed on the non-continuum of maternal care. In addition to modeling the overall non-continuum, we also performed modeling for each stage of the continuum ("Non-continuum of maternal care from ANC 1 to ANC 4+" and "Non-continuum of maternal care from ANC 4 + to delivery assisted by skilled health personnel").

Covariates for logistic regression were selected based on a *p*-value of less than or equal to 0.20 in bivariate analysis. We adjusted for multiple variables simultaneously in the models to ensure the validity of the observed associations.

3 Results

3.1 Sociodemographic characteristics of participants

The investigators received a response from a total of 5,335 women who had completed the provided questionnaire, resulting in a response rate of 98.79%. It was observed that the median age of the surveyed women was 29 years with an interquartile range (IQR) of 24–36. The majority of the surveyed women, accounting for 91.6%, were married. Additionally, it was noted that 94.5% of the women surveyed were Muslim, while 49.7% belonged to the Fulani tribe. In terms of the women's educational background, 46.3% of the surveyed women had not received any formal education (Table 1).

3.2 Obstetric history and use of antenatal and postnatal visits

This study found that the majority (76.6%) of surveyed women were multiparous, with 50% having two or more living children. The report also revealed that 89.6% of women attended their first antenatal visit, while only 55.4% attended the fourth. During the initial antenatal visit, 85.4% and 80.7% of women respectively received sulfadoxine-pyrimethamine and mosquito nets free of charge. Regarding childbirth, 91.2% of women gave birth in a healthcare facility, with a cesarean section rate of 15.1%. The study also observed that 64.4% of women delivered under the care of

TABLE 1 Sociodemographic characteristics of 5,335 women who gave birth in the last 12 months before the 2022 survey in Conakry, Guinea.

Variables	Number (%)	Continuum of maternal health care	
		No (%)	Yes (%)
Survey communes			
Dixinn	997 (18.69)	71.70	28.30
Kaloum	896 (16.79)	73.90	26.10
Matoto	1,085 (20.34)	75.60	24.40
Ratoma	1,336 (25.04)	76.70	23.30
Matam	1,021 (19.14)	69.90	30.10
Median age	29 (24, 36)		
Age groups			
25–49 years old	3,204 (60.1)	77.87	22.13
15–24 years old	2,131 (39.9)	67.40	32.60
Educational level			
Not attended school	2,472 (46.3)	83.40	16.60
Attended school	2,863 (53.7)	59.70	40.30
Job			
Unemployed	2,714 (50.9)	84.90	15.10
Employed	2,615 (49.0)	54.80	45.20
Not registered	6		
Marital status			
Married	4,886 (91.6)	72.8	27.2
Unmarried	449 (8.4)	74.4	25.6
Ethnic group			
Soussou	1,597 (29.9)	72.50	27.50
Malinke	725 (13.6)	74.20	25.80
Other	54 (1.0)	72.60	27.40
Fulani	2,649 (49.7)	75.40	24.60
Forester	310 (5.8)	69.90	30.10
Religion			
Muslim	5,041 (94.5)	74.10	25.90
Christian	294 (5.5)	70.68	29.32

qualified personnel, with 58.1% receiving postnatal care within the recommended timeframe. Additionally, it was noted that 70.06% of the 922 women who did not receive insecticide-treated bed nets during the first antenatal care (ANC1) had no education, which constituted 12.11% of the total study sample (Table 2).

3.3 Reception of LLINs at ANC1

The distribution of insecticide-treated bed nets is one of the ways to encourage pregnant women to attend antenatal visits. We hypothesized that the provision of nets to women at the first ANC would act as an incentive to continue maternal health care. This is because of Guinea's poverty challenge. In the course of this study, we observed that 19.28% of women who gave birth in the last 12 months before the survey did not receive insecticide-treated bed nets free of charge during their initial antenatal visits. This proportion varies based on sociodemographic characteristics and obstetric history. It is 13.18% among women aged 25–49, compared to 25.37% among women aged 15–24. Likewise, it is 8.45% among educated women, while it reaches 30.11% among non-educated women. Regarding the "employment" variable, we found that the proportion of women not receiving bed nets during their initial antenatal visits was 6.11% among those employed, compared to 32.46% among those unemployed (Table 3).

Our research has revealed that distributing insecticide-treated bed nets can effectively encourage pregnant women to attend antenatal appointments. However, we also discovered that nearly one-fifth (19.28%) of women who gave birth within the past year did not receive these bed nets at no cost during their initial antenatal visits. This percentage varied depending on sociodemographic factors and obstetric history. Notably, the percentage was lower among women aged 25–49 (13.18%) than those aged 15–24 (25.37%), as well as among educated women (8.45%) compared to non-educated women (30.11%). Additionally, our findings showed that employed women were significantly less likely to have missed out on bed nets during their initial antenatal visits (6.11%) compared to unemployed women (32.46%).

3.4 Continuum and proportions of loss in maternal healthcare continuum

This study showed that the (weighted) proportion of women who had completed the various stages of the health care continuum, i.e., the proportion of women who had completed the four prenatal visits, given birth under the care of qualified personnel and received postnatal care within 42 days of delivery" was 26.90% (IC 95%: 22.4–31.3), while 73.1% of women had not completed the various stages of the continuum. Among the 5,335 women surveyed, 56.70% had completed all four prenatal visits ($n = 2,955$). Still using the same denominator ($n = 5,355$), we found that 29.50% of the women surveyed had completed the 4 prenatal visits and had given birth in the hands of qualified health personnel. Finally, using the same denominator (5,355), we found that only 26.90% of women had completed the different stages of the maternal health care continuum (attended the 4 prenatal visits, gave birth in the hands of a professional qualified and had received postnatal care within 42 days of delivery (Figure 1). This last proportion

TABLE 2 Obstetric history and utilization of antenatal and postnatal visits among 5,335 women who gave birth in the last 12 months preceding the 2022 survey in Conakry, Guinea.

Variables	Number (%)	Continuum of maternal health care	
		No (%)	Yes (%)
Parity			
Multiparous	4,085 (76.6)	73.2	26.8
Primiparous	1,250 (23.4)	72.8	27.20
Children born alive			
>2 children	2,666 (50.0)	73.2	27.2
1 to 2 children	2,664 (49.9)	73.5	26.5
Not registered	5		
Stillborn			
>2 children	31 (0.6)	73.6	26.4
1 to 2 children	5,302 (99.4)	73.02	26.98
Not registered	2		
Children alive			
>2 children	2,599 (48.7)	84.50	15.50
1 to 2 children	2,733 (51.2)	68.80	31.20
Not registered	3		
Antenatal care			
ANC1	4,781 (89.6)		
ANC2	4,648 (87.1)		
ANC3	3,273 (61.3)		
ANC4	2,958 (55.4)		
ANC 5 and above	2,492 (46.7)		
SP/Fansidar at ANC1			
Yes	4,083 (85.4)	73.69	26.31
No	695 (14.5)	72.39	27.61
vNot registered	3		
Reception of LLIN at ANC1			
No	922 (19.28)	77.30	22.70
Yes	3,857 (80.67)	68.80	31.20
Not registered	2		
Combination of education and bed net reception			
Non-educated women who have not received LLIM at ANC 1	646 (12.11)	85.33	14.67
Other women	4,689 (87.89)	44.60	55.40
Place of delivery			
No Health facility	467 (8.8)	73.4	26.6
Health facility	4,868 (91.2)	72.6	27.4
Cesarean delivery			
Yes	805 (15.1)	74,8	25,2
No	4,527 (84.9)	72,99	27,01
Not registered	3		
Assisted Childbirth			
No	1,899 (35.6)		
Yes	3,436 (64.4)		
Postnatal care			
No	2,238 (41.9)		
Yes	3,097 (58.1)		

ANC, antenatal care; SP, sulfadoxine and pyrimethamine; LLIN, long-lasting insecticidal net.

TABLE 3 Reception of LLINs at ANC1 based on the characteristics of 5,333 women who gave birth in the last 12 months before the 2022 survey in Conakry, Guinea.

Variables	Reception of LLINs at ANC1	
	Yes *n* (%)	No *n* (%)
Survey communes		
Dixinn	788 (78.99)	209 (21.01)
Matam	836 (81.90)	185 (18.10)
Kaloum	752 (83.88)	144 (16.12)
Matoto	851 (78.39)	234 (21.61)
Ratoma	1,075 (80.44)	261 (19.56)
Age groups		
25–49 years old	2,782 (86.82)	422 (13.18)
15–24 years old	1,590 (74.63)	541 (25.37)
Educational level		
Not attended school	1,728 (69.89)	744 (30.11)
Attended school	2,621 (91.55)	242 (8.45)
Job		
Unemployed	1,833 (67.54)	881 (32.46)
Employed	2,455 (93.89)	160 (6.11)
Marital status		
Married	3,903 (79.88)	983 (20.12)
Unmarried	366 (81.58)	83 (18.42)
Ethnic group		
Soussou	1,354 (84.80)	243 (15.20)
Malinke	571 (78.75)	154 (21.25)
Other	44 (81.52)	10 (18.48)
Fulani	2,165 (81.74)	484 (18.26)
Forester	238 (76.82)	72 (23.18)
Religion		
Muslim	4,120 (81.73)	921 (18.27)
Christian	234 (79.71)	60 (20.29)
Parity		
Multiparous	3,303 (80.86)	782 (19.14)
Primiparous	1,007 (80.57)	243 (19.43)
Children born alive		
>2 children	2,189 (82.12)	477 (17.88)
1 to 2 children	2,114 (79.34)	550 (20.66)
Stillborn		
>2 children	26 (83.63)	5 (16.37)
1 to 2 children	4,124 (77.79)	1,178 (22.21)
Children alive		
>2 children	2,120 (81.56)	479 (18.44)
1 to 2 children	2,184(79.90)	584(20.10)

AN, antenatal care; LLIN, long-lasting insecticidal net.

represents the proportion of women who have completed the different stages of the care continuum d (as shown in Figure 1). The study highlights that many women discontinued their care during the postnatal period (29.80%) and at the time of delivery (27.20%), indicating discontinuity in maternal healthcare services (Figure 2).

3.5 Factors associated with non-continuum

In our multivariable logistic regression, we found that several factors were associated with the non—continuum of maternal health care (non—completion of the various stages of the continuum by women). These factors include: not having an education compared to having an education (AOR 1.712: 1.456–2.185); being unemployed compared to being employed (AOR 4.232: 3.886–5.562); having two or more living children compared to having one to two living children (AOR 1.198: 1.081–1.453); not receiving a free Long-Lasting Insecticidal Net during the first antenatal care (AOR 2.117: 1.012–2.345); and a combination of not having an education and not receiving LLIM at ANC1 (AOR 6.216: 4.341–8.543) (Table 4).

4 Discussion

This study was conducted to estimate the proportion of women who had completed the various stages of the continuum of maternal health care, i.e., those who had completed the four antenatal visits, given birth under the care of qualified personnel, and received postnatal care within 42 days of delivery, during the 12 months preceding the survey in Conakry, as well as to identify the factors associated with non-completion of the various stages of the continuum of maternal care. A total of 5,335 women were interviewed during the study, and the results indicate that only 26.90% had completed the various stages of the maternal care continuum, while 73.1% had not. These statistics are better than those found by Camara BS et al. in Guinea in 2018, where only 20% of women had completed the various stages of the maternal healthcare continuum compared with 80% of non-completion of the various stages. The findings of this study hold significant implications for maternal healthcare policies and programs in Guinea and other countries with similar contexts (14). Based on these results, we can conclude that the level of non-continuum of maternal health care has decreased slightly, from 80% in 2018 to 73.1% in 2022. Despite this improvement, the result is still far from the national target. Guinea's 2015–2024 National Health Development Plan aims to achieve a continuum level of 73% against a non-continuum level of 27% by 2022 (16).

Several studies carried out in different regions have produced similar results regarding the continuum of maternal healthcare. In particular, a study carried out in Pakistan in 2021 (22) and another in Ethiopia in 2020 (12) determined that the probabilities of women completing the various stages of the continuum of care were 22.3% vs. 77.7% non-completion and 21.6% vs. 78.4%, respectively. In contrast, Charlotte et al. conducted a study in Benin in 2022 and obtained higher results, with 30% of women having completed the various stages of the continuum of care, compared with 70% who had not (21, 23).

The variations in estimates of the level of maternal healthcare continuum observed in the aforementioned studies could be attributed to differences in sample size and sociocultural variations. Another possible explanation could be the study period; in our study, we utilized a recall period of 12 months, whereas other studies used a recall period of 5 years. The use of a longer study period to retrospectively evaluate the utilization of

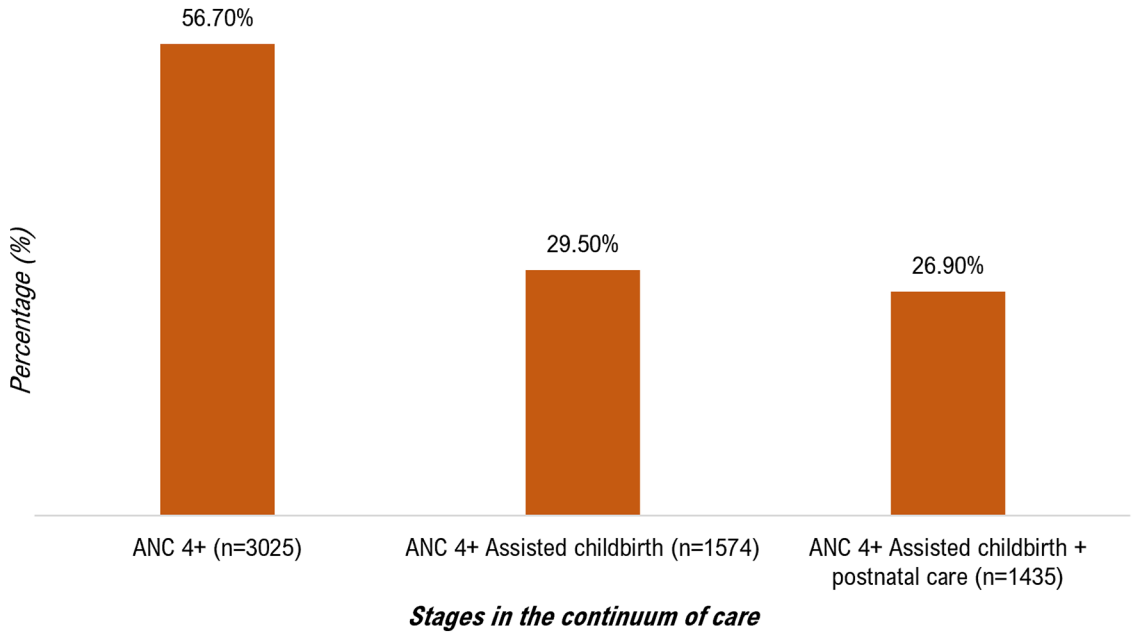

FIGURE 1
Stages of the continuum of maternal healthcare among 5,335 women who gave birth in the last 12 months before the 2022 survey in Conakry, Guinea.

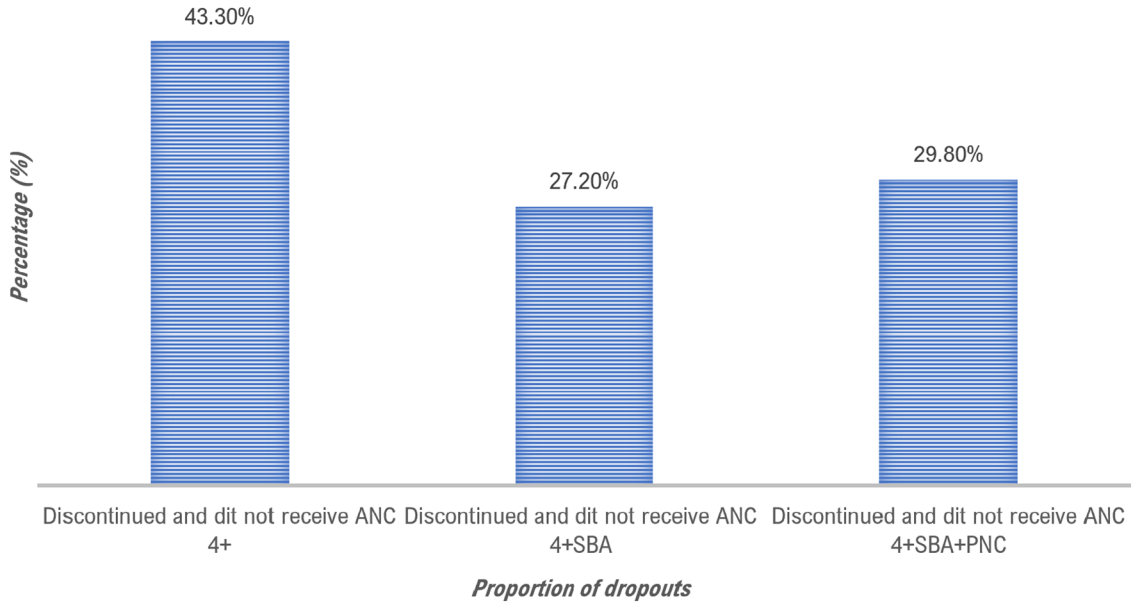

FIGURE 2
Proportion of losses in the continuum of maternal healthcare among 5,335 women who gave birth in the last 12 months before the 2022 survey in Conakry, Guinea.

maternal healthcare services before the survey could potentially increase recall bias among the women involved.

There are several reasons why certain women may not receive the appropriate maternal healthcare services they require. One of these reasons is the lack of access to healthcare services, which can be dependent on a number of factors. These may include widely held beliefs or traditional practices, as well as financial constraints that can make it difficult for women to pay for consultations, standard delivery fees, or care in private facilities for ultrasounds.

Our study showed that multiple factors contribute to non-completion of the different stages of the maternal care

TABLE 4 Factors associated with non-continuum of maternal healthcare services among 5,335 women who gave birth in the last 12 months before the 2022 survey in Conakry, Guinea.

Variables	Continuum of maternal Health care in weighted value (*n* = 5,335)		Multivariate analysis of the non-continuum of maternal care								
			Non-continuum of maternal Health care from ANC 1 to ANC 4+ (*n* = 2,955)			Non-continuum of maternal health care from ANC4 + to Assisted Childbirth (*n* = 1,462)			Non-Continuum of maternal Health care (ANC4 + Assisted childbirth + postnatal care) = global non-continuum of maternal Health care (*n* = 1,302)		
	No (%)	Yes (%)	AOR	95% CI	*p*-value	AOR	95% CI	*p*-value	AOR	95% CI	*p*-value
Survey communes											
Dixinn	71.70	28.30	0.981	(0.752–1.021)	0.421	1.064	(0.97–1.240)	0.061			
Kaloum	73.90	26.10	1.060	(0.901–1.231)	0.073	1.072	(0.99–1.310)	0.081			
Matoto	75.60	24.40	1.101	(0.672–1.302)	0.069	1.231	(1.106–1.431)	0.003			
Ratoma	76.70	23.30	1.450	(1.246–2.061)	0.006	1.651	(1.321–1.125)	0.002			
Matam	69.90	30.10	1			1					
Age groups											
25–49 years old	77.87	22.13	1.224	(1.098–1.712)	0.004	1.122	(1.043–1.69)	0.008	1.24	(1.041–1.63)	0.007
15–24 years old	67.40	32.60	1			1			1		
Ethnic group											
Soussou	72.50	27.50	1.046	(0.971–1.123)	0.235	1.086	(0.652–1.212)	0.235			
Malinke	74.20	25.80	0.871	(0.076–0.982)	0.321	0.972	(0.064–1.021)	0.453			
Other	72.60	27.40	1.225	(1.086–1.367)	0.009	1.0761	(0.954–1.211)	0.067			
Fulani	75.40	24.60	0.982	(0.543–1.157)	0.561	0.773	(0.651–1.235)	0.081			
Forester	69.90	30.10	1			1					
Religion											
Muslim	74.10	25.90	1.121	(0.965–1.231)	0.432	1.250	(0.991–1.311)	0.421			
Christian	70.68	29.32	1			1					
Educational level											
Not attended school	83.40	16.60	1.842	(1.541–1.762)	<0.001	1.657	(1.5431–2.451)	<0.001	1.712	(1.456–2.185)	<0.001
Attended school	59.70	40.30	1			1			1		
Job											
Unemployed	84.90	15.10	3.65	(3.210–5.231)	<0.001	4.561	(3.543–612)	<0.001	4. 232	(3.886–5.562)	<0.001
Employed	54.80	45.20	1			1			1		
Children alive											
>2 children	84.50	15.50	1.218	(1.0981–1.561)	0.001	1.177	(1.086–1.361)	0.001	1.198	(1.081–1.453)	0.001
1 to 2 children	68.80	31.20	1			1			1		
Reception of LLIN at ANC 1											
No	77.30	22.70	2.353	(1.010–2.216)	0.030	2.101	(1.03–2.123)	0.041	2.117	(1.012–2.345)	0.032
Yes	68.80	31.20	1			1			1		
Combination of education and bed net reception											
Non-educated women who have not received LLIM at ANC 1	85.33	14.67	5.651	(3.546–7.651)	<0.001	7.023	(5.651–8.892)	<0.001	6.216	(4.341–8.543)	<0.001
Other women	44.60	55.40	1			1			1		

(*Continued*)

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TABLE 4 Continued

Variables		Continuum of maternal Health care in weighted value (n = 5,335)	Multivariate analysis of the non-continuum of maternal care									
			Non-continuum of maternal Health care from ANC 1 to ANC 4+ (n = 2,955)			Non-continuum of maternal health care from ANC4 + to Assisted Childbirth (n = 1,462)			Non-Continuum of maternal Health care (ANC4 + Assisted childbirth + postnatal care) = global non-continuum of maternal Health care (n = 1,302)		
	No (%)	Yes (%)	AOR	95% CI	p-value	AOR	95% CI	p-value	AOR	95% CI	p-value
SP/Fansidar at ANC 1											
Yes	77.70	22.30	1.231	(1.120–1.651)	0.0024	1.103	(0.876–1.452)	0.354	1.114	(0.930–1.335)	0.240
No	67.60	32.40	1			1			1		

SP, sulfadoxine and pyrimethamine; ANC, antenatal care; LLIN, long-lasting insecticidal net, AOR, adjusted odds ratio; DK, don't know; CI, confidence interval.

continuum. Specifically, women with no education are 1.83 times more likely (or 83% more likely) to fail to complete the various stages of the maternal care continuum than other women with some level of education. This finding highlights the negative impact that a lack of education can have on healthcare utilization. It's logical that the less educated a woman is, the less likely she is to take advantage of healthcare services. A study conducted by Atnafu et al. in 2020 in Ethiopia confirms this conclusion. This study revealed that women who could read and write were 2.70 times more likely to benefit from the full range of maternal health services than those who could not read and write (12).

Our findings suggest that the low level of education among young girls in Guinea (13); may explain our results. Education can improve women's knowledge, access to information, and ability to understand advocacy messages through media and healthcare providers. Additionally, women with more education may have greater awareness of the maternal and child health services that are exempt.

This study also revealed that unemployment seems to be a significant factor associated with discontinuous maternal healthcare. In your sample, women without formal employment are 4.2 times more likely not to complete the various stages of the maternal care continuum than women with formal employment. This indicates that employment status may influence access to and the continuity of maternal healthcare. A study by Tesfa et al. in Ethiopia in 2022 also found that unemployment was significantly associated with incomplete use of maternal healthcare services (not continuum) (24). Women without employment may be preoccupied with the daily struggle for survival through informal activities, making it difficult for them to prioritize healthcare service utilization. This information suggests designing specific interventions aimed at improving access to and continuity of maternal healthcare among unemployed mothers. This result underlines the importance of considering socio-economic conditions in public health strategies aimed at improving maternal health.

In addition, the study showed that the number of children is a factor significantly associated with interruption of the maternal health care continuum. Mothers with two or more living children were 1.198 times more likely (or 20% more likely) not to complete the various stages of the maternal health care continuum than those with fewer than two children. Women with multiple children may prioritize their childbirth experience over the completeness of maternal healthcare services. It is therefore essential to offer education and information sessions to women during antenatal care visits, whatever their previous childbirth experience, in order to improve the continuum of maternal health care aimed at reducing maternal and neonatal deaths.

Finally, mothers who did not receive an insecticide-treated bed net during their initial prenatal visits are 2.117 times more likely to not complete the various stages of the maternal healthcare continuum compared to those who did receive one. This result shows that the lack of encouragement for women during maternal healthcare consultations could also limit women's use of healthcare services. This is the case for women in this study who did not

receive the bed net during their first antenatal visits. The above result suggests that the distribution of mosquito nets encourages pregnant women to attend regular prenatal consultations, which are essential for screening, prevention of complications, health education and fetal monitoring. Greater participation improves maternal and neonatal health outcomes. Incorporating this distribution reinforces the integrated approach to care, showing that prenatal services can address multiple needs simultaneously, increasing confidence and adherence to ongoing care. In summary, this holistic strategy improves malaria prevention, antenatal care uptake, confidence in the health system and maternal and child health outcomes, strengthening the continuum of care.

The various results related to factors associated with the non-continuum of maternal healthcare highlight how sociodemographic characteristics and other factors like the organization of healthcare services can influence the continuum of maternal healthcare. After combining the variables "education and the distribution of insecticide-treated bed nets during ANC," we observed a significant increase in the likelihood of not completing maternal care. Thus, the chance of not completing maternal health care was 6.216 times higher among uneducated mothers who did not receive insecticide-treated nets during ANC1 than among those who did. This result underscores how the lack of incentive for non-educated women can exacerbate the low utilization of maternal and child health services, highlighting the need for the country to develop and implement health promotion initiatives.

4.1 Strengths and limitations of the study

This study provides new data on the continuum of maternal healthcare in Conakry, Guinea. The sample size of interviewed women was sufficient. However, waiting five years between each demographic and health survey to assess performance and make necessary adjustments seems too long for a healthcare system that aims to reduce maternal and infant mortality efficiently. Many gaps could persist, and they might only become evident after five years. To our knowledge, our study is the first to present results on the continuum of maternal healthcare outside the typical cycle of demographic and health surveys in Guinea. Thus, the findings of this study can help decision-makers in the Guinean health department adjust interventions for women and children while awaiting a new demographic and health survey.

One possible limitation of this study is social desirability bias, as the interviews were conducted by medical students at the end of their training cycle. To mitigate this, we encouraged women to feel comfortable and tell the truth. Also, to reduce desirability bias, we took gender into account in forming the data collection teams. Each team consisted of one woman and one man. In certain instances, when the interviewed women preferred, only the female interviewer conducted the interview. Such cases were rare in this study (less than 1% of the sample). Another potential bias could result from women's recall due to the extended duration of the study. Women might have difficulty remembering the services they received during their previous obstetric visits, leading to overestimations or underestimations of the level of care. We minimized this issue by teaching women recall techniques repeatedly.

Another limitation of this study is that it only collected data from Conakry. Considering the prefectures in the interior of the country could change the estimation of the level of continuum. However, given that the level of continuum is low in Conakry (where access to healthcare services is better), the situation is probably even more concerning in the interior of the country, especially in rural areas. This leads us to claim that the completeness of maternal healthcare remains a significant health problem in Guinea.

Furthermore, since this study is cross-sectional, it does not allow for the examination of causality between the studied independent variables and the non-continuum of maternal healthcare. Additionally, we did not explore women's satisfaction with maternal healthcare services received during pregnancy, childbirth, and postpartum. A study exploring customer satisfaction and the quality of maternal and child healthcare services would be interesting to better understand the challenges related to the continuum of maternal healthcare.

5 Conclusion

According to a recent study, only 26.90% of women who had given birth in the 12 months prior to the survey had completed the various stages of the maternal health continuum, while 73.1% had not. These figures are well below the national target of 73% completion, which is essential to reduce maternal and infant morbidity and mortality rates. The study found that several factors, including not attending school, being unemployed, having two or more living children, and not receiving a bed net during the first antenatal visit, were associated with the non-continuity of maternal healthcare. To address these issues, significant additional efforts are needed in Guinea, particularly in improving maternal healthcare continuity. This can be achieved by strengthening education and information for pregnant women during early antenatal visits through interpersonal communication, implementing financial support measures for certain women, digitizing the antenatal visits registry, and creating an appointment reminder system. These measures can help reduce losses between the first and fourth antenatal visits and increase the proportion of women returning to healthcare facilities for postpartum care within the required timeframe. Moreover, improving the availability of quality human resources such as doctors, nurses, and midwives at peripheral healthcare facilities such as health centers and health posts, and increasing healthcare coverage by establishing new health centers and promoting the private sector, could enhance the proportion of women delivering under the care of qualified personnel.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The study was non-interventional and posed no risk of adverse effects. However, before its launch, the research protocol was approved by the 'National Ethics Committee for Health Research' of Guinea and registered under the number 141/CNERS/22. The municipal authorities in the five districts of Conakry were approached and permissions were obtained before data collection in the field. During the interviews, investigators encouraged women to ask questions and ensured their comfort before signing the consent form. The women were informed that they could terminate the interview at any point during the administration of the questionnaire. The participants in the study were not required to answer any questions if they did not wish to do so. Prior to administering the questionnaire, written informed consent was obtained from all women who agreed to participate. Each woman who was interviewed signed two copies of the informed consent form. One copy was kept by the woman, and the other copy was collected by the investigators for record-keeping purposes. The study included women between 15–24 yo. Consent from their legal guardian was waived by the the 'National Ethics 530 Committee for Health Research' of Guinea. The methods used in the study followed valid and standard methodological guidelines. To ensure confidentiality, all collected data was anonymized and only accessible to the investigators.

Author contributions

NL: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Software, Writing – original draft, Writing – review & editing. DL: Conceptualization, Methodology, Supervision, Writing – review & editing. AS: Writing – review & editing, Visualization. GK: Investigation, Methodology, Software, Writing – original draft. AC: Conceptualization, Methodology, Supervision, Validation, Writing – review & editing. SM: Writing – original draft, Writing – review & editing, Conceptualization. AD: Conceptualization, Methodology, Supervision, Validation, Visualization, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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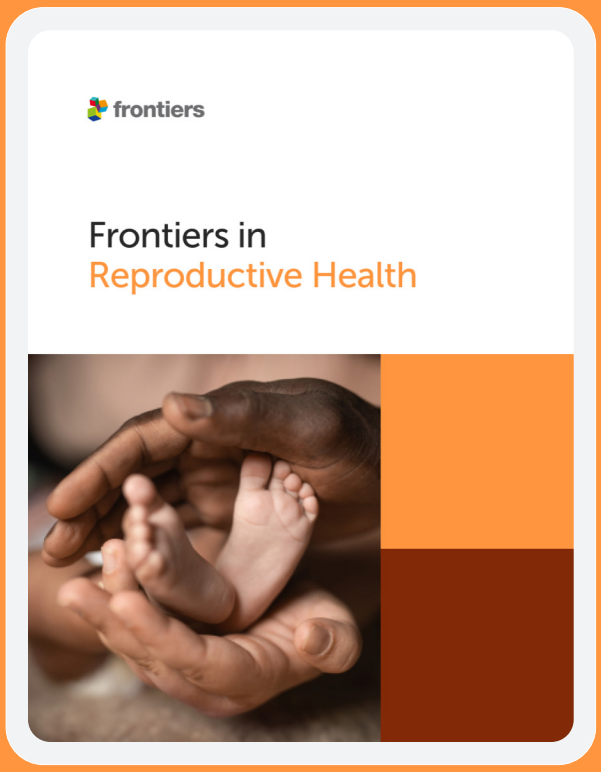

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