Impact of Exposure to Air Pollution on Cervicovaginal Microbial Communities

Inumidun Oyebode
Mentor: Heather Burris

Introduction

- Vaginal microbial communities can be dominated by anaerobic (CST IV) or *Lactobacillus* (other CSTs) species[1]
- CST IV is a risk factor for spontaneous preterm birth (sPTB) and is more common among Black than White populations[2]
- Aims:
  - (1) quantify associations of air pollution, specifically particulate matter <2.5μ in diameter ($PM_{2.5}$), with vaginal microbiota
  - (2) explore the extent to which racial disparities in $PM_{2.5}$ exposure might explain racial differences in the prevalence of CST IV

Methods

- Secondary analysis of 569 participants of the *Motherhood & Microbiome* study
- $PM_{2.5}$ exposures from NASA satellite and EPA ground monitor data
- Vaginal swabs from 16-20 weeks' gestation were analyzed using 16S rRNA sequencing and hierarchical clustering assigned CSTs.
- Multivariable logistic regression models calculated adjusted odds ratios of CST IV (vs. other CSTs) per interquartile range (IQR) increment of $PM_{2.5}$
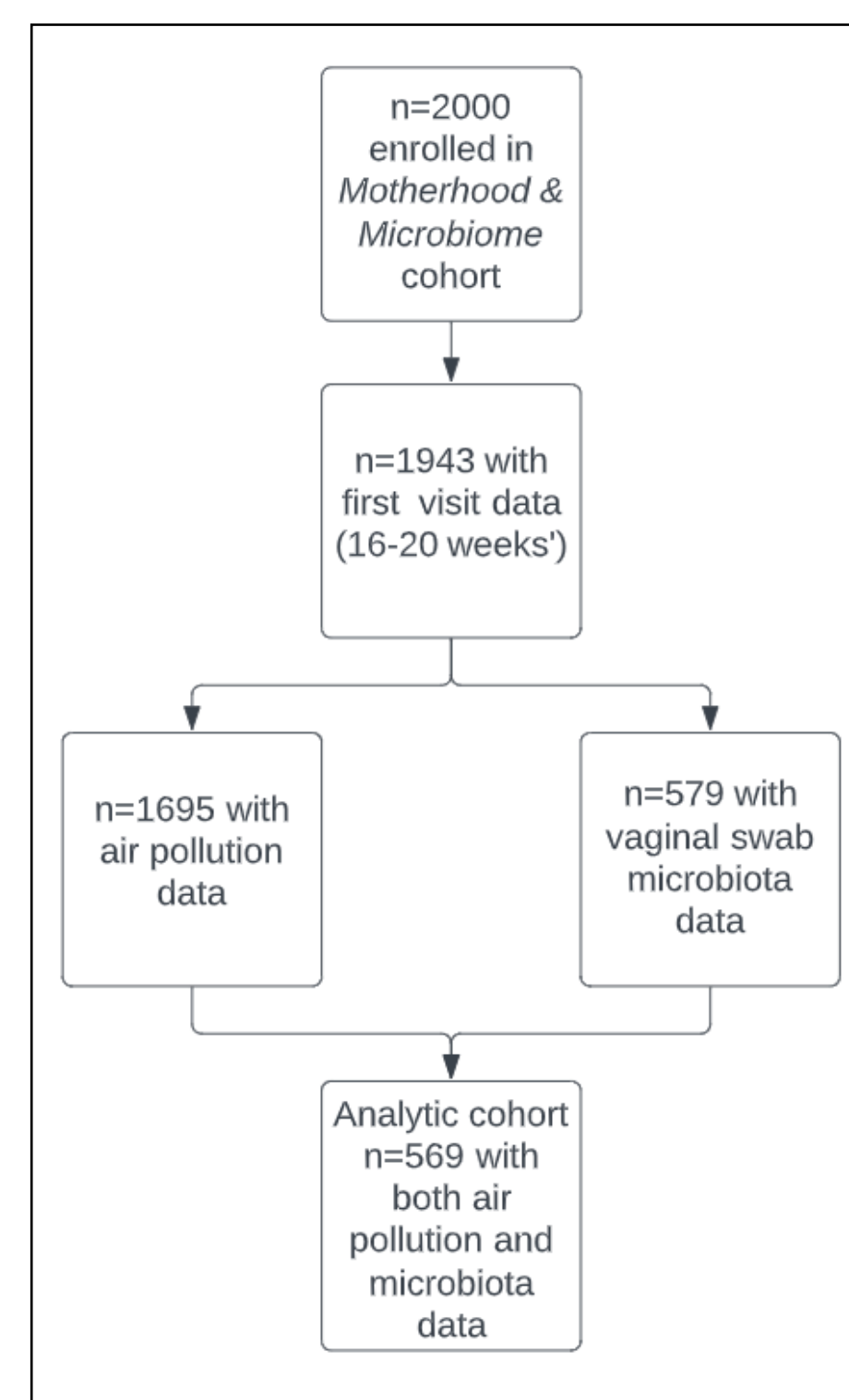- Race-stratified and mediation analyses

Figure 1. Development of analytic cohort

Flowchart:
- n=2000 enrolled in *Motherhood & Microbiome* cohort
- n=1943 with first visit data (16-20 weeks')
- n=1695 with air pollution data
- n=579 with vaginal swab microbiota data
- Analytic cohort n=569 with both air pollution and microbiota data

Table 2: Unadjusted and adjusted associations of $PM_{2.5}$ exposure with high risk cervicovaginal microbiota (Community State Type IV [CST IV]). Odds ratios presented per interquartile range increment of $PM_{2.5}$ exposure.

	OR (95% CI)
All participants (n=569)	
Model 1[a]	1.49 (1.16-1.90)
Model 2[b]	1.41 (1.04-1.92)
Model 3[c]	1.35 (0.99-1.86)
Race/ethnicity-stratified models	
Non-Hispanic Black (n=418)	
Model 1[a]	1.37 (0.98-1.92)
Model 2[b]	1.31 (0.93-1.87)
Non-Hispanic White[d] (n=107)	
Model 1[a]	2.84 (0.99-9.32)
Hispanic/Asian/Other[d] (n=44)	
Model 1[a]	1.21 (0.34-4.18)
Hispanic, Non-Hispanic Asian/Other/White (n=151)[e]	
Model 1[a]	1.85 (0.91-3.86)
Model 2[b]	2.05 (0.88-4.90)

[a]Unadjusted (adjusted only for season)
[b]Additionally adjusted for age, body mass index, parity, insurance, smoking status, gestational age at time of swab collection,
[c]Additionally adjusted for age, body mass index, parity, insurance, smoking status, gestational age at time of swab collection, race/ethnicity
[d]Sample size too small for adjusted model to run
[e]Group combined in order to perform multivariable adjustment

Figure 2. Annual mean $PM_{2.5}$ in the Philadelphia, PA region in 2015

Results

- Higher $PM_{2.5}$ exposure was associated with CST IV (aOR 1.41, 95% CI 1.04-1.92).
- Black participants (vs. White) had higher median $PM_{2.5}$ exposure (10.6 vs. 9.6 μg/m³, P< 0.001) and higher prevalence of CST IV (46% vs. 11%, P< 0.001).
- Mediation analysis revealed that higher $PM_{2.5}$ exposure may explain 5.4% (P=0.028) and 4.9% (P=0.066) of the Black-White disparity in CST IV in unadjusted and adjusted models.

Conclusion

- $PM_{2.5}$ was associated with CST IV, a risk factor for sPTB.
- $PM_{2.5}$ exposure may partially explain racial differences in CST IV.

Table 1: Characteristics of 569 participants in Motherhood and Microbiome pregnancy cohort with vaginal microbiota data at 15-20 weeks' gestation and $PM_{2.5}$ data and 1st trimester.

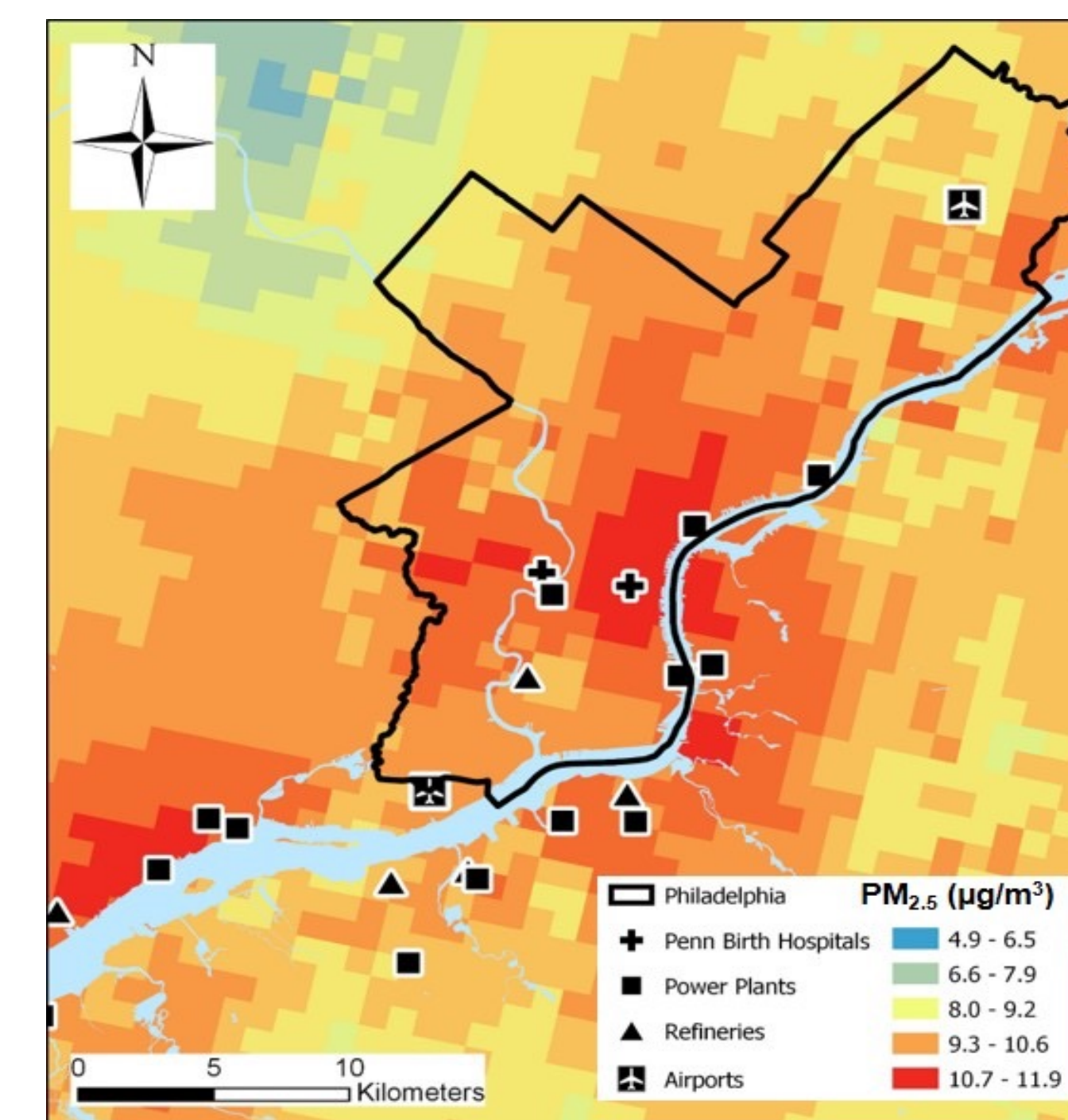| Characteristics	All participants (n=569) n (col%)	CST IV (n=218) n (col%)	Other CSTs (n=351) n (col%)	P	1st Trimester PM2.5 (ug/m3) Median [IQR]	P
Age (years)				<0.001		0.54
< 25	176 (30.9)	85 (39.0)	91 (25.9)		10.6 [1.2]	
25 to < 35	295 (51.8)	109 (50.0)	186 (53.0)		10.3 [1.9]	
≥ 35	98 (17.2)	24 (11.0)	74 (21.1)		10.2 [1.6]	
Race/ethnicity				<0.001		<0.001
Black	418 (73.5)	194 (89.0)	224 (63.8)		10.6 [1.5]	
White	107 (18.8)	12 (5.5)	95 (27.1)		9.6 [2.0]	
Asian/Hispanic/Other	44 (7.7)	12 (5.5)	32 (9.1)		10.0 [1.5]	
BMI Category (kg/m²)				0.007		0.45
< 25	191 (33.6)	60 (27.5)	131 (37.3)		10.4 [1.7]	
25 to < 30	159 (27.9)	57 (26.1)	102 (29.1)		10.3 [1.8]	
≥ 30	219 (38.5)	101 (46.3)	118 (33.6)		10.6 [1.5]	
Parity				0.4		0.49
Nulliparous	240 (42.2)	84 (38.5)	156 (44.4)		10.5 [1.8]	
Parous	329 (57.8)	134 (61.5)	195 (56.6)		10.4 [1.7]	
Smoked in Pregnancy				0.09		0.05
Yes	47 (8.3)	24 (11.0)	23 (6.6)		10.9 [1.5]	
No	522 (91.7)	194 (89.0)	328 (93.4)		10.4 [1.7]	
Insurance				0.51		<0.001
Private	265 (46.6)	66 (30.3)	199 (56.7)		10.0 [1.9]	
Medicaid/uninsured	304 (53.4)	152 (69.7)	152 (43.3)		10.7 [1.4]	

Works Cited

(1) Ravel, J., Gajer, P., Abdo, Z., Schneider, G. M., Koenig, S. S. K., McCulle, S. L., Karlebach, S., Gorle, R., Russell, J., Tacket, C. O., Brotman, R. M., Davis, C. C., Ault, K., Peralta, L., & Forney, L. J. (2011). Vaginal microbiome of reproductive-age women. *Proceedings of the National Academy of Sciences, 108*(supplement_1), 4680–4687. https://doi.org/10.1073/pnas.1002611107
(2) Elovitz, M. A., Gajer, P., Riis, V., Brown, A. G., Humphrys, M. S., Holm, J. B., & Ravel, J. (2019). Cervicovaginal microbiota and local immune response modulate the risk of spontaneous preterm delivery. *Nature Communications, 10*(1), 1305. https://doi.org/10.1038/s41467-019-09285-9