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The Effects of Opioid Use on Maternal Health and Infant Growth in the First 3 Years

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Abstract

Background: The effects of opioid use disorder (OUD) on maternal-infant health are understudied.

Methods: A retrospective review of 174 infants born at 34-42 weeks' gestational age (GA) examined the association between OUD and maternal body mass index (BMI; primary outcome) and infant growth parameters in the first 3 years of life (secondary outcome). Multivariable linear regression and linear mixed-effects models were used.

Results: Maternal pre-pregnancy, pregnancy, and ΔBMI did not differ by opioid exposure, but the cohort with OUD had greater variance in ΔBMI (p=0.0003). Opioid-exposed infants (n=92) were born smaller, but by 3 years, their BMIs surpassed those of non-exposed infants (β Yr2=1.4; β Yr3=1.46, both p<0.01). This pattern remained even after adjusting for GA, pre-pregnancy BMI, and ΔBMI. Opioid-exposed males grew more slowly over the first 3 years than their female counterparts (sex*time interaction β=-0.53, p=0.037).

Conclusion: OUD may compromise maternal health during pregnancy and alter infant growth.

Impact

- Maternal opioid use disorder was associated with greater BMI variability during pregnancy and greater social and clinical vulnerability.
- The current study expands on previous evidence of aberrant growth in opioid-exposed infants during the first year of life by demonstrating altered BMI trajectories through 3 years of age.
- Prenatal opioid exposure was associated with sex-specific BMI trajectories in the first 3 years of life, highlighting the importance of considering sex as a biological variable and the need for longitudinal growth monitoring.

INTRODUCTION

There has been a fourfold increase in pregnant women with opioid use disorder (OUD) from 1999 to 2014 (1, 2). Paralleling this trend is the 82% increase in neonatal opioid withdrawal syndrome (NOWS) between 2010 and 2017 (1). Compared to healthy infants, opioid-exposed infants are often born smaller and prematurely (3, 4). They also experience feeding difficulties and gastrointestinal issues (5, 6). However, growth trajectories following prenatal opioid exposure are not well studied.

Compared with healthy infants without prenatal opioid exposure, those with NOWS exhibited greater variation in growth trajectories during the first year of life, with more infants growing at either the higher (90th) or lower (10th) weight percentiles (7). Further, despite being born leaner, opioid-exposed infants had a comparable fat mass gain as their non-exposed counterparts (8), evidence of catch-up growth in the exposed group. Because aberrant growth in early childhood has been associated with adverse

cardiometabolic health in adulthood, it is important to understand early factors that may contribute to this predisposition.

Recognizing the role of maternal health on infant health, the World Health Organization categorizes maternal pre-pregnancy weight as the following: underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25.0-29.9 kg/m^2), and obese (BMI > 30.0 kg/m^2) (9, 10). For each of these BMI categories, the National Academy of Medicine (NAM; previously known as the Institute of Medicine) recommend appropriate gestational weight gain as 12.5–18.0 kg (28–40 pounds [lbs]) for the underweight category, 11.5–16.0 kg (25–35 lbs) for the normal weight category, 7.0-11.5 kg (15–25 lbs) for the overweight category, and 5.0–9.0 kg (11–20 lbs) for the obese category (11). Based on the association between maternal health before and during pregnancy and offspring weight and growth, we hypothesized that OUD adversely affected maternal BMI during pregnancy (primary outcome) and infant growth trajectory in the first 3 years of life (secondary outcome). Because social-environmental factors are shown to affect birth outcomes (12), we also explored these effects on BMI outcomes in mother-infant dyads affected by OUD.

SUBJECTS AND METHODS

We conducted a retrospective electronic medical record (EMR) review of 174 infants with and without prenatal opioid exposure born at our center between September 2021 and July 2024 who were enrolled in a study approved by the Tufts Medical Center Institutional Review Board. Infants were born between 34 and 42 weeks' gestational age (GA). We extracted demographic and clinical data for mother-infant dyads. Prenatal opioid exposure was defined as positive maternal urine toxicology, documented maternal opioid use throughout the pregnancy, and/or positive neonatal toxicology (urine and/or meconium) testing. We excluded infants with known or suspected congenital malformations or chromosomal anomalies and death before 48 hours of life.

Maternal data include pre-pregnancy BMI (the last recorded BMI within one month before pregnancy), pregnancy BMI (the last recorded BMI within one month before delivery), change in pre-pregnancy to pregnancy BMI (ΔBMI), gestational weight gain, delivery type (vaginal vs. cesarean/C-section), comorbid physical conditions (general hypertension [HTN], chronic HTN, gestational HTN, preeclampsia [PEC], gestational diabetes, hypothyroidism, pregnancy-induced cholestasis, infectious diseases, other health conditions), and mental health conditions (depression, anxiety, post-traumatic stress disorder [PTSD], bipolar, attention deficit disorder [ADD], attention-deficient hyperactivity disorder [ADHD], other mental health), race, ethnicity, cigarette smoking, and hepatitis C status. Infant data included sex and anthropometric measurements (weight, length, head circumference, percentiles, and BMI) at birth and in the first 3 years of life. Social-environmental factors included insurance type (public vs. private), area deprivation index (ADI) obtained using the Neighborhood Atlas mapping tool (13), and housing status (stable vs. unstable, with unstable defined as homelessness, sheltered living, sober house, or transitional housing). We also evaluated primary language and the need for an interpreter.

Descriptive statistics (means and standard deviations, counts and percentages) were calculated for demographic and clinical variables stratified by opioid exposure group. T-tests and Fisher's exact tests were used to test associations between variables and opioid exposure. Univariate and multivariable associations of opioid exposure with pre-pregnancy BMI, pregnancy BMI, ΔBMI, and infant BMI at birth were measured using linear regression models. Covariates for multivariable models were selected via backward selection, using candidate variables with $p < 0.2$ in univariate associations with the outcome, and keeping covariates with adjusted $p < 0.2$ in the multivariable model. Of the clinical and demographic variables listed above, any measurements occurring after the outcome were not included as candidate predictors (e.g., conditions occurring during pregnancy could not predict pre-pregnancy BMI). We performed diagnostic assessments for the final models, including visual inspection of residuals and calculation of variance inflation factors to assess potential multicollinearity among predictors. We assessed homogeneity of variance in the outcomes by opioid exposure status using Levene's test. For covariates that were associated with outcomes and were highly unbalanced between exposure groups (e.g., smoking), we performed sensitivity analyses among those who had sufficient numbers in both exposure groups (e.g., non-smokers).

We measured associations of opioid exposure with infant BMI trajectories over the first 3 years of life using linear mixed-effects models. We included time, time squared (to account for non-linear growth trajectories), sex, GA, pre-pregnancy BMI, and ΔBMI as fixed effects, as well as fixed effects for interactions between linear time and each covariate, and a random intercept for each child. This allows us to examine the effect of each covariate on birth BMI and on the rate of change in BMI over the first 3 years of life. We did not consider additional covariates due to concerns about potential overfitting. We also measured associations between opioid exposure and child BMI at each year separately using linear regression models adjusting for sex, GA, pre-pregnancy BMI, and ΔBMI.

For the outcomes of child BMI at birth and trajectories over the first 3 years of life, we examined sex-specific effects within opioid-exposed children. In both cases, we used the same models as described above, but we limited the sample to opioid-exposed children and considered the effect of sex (and the interaction of sex with time, for trajectory models) as the variable of interest. All statistical analyses were carried out in R (version 4.5.3).

RESULTS

We included 82 mother-infant dyads without opioid exposure and 92 dyads with opioid exposure. As shown in Table 1, mothers with OUD had unique characteristics, with a higher proportion of White race, cigarette smoking, and positive hepatitis C. More of these mothers were on public insurance, reported housing instability, and had higher state decile and national percentile ADI scores. Mothers with OUD also had higher rates of general hypertension and mental health conditions (anxiety, depression, PTSD, bipolar, ADD/ADHD, and any mental health problems). Infants in the opioid cohort were born smaller than those in the non-opioid cohort. The exposed cohort had a trend towards a higher SGA proportion.

Table 1
Demographic and Clinical Data

VARIABLES	NON-EXPOSED (N = 82)	OPIOID-EXPOSED (N = 92)	P
Maternal Data			
Age (years)	31.27 (5.20)	32.39 (3.75)	0.115
Race	45 (54.9)	77 (83.7)	**< 0.001**
White	12 (14.6)	4 (4.3)	
Black	25 (30.5)	11 (12)	
Other/Unknown			
Ethnicity	65 (79.3)	72 (78.3)	1.000
Not Hispanic/Latino	8 (9.8)	10 (10.9)	
Hispanic/Latino	9 (11.0)	10 (10.9)	
Unknown			
Smoking	67 (81.7)	36 (39.1)	**< 0.001**
No	0 (0.0)	47 (51.1)	
Yes	15 (18.3)	9 (9.8)	
Unknown			
Hepatitis C	52 (63.4)	48 (52.2)	**< 0.001**
Negative	1 (1.2)	35 (38.0)	
Positive	29 (35.4)	9 (9.8)	
Unknown			
Maternal Opioid	NA	40 (43.5)	NA
Methadone	NA	45 (48.9)	
Buprenorphine	NA	7 (7.6)	
Other			
Cesarean Section	30 (36.6)	39 (42.4)	0.443

Data are presented as mean (standard deviation) for continuous measures and N (%) for categorical measures. Bold p value indicates significance. ADI: area deprivation index, BMI: body mass index, GWG: gestational weight gain, HTN: hypertension, PEC: pre-eclampsia, PTSD: post-traumatic stress disorder, ADD: attention deficit disorder, ADHD: attention-deficient hyperactivity disorder, HC: head circumference, SGA: small for gestational age.

VARIABLES	NON-EXPOSED (N = 82)	OPIOID-EXPOSED (N = 92)	P
Maternal Data			
Insurance Type	23 (28.0)	66 (77.6)	**< 0.001**
Public	50 (61.0)	10 (11.8)	
Private	9 (11.0)	9 (10.6)	
Unknown			
State Decile ADI	4.83 (2.39)	5.67 (2.12)	**0.017**
National Percentile ADI	20.04 (11.97)	24.37 (11.80)	**0.021**
Housing Stability (%)	65 (80.2)	51 (61.4)	**< 0.001**
Stable	7 (8.6)	32 (38.6)	
Unstable/homeless	9 (11.1)	0 (0.0)	
Unknown			
Pre-pregnancy BMI (kg/m^2)	26.46 (4.61)	27.59 (6.60)	0.235
Pre-pregnancy Weight (kg)	154.09 (28.41)	155.54 (36.12)	0.790
BMI (kg/m^2)	0 (0.0)	2 (2.7)	0.253
<18.5	29 (42.0)	26 (34.7)	
18.50–24.9	27 (39.1)	31 (41.3)	
25-29.9	10 (14.5)	6 (8.0)	
30-34.9	2 (2.9)	6 (8.0)	
35-39.9	1 (1.4)	4 (5.3)	
40+			
Pregnancy BMI (kg/m^2)	31.92 (5.68)	31.79 (6.51)	0.891
Pregnancy Weight (kg)	184.60 (33.35)	181.38 (35.54)	0.555

Data are presented as mean (standard deviation) for continuous measures and N (%) for categorical measures. Bold p value indicates significance. ADI: area deprivation index, BMI: body mass index, GWG: gestational weight gain, HTN: hypertension, PEC: pre-eclampsia, PTSD: post-traumatic stress disorder, ADD: attention deficit disorder, ADHD: attention-deficient hyperactivity disorder, HC: head circumference, SGA: small for gestational age.

VARIABLES	NON-EXPOSED (N = 82)	OPIOID-EXPOSED (N = 92)	P			
Maternal Data						
Delta BMI (kg/m^2)	5.29 (2.82)	4.73 (5.40)	0.486			
GWG (kg)	33.29 (24.72)	26.69 (29.69)	0.178			
HTN	25 (30.5)	13 (14.1)	**0.010**			
Gestational HTN	17 (20.7)	9 (9.8)	0.055			
Chronic HTN	9 (11.0)	4 (4.3)	0.147			
PEC	10 (12.2)	9 (9.8)	0.635			
Gestational Diabetes	1 (1.2)	1 (1.1)	1.000			
Cholestasis in Pregnancy	0 (0.0)	5 (5.4)	0.061			
Hypothyroidism	7 (8.5)	5 (5.4)	0.552			
Infectious Disease	9 (11.0)	8 (8.7)	0.621			
Other Health Conditions	25 (30.5)	34 (37.0)	0.424			
Anxiety	11 (13.4)	29 (31.5)	**0.006**			
Depression	9 (11.0)	26 (28.3)	**0.005**			
PTSD	0 (0.0)	10 (10.9)	**0.002**			
Bipolar	1 (1.2)	9 (9.8)	**0.020**			
ADD/ADHD	1 (1.2)	9 (9.8)	**0.020**			
Other Mental Health	1 (1.2)	3 (3.3)	0.623			
Any Mental Health	17 (20.7)	43 (46.7)	**< 0.001**			
Neonatal Data						
Male Sex	42 (51.2)	49 (53.3)	0.879			
Gestational Age (weeks)				38.35 (1.51)	38.06 (1.64)	0.220

Data are presented as mean (standard deviation) for continuous measures and N (%) for categorical measures. Bold p value indicates significance. ADI: area deprivation index, BMI: body mass index, GWG: gestational weight gain, HTN: hypertension, PEC: pre-eclampsia, PTSD: post-traumatic stress disorder, ADD: attention deficit disorder, ADHD: attention-deficient hyperactivity disorder, HC: head circumference, SGA: small for gestational age.

VARIABLES	NON-EXPOSED (N = 82)	OPIOID-EXPOSED (N = 92)	P
Maternal Data			
Birth Weight (grams)	3195.48 (480.12)	2996.03 (583.27)	**0.014**
Birth Weight %	49.37 (26.49)	40.71 (27.26)	**0.035**
Birth Length (cm)	49.90 (3.34)	48.71 (3.15)	**0.017**
Birth Length %	61.09 (26.63)	46.92 (29.04)	**0.001**
Birth HC (cm)	34.10 (2.96)	33.28 (2.02)	0.037
Birth HC %	44.98 (28.95)	40.34 (28.87)	0.292
Birth BMI (kg/m^2)	12.98 (3.11)	12.53 (1.53)	0.230
SGA	15 (18.3)	28 (30.4)	0.079

Data are presented as mean (standard deviation) for continuous measures and N (%) for categorical measures. Bold p value indicates significance. ADI: area deprivation index, BMI: body mass index, GWG: gestational weight gain, HTN: hypertension, PEC: pre-eclampsia, PTSD: post-traumatic stress disorder, ADD: attention deficit disorder, ADHD: attention-deficient hyperactivity disorder, HC: head circumference, SGA: small for gestational age.

Maternal BMI

Pre-pregnancy BMI

did not differ by maternal OUD status using the unadjusted model (β = 1.13, 95% CI [-0.77, 3.02], p = 0.24) and adjusted models (β = 0.09, 95% CI [-2.21, 2.39], p = 0.94) accounting for maternal age, cigarette smoking, state decile ADI, anxiety, and ADD/ADHD.

Pregnancy BMI

did not differ by maternal OUD status using the unadjusted (β=-0.13, 95% CI [-2.03, 1.77], p = 0.89) and adjusted models (β=-0.33, 95% CI [-2.26, 1.60], p = 0.74) accounting for chronic HTN, PEC, cholestasis, and national percentile ADI.

Change in BMI During Pregnancy (ΔBMI)

did not differ by maternal OUD status using the unadjusted (β=-0.56, 95% CI [-2.06, 0.95], p = 0.47) and adjusted models (β = 0.18, 95% CI [-1.61, 1.96], p = 0.84) accounting for maternal race, cigarette smoking, other health problems, and pre-pregnancy BMI. While there was no significant effect of opioid use on

mean ΔBMI, Levene's test for homogeneity of variance showed greater variability in ΔBMI for mothers with OUD than without (p = 0.0003) (Fig. 1).

Gestational Weight Gain

significantly fewer mothers in the opioid group had appropriate gestational weight gain within the NAM guidelines than in the non-opioid group (13.8% vs. 30.9%, $\chi^2 = 4.24$, df = 1, p = 0.04). When gestational weight gain falls outside of the NAM guidelines, 40% of mothers in the opioid group compared to 25.5% of mothers in the non-opioid group had suboptimal gestational weight gain ($\chi^2 = 1.69$, df = 1, p = 0.19), with an odds ratio of 1.94 (95% CI [0.82–4.6]).

Infant BMI

BMI at Birth and Trajectories in the First 3 Years

although opioid-exposed infants were born smaller, their birth BMI did not differ from the non-exposed group using the unadjusted (β=-0.46, 95% CI [-1.17, 0.26], p = 0.21) and adjusted models (β=-0.24, 95% CI [-1.05, 0.57], p = 0.56) accounting for GA, ethnicity, cigarette smoking, pre-pregnancy BMI, and ΔBMI. BMI in Year 1 did not differ by opioid exposure status (β = 0.61, 95% CI [-0.07, 1.28], p = 0.077), but the opioid-exposed cohort had significantly greater BMI in Year 2 (β = 1.44, 95% CI [0.38, 2.49], p = 0.009) and Year 3 (β = 1.46, 95% CI [0.55, 2.36], p = 0.003) after adjusting for sex, GA, birth BMI, pre-pregnancy BMI, and ΔBMI. Retention of participants was 66% at Year 1, 43% at Year 2, and 25% at Year 3, with no differences in retention rates between OUD exposure groups (chi-square p > 0.05).

Interaction Between Opioid Exposure and Time

modeling BMI from birth to Year 3 together, the opioid-exposed cohort had greater BMI slopes than the non-exposed cohort, as evidenced by a significant opioid exposure * time effect on BMI trajectories (β = 0.52, 95% CI [0.21, 0.85], p = 0.002) after adjusting for time squared, GA, pre-pregnancy BMI, ΔBMI and time interactions with GA, pre-pregnancy BMI, and ΔBMI (Fig. 2).

Sex-specific Effects

within the opioid-exposed cohort, male sex was associated with significantly higher birth BMI (β = 1.09, 95% CI [0.32, 1.85], p = 0.006), adjusting for the same covariates as the full-cohort birth BMI analysis. There was also a significant male sex * time effect on BMI trajectories (β=-0.53, 95% CI [-1.03, -0.06], p = 0.037), suggesting slower growth in opioid-exposed males than opioid-exposed females (Fig. 3).

DISCUSSION

Maternal outcomes

Despite the similar pre- and pregnancy BMI profiles between groups, the significantly greater variance in ΔBMI in women with OUD compared to those without OUD suggests the greater tendency for over- or undernutrition in the OUD cohort. The BMI variance in mothers affected by OUD paralleled the previously reported wider variation in growth trajectories of opioid-exposed infants (7). Together, these data suggest that OUD may alter health trajectories of mother-infant dyads. Such OUD-related vulnerability is also reflected in the significantly higher proportion of pregnant women with OUD who failed to meet the NAM standard of healthy gestational weight gain compared to those without OUD (86.2% vs 69.1%). Although not significant, among those who did not meet the NAM standard of healthy gestational weight gain, almost twice as many mothers with OUD had gestational weight gain below the NAM standard as the mothers without OUD. Although BMI is not an accurate metric for global health, it is often used as a proxy for adiposity and obesity because of its convenience (14). Therefore, our data suggest that OUD may adversely affect maternal health and weight during pregnancy. Because suboptimal gestational weight gain has been linked to adverse short- and long-term infant outcomes (15, 16), future studies should elucidate such effects.

The retrospective nature of our study makes it impossible to identify the causal mechanisms underlying the greater variance in maternal ΔBMI and the inability to meet the NAM standard. However, we speculate that several factors may contribute to this association. The significantly higher proportions of public insurance and housing instability and higher ADI scores at both the state and national levels in the OUD cohort suggest that OUD was associated with more adverse social-environmental factors. These factors may compromise a healthy lifestyle and lead to either excessive or inadequate weight gain during pregnancy (17, 18). Additionally, the significantly greater proportion of comorbid mental health conditions in the OUD cohort likely compromises the ability to maintain healthy nutritional profiles (19–22). Future studies should focus on social and environmental factors as determinants of, and barriers to, a healthy lifestyle and optimal gestational weight gain.

The trend towards greater incidence of gestational HTN in the OUD cohort is consistent with prior reports and is associated with smaller infant size at birth (23). In our cohort, the incidence of gestational diabetes was relatively low, which may reflect missing data or underreporting. Studies on the link between OUD and gestational diabetes have been conflicting, with some showing a lower incidence of gestational diabetes in pregnant women with substance use disorder (24). In contrast, others reported varying effects of opioids from harmful to protective (25). Some others asserted that the increased incidence of metabolic syndrome and gestational diabetes may result from the unhealthy lifestyle and diets related to OUD rather than the direct effect of opioid use (26). The role of nutrition, diets, and lifestyle in the association between OUD and pregnancy-related comorbid conditions warrants further study.

A significantly greater proportion of women with OUD had hepatitis C infection, supporting prior studies, which may affect maternal and neonatal outcomes (27, 28). A diagnosis of hepatitis C may predispose individuals with OUD to altered immune profiles compared to those without a hepatitis C diagnosis (29). While OUD is associated with a hyper-reactive immune state compared with no OUD, co-occurring OUD

and hepatitis C heighten stress stimulation and disrupt immune cell production and function, leading to attenuated responses compared with OUD alone. Further research is needed to examine the interplay between hepatitis C and OUD and its effect on mother-infant outcomes.

Infant outcomes

In addition to the effects on maternal health, opioid use during pregnancy also affects offspring outcomes. As shown in our cohort, infants with prenatal opioid exposure were born significantly smaller, which supports prior research (3). The smaller size at birth may be linked to greater maternal ΔBMI variance and lower gestational weight gain in the OUD cohort.

Because BMI estimates childhood obesity risk (30), our finding of comparable BMI despite lower birth weight in the opioid-exposed cohort may indicate excess adiposity in this population. This result supports recently published data from our laboratory, showing that despite significantly lower birth weight, opioid-exposed infants had relative excess adiposity measured using air displacement plethysmography (31). Together, these data suggest that opioid-exposed infants may have greater fat mass at birth. It is unclear if such excess adiposity may predispose these infants to metabolic syndrome in adulthood. Future studies should examine these programming effects prospectively.

While BMI at birth was comparable between groups, the BMI for opioid-exposed infants surpassed that of non-exposed infants in Years 2 and 3, evidence of catch-up growth in this population. Further, the interaction between opioid exposure and time suggests that opioid-exposed infants have a distinct growth pattern compared to non-exposed infants over time, highlighting the need to elucidate whether such trajectory predisposes these infants to overgrowth and metabolic syndrome later in life. Previous studies have also demonstrated opioid-related catch-up growth in the first few months of life and aberrant growth trajectory in the first year of life (7, 8). However, by expanding to the first 3 years of life, our study represents the longest longitudinal growth-trajectory study in this high-risk population. Such a unique catch-up growth trajectory in opioid-exposed infants may predispose them to a well-known phenomenon called the Developmental Origins of Health and Disease (DOHaD), where an in-utero adverse environment determines susceptibility to adult-onset and chronic diseases (32). Therefore, the longitudinal and developmental programming effects of prenatal opioid exposure on infant growth warrant further study.

In addition to the BMI changes over time, prenatal opioid exposure is also linked to sex-specific BMI alterations in our study. Although opioid-exposed males had greater BMI at birth, they had slower growth in the first 3 years of life compared to opioid-exposed females. Our sex-specific findings are consistent with human and animal data showing the sex-specific effects of in-utero opioid exposure on perinatal and postnatal growth (31, 33). While understudied, such early sex-specific differences may explain why adult females on medications for OUD have higher BMI and greater weight gain during treatment than their male counterparts (34).

Strengths and Limitations

Our retrospective and single-center design limits the generalizability of our findings. Use of EMR to collect data may be subject to human and system errors during data recording and extraction. Additionally, residual confounding factors may affect our results. For instance, breast milk use has been shown to improve childhood BMI (35), but we did not collect feeding data as a potential modifier of the impact of OUD on infant health. Future studies should include this important variable to understand the protective effect of breast milk use. The high attrition rates introduce potential selection bias. Additionally, some covariates were so unbalanced by OUD exposure groups that distinguishing between OUD and these co-occurring conditions (e.g., smoking, housing instability) was not possible.

Despite these limitations, our study represents the longest longitudinal study to date examining the impact of maternal OUD on infant BMI and growth trajectory in the first 3 years of life. Using a retrospective chart review, we conducted our study cost-effectively. Incorporating maternal mental health conditions and social-environmental factors provides important context that can be validated in future studies. The sex-specific effects highlight the importance of including sex as a biological variable in biomedical research. While it is known that males and females encounter distinct challenges related to OUD, findings such as ours demonstrate early predisposition to these unique, sex-specific risks. Such understanding is an important step toward developing personalized medicine.

CONCLUSION AND FUTURE DIRECTIONS

This retrospective chart review provides novel insights into the adverse effects of OUD on maternal health during pregnancy, which may impact infant anthropometrics at birth and early growth trajectories in the first 3 years of life. While our study warrants further validation in prospective studies with larger sample sizes, the current findings highlight important public health measures that may alter vulnerability and risk profiles of mother-infant dyads affected by the opioid epidemic to improve intergenerational health across the lifespan. The association between maternal OUD and social and mental health vulnerability and potential impact on pregnancy-related health suggests the need for prenatal nutrition support programs and weight monitoring during pregnancy. Additionally, the evidence of aberrant growth trajectory in opioid-exposed infants and the predisposition to adverse metabolic outcomes can inform current practice and develop targeted strategies, such as early nutritional counseling, feeding support, and healthy lifestyle interventions, to prevent long-term chronic health problems. While our study focuses on maternal health, including paternal health in future studies is important for achieving optimal outcomes for offspring (36). Finally, because of the known risk of poor cognitive development and mental health conditions in pregnancy-related and childhood undernutrition (37), future efforts should focus on understanding the neurodevelopmental and mental health outcomes related to prenatal opioid exposure.

Declarations

consent declaration: All parents or legal guardians of the minors involved in this study have consented to participate in the study.

Conflict of Interest: The authors declare no competing financial interests.

Data Availability: Materials described in the manuscript, including all relevant raw data, are available for research and non-commercial purposes upon reasonable request, without breaching participant confidentiality.

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Ethics Approval and Consent to Participate: IRB Exempt.

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Figures

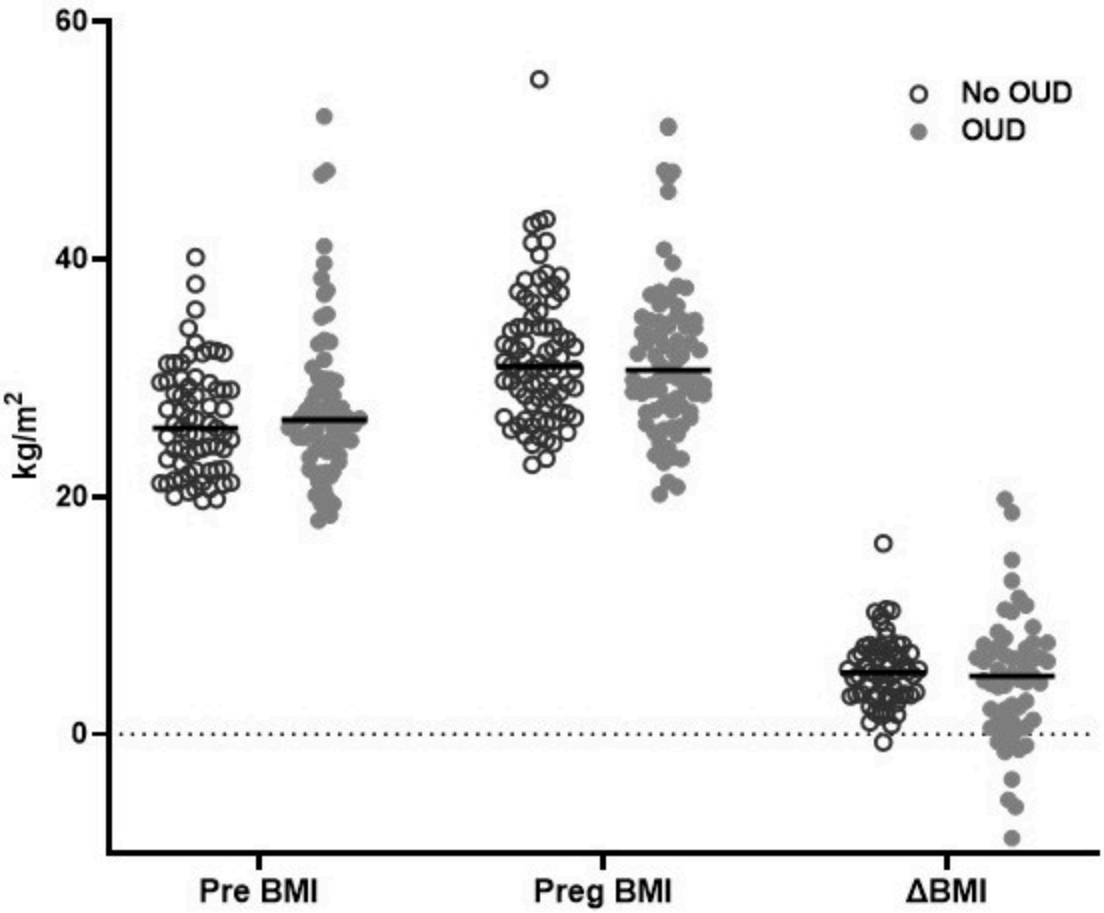

Figure 1

Maternal BMI measurements by OUD status. Pre-pregnancy, pregnancy, and delta BMI did not differ significantly between mothers with and without OUD. However, OUD was associated with significantly greater variability in delta BMI (Levene's test; p=0.0003). Dots represent individual data points, and lines represent group medians and interquartile ranges. ΔBMI: change in pre-pregnancy and pregnancy BMI.

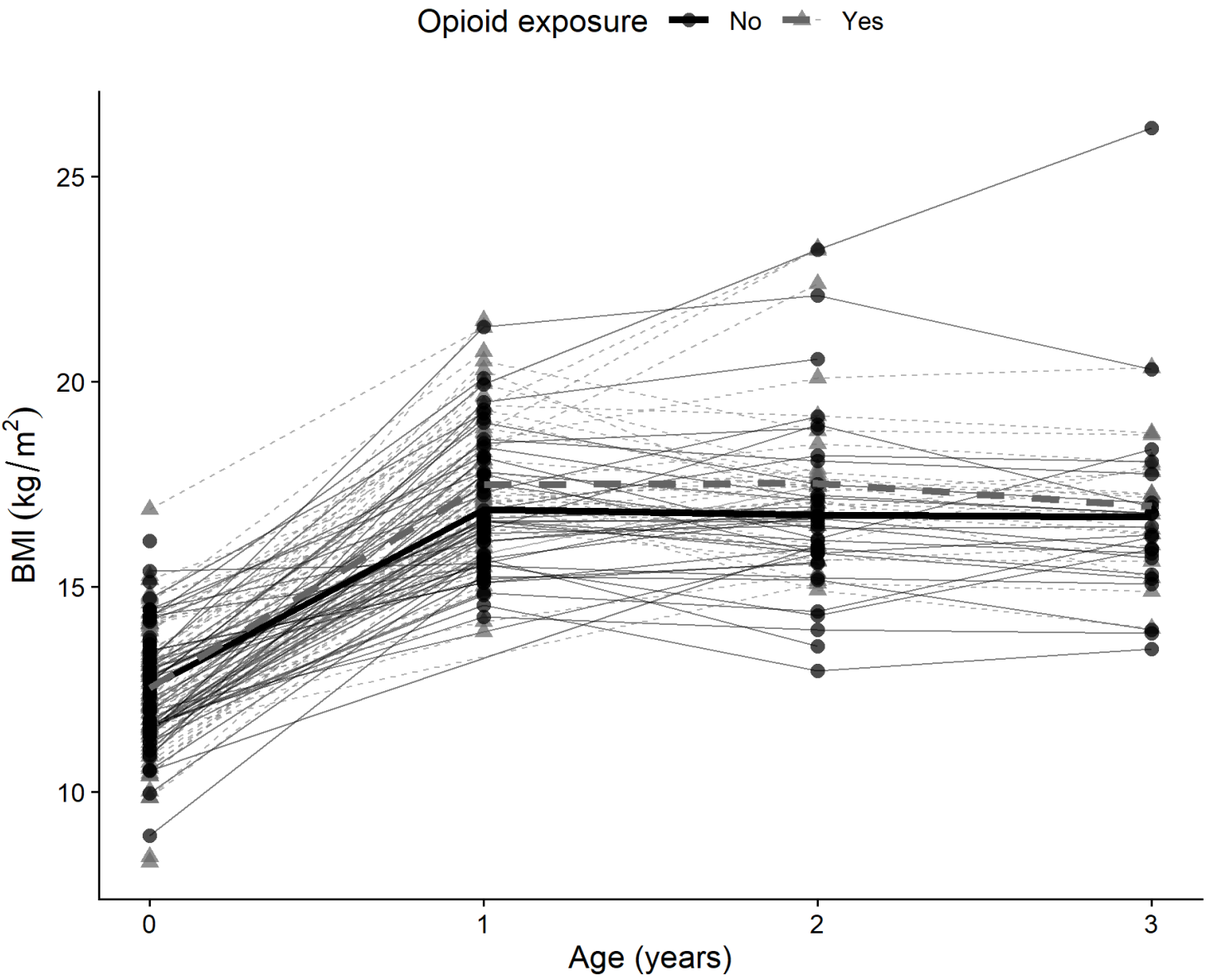

Figure 2

BMI trajectories from birth to age 3 by opioid exposure status. Each line represents BMI measurements for an individual infant over time. Opioid-exposed children are represented with red triangles and dotted lines, and non-exposed children are represented with blue circles and solid lines. Opioid-exposed children demonstrate a distinct growth pattern compared to non-exposed infants' growth pattern, with greater BMI slopes over the first 3 years. The thick dotted and solid lines represent the average BMI trajectories for opioid-exposed and non-opioid-exposed children, respectively.

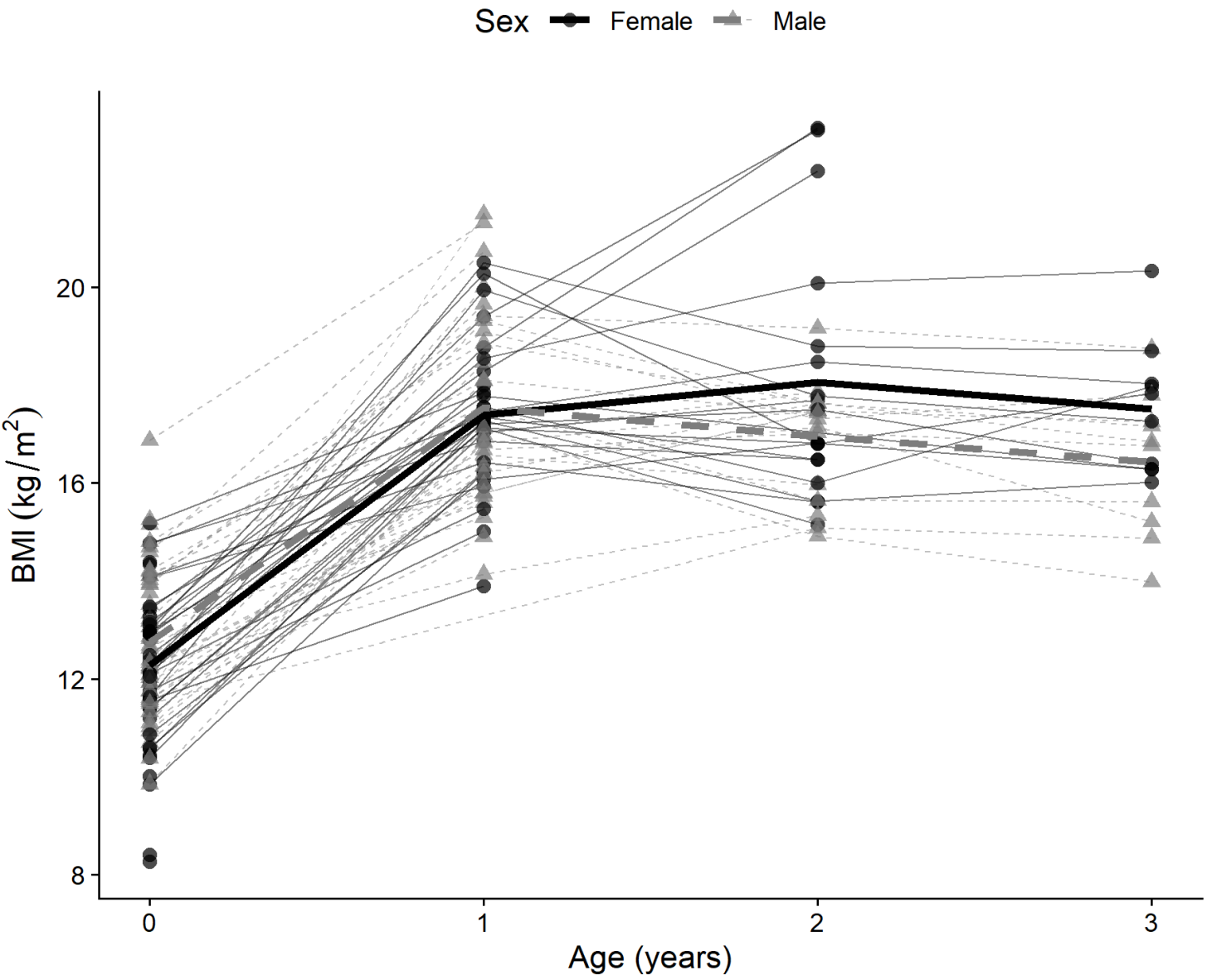

Figure 3

Sex-specific BMI trajectories from birth to age 3 in opioid-exposed infants. Each line represents BMI measurements for an individual infant over time. Opioid-exposed female infants are represented by red circles and solid lines, and opioid-exposed male infants are represented by blue triangles and dotted lines. Opioid-exposed males had higher BMI at birth but had a slower increase in BMI over the first 3 years compared to opioid-exposed females. The thick dotted and solid lines represent the average BMI trajectories for opioid-exposed males and non-opioid-exposed females, respectively.