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Body composition during the first 4 months in infants affected by neonatal abstinence syndrome: a pilot study

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Original Article

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Abstract

Newborns with neonatal abstinence syndrome (NAS) display symptoms related to neurologic excitability and autonomic dysfunction that result in increased metabolic demands. These infants also exhibit feeding difficulties and/or hyperphagia. Because the effects of these symptoms and behaviors on growth are unknown, we sought to measure serial body composition measurements over the first 4 months in infants with NAS requiring pharmacologic treatment using air displacement plethysmography. Fourteen infants of singleton birth with appropriate-for-gestational-age (AGA) weight and a gestational age of ≥35 weeks and <42 weeks were evaluated. In mixed-effects models, per week, infants increased in mean fat percent by 1.1% (95% confidence interval [CI]: 0.85–1.43), fat mass by 90 g (CI: 70–100), and fat-free mass by 140 g (CI: 130–150). The subgroup of infants ($N = 5$) requiring multidrug therapy for symptom control had lower mean fat percent (−1.2%, CI: −5.2–2.1), fat mass (−60 g, CI: −25–13), and fat-free mass (−270 g, CI: −610–80) across time compared to infants requiring monotherapy. We are the first to report how body composition measures change over time in a small group of patients with NAS. Infants with NAS were smaller and leaner in the first several weeks compared to previously reported body composition measurements in term infants, but grew similarly to their healthy counterparts by 16 weeks. Infants with more severe NAS may be at risk for abnormalities in longer term growth.

Introduction

Neonatal abstinence syndrome (NAS) remains a global public health problem.[1–5] Newborns with NAS display symptoms such as hypertonicity and tremors, hyperthermia, persistent crying, and prolonged awake time related to autonomic instability and neurologic excitability.[6] These symptoms, combined with poor feeding, emesis, and loose stools may lead to weight loss,[7,8] hyperphagia,[9] or even increased enteral intake with excessive weight gain.[10]

As infants with a history of NAS move beyond the newborn period, little is known about the long-standing effects earlier established feeding behaviors have on subsequent growth, particularly as the symptoms of withdrawal resolve.[11,12] Though infants have a natural ability to regulate their caloric intake,[13,14] feeding behaviors can be modified by caregiver feeding habits and influence weight gain.[15] Initial hyperphagia along with a caretaker's propensity to comfort feed these characteristically irritable infants may affect the long-term feeding habits and qualitative growth of an infant with NAS. Thus, in this pilot study, we sought to use air displacement plethysmography to obtain serial body composition measurements, including percent body fat, fat mass, and fat-free mass, over the first 4 months in infants affected by NAS.

Methods

Design

Infants with a diagnosis of NAS requiring pharmacologic treatment were recruited from the Penn State Milton S. Hershey Medical Center (HMC; Hershey, PA, USA) between January 2016 and July 2018. HMC is a tertiary care, academic institution with a level IV neonatal intensive care unit (NICU) and an active maternal–fetal medicine program. Infant body composition measurements including fat percent, fat-free mass percent, fat mass, fat-free mass, body mass, body volume, and body density were obtained weekly using the whole-body air displacement plethysmography machine, PEA POD (COSMED, Rome, Italy), in addition to standard growth measurements including weight, length, and head circumference. Air displacement plethysmography measurements, which have strong reliability, reproducibility, and validity in infants,[16–18] were obtained by trained pediatric research nurses weekly until patient discharge, and then again at 2 months and 4 months after birth. The research nurses received in-person, on-site

training by a COSMED representative to ensure competence in the use of the PEA POD machine, and each member demonstrated aptitude in the technology at the completion of the training. Body composition measurements were not obtained beyond 4 months as the PEA POD is limited to infants ≤8 kg, and babies beyond this age are more likely to surpass this weight limit.

Data extracted from the electronic medical record (EMR) for the infant included demographic information, birth weight, birth length, results of meconium drug screening, daily vital signs, Finnegan scores, type of pharmacologic treatment, and breast-feeding frequency. Maternal data extracted from the EMR included maternal health and demographic information as well as licit and illicit drugs used during pregnancy. Data regarding the mother's health, medication use, illicit drug use, and socioeconomic status were also collected using a questionnaire at the time of enrollment. Additional information on infant feeding was obtained via a follow-up questionnaire at 1 week after discharge, and 2 months and 4 months after birth.

Participants

Study participation was limited to infants of singleton birth with an appropriate-for-gestational-age (AGA) weight and a gestational age of ≥35 weeks and <42 weeks who were admitted to the NICU with a diagnosis of NAS requiring pharmacological therapy for symptom control. Over the past 4 years, our institution has treated 43%–60% of infants admitted for observation of NAS with medications. The need for pharmacologic treatment was defined by three consecutive Finnegan scores > 8 or a sum of three consecutive Finnegan scores > 24 on the Modified Finnegan Scoring Scale. While it has been established that late preterm or early term infants are at risk for differences in growth,[19] infants of 35–36 weeks completed gestational age were included because infants with *in utero* drug exposure are at greater risk for premature birth.[6,20,21] Thus, their exclusion would eliminate an important subset of the study population. Subjects with congenital malformations, known chromosomal abnormalities, endocrinological disorders, or infants of diabetic mothers were excluded due to the influence these disorders can have on growth. Informed parental consent was obtained for each mother–infant pair. Study approval was obtained from the Penn State College of Medicine Institutional Review Board.

Data analysis

Descriptive statistics (medians and interquartile ranges for continuous variables and frequency counts and percentages for categorical variables) were reported for patient characteristics. For measurements of growth, obvious errors for fat mass (<0.03%), length (<35.7 cm), and head circumference (>50 cm) were set to missing. Body composition measures were modeled using mixed-effects regression models. For each measure, we fit two models. The first model included time after birth as a linear fixed effect and random intercept and slope effects for each infant. The second model included an additional fixed effect for the most severely symptomatic infants, defined as those requiring adjuvant pharmacotherapy in addition to morphine for symptom control, compared to less severe infants that required only morphine. Given the small sample size, we were unable to include additional variables, such as gestational age, in the models in order to retain the primary focus on growth patterns over time.

Table 1. Demographic and birth characteristics of infants with NAS[a]

Variable	Total (%) ($N = 14$)
Sex	
Male	10 (71%)
Female	4 (29%)
Gestational age (weeks)	
Median (Interquartile range)	39.2 (38.4–40.0)
Birth weight (kg)	
Median (Interquartile range)	2.933 (2.690–3.296)
Birth length (cm)	
Median (Interquartile range)	49.0 (47.0–51.5)
Type of delivery	
Vaginal	8 (57%)
Cesarean	6 (43%)
Total length of stay (days)	
Median (Interquartile range)	25 (21–58)
Total length of pharmacologic treatment (days)	
Median (Interquartile range)	23 (17–54)
Meconium toxicology results[b]	
Buprenorphine	2 (14%)
Methadone	9 (64%)
Opiates	4 (29%)
Cannabinoids	4 (29%)
Missing	1 (7%)
Maternal licit opioid use[c]	
Buprenorphine	2 (14%)
Methadone	9 (64%)
Prescribed opioid	1 (7%)
None	2 (14%)

[a]NAS, Neonatal abstinence syndrome.
[b]Toxicology results are not mutually exclusive categories and a subject may have positive results in more than one category.
[c]Percentages may not add to 100 secondary to rounding.

Results

A total of 14 newborns met the inclusion criteria for the study. The majority were male (71%), and the median gestational age was 39.2 weeks (range: 35.0–41.0). The median birth weight and length were 2.933 kg and 49.0 cm, respectively. Infants had a median length of stay of 25 days. All mothers had opioid exposure. Eleven (79%) mothers were receiving an opioid replacement therapy, one mother was taking a prescribed opioid, and two mothers had no record of provider-directed opioid use. Consistent with maternal history, 11 (79%) infant meconium drug screens were positive for buprenorphine or methadone, while an additional 8 (57%) infants had drug screens positive for opiates or cannabinoids (Table 1). On an administered, health-related questionnaire, eight mothers (57%) admitted to illegal drug use during pregnancy, two mothers denied illegal drug use, and four mothers declined to answer. Maternal medical records indicate the use of heroin by four

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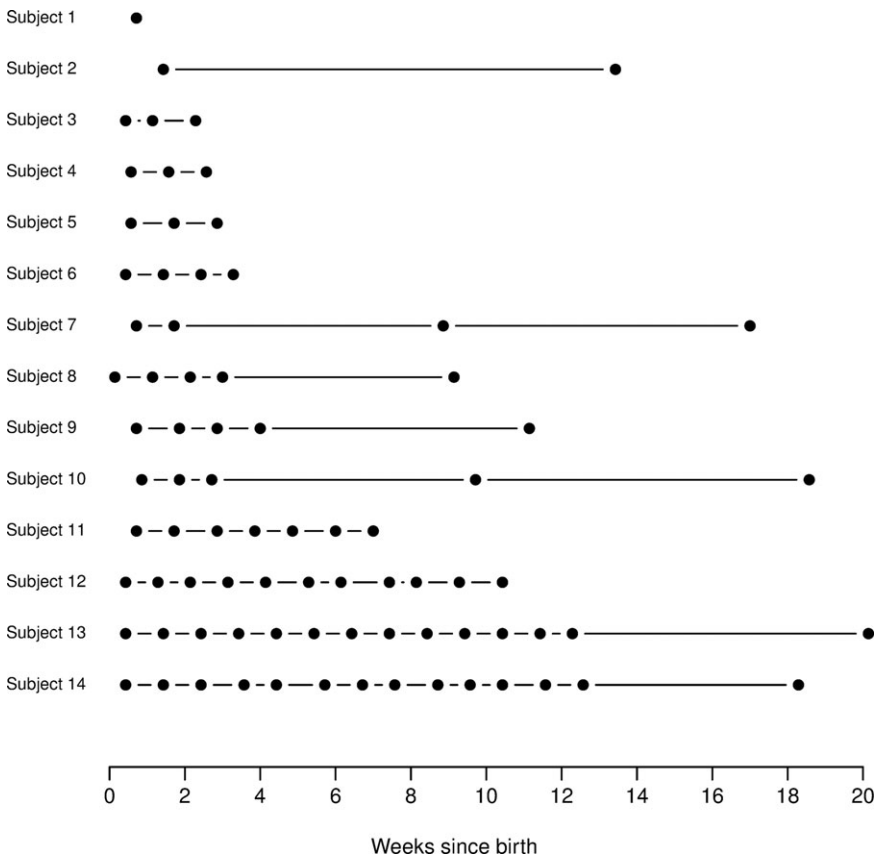

Fig. 1. Timing of body plethysmography measurements for each patient. Patients are ordered top to bottom by the number of measurements obtained.

women, marijuana by two women, and cocaine by one woman. Of women with a diagnosed substance use disorder, four (31%) mothers were converted to medication-assisted treatment of their addiction during pregnancy, seven (54%) mothers were on medication-assisted treatment prior to pregnancy, and two (15%) mothers received no opioid replacement therapy. Twelve (86%) mothers used nicotine or admitted to smoking during the pregnancy.

Four out of the 10 mothers who completed a demographic questionnaire indicated they were married, 3 were living with a partner, 1 was single, and 2 were divorced. The majority of mothers were insured by Medicaid (90%) and the remaining 10% were uncertain of their insurance status. Ninety percent of women indicated they were unemployed during their pregnancy. Fifty percent of mothers did not know their annual household income prior to taxes, and of the remaining 50%, four out of the five made less than $50,000 per year.

The majority of infants participated in some breastfeeding (71%). There was no association between the amount of breastfeeding during the birth hospitalization (never breastfed [$N = 5$], breastfed <50% of days [$N = 5$], and breastfed >90% of days [$N = 4$]) and body plethysmography measurements. On a follow-up questionnaire administered 1 week after discharge ($N = 4$), at 2 months ($N = 6$), and at 4 months ($N = 4$), one, three, and one of the infants, respectively, were still breastfeeding. None of the infants in the study exclusively breastfed. Post-hospitalization, infants consumed 3–10 bottles of breastmilk or formula per day with each bottle containing 2–8 oz. Two out of the four mothers were questioned at 1 week after discharge and were urging their infant to finish a bottle if not entirely consumed, but at 4 months of age, none of the mothers were encouraging completion of the bottle.

No infants were receiving solid food at 2 months of age. At 4 months old, cereal was introduced to two of the four infants and beverages other than breastmilk or formula to one of the four infants of mothers surveyed. At 1 week after discharge, 2 months, and 4 months, two of the four, five of the six, and four of the four mothers, respectively, noted that they let their baby determine how much to eat "most of the time" or "always". Overall, mothers felt their infant was content while feeding with 100% answering "often" or "always" to the inquiry at 1 week after discharge and 2 months of age, and two of the three answering affirmatively at 4 months.

Of the 81 air displacement plethysmography measurements obtained over 4 months, 45 (56%) of the measurements were obtained in the first 30 days, and infants had a mean of 5.8 plethysmography measurements (range of 1–14 measurements) during the study (Fig. 1). Individual trajectories of specific growth parameters for each infant along with the mean estimates from fitted mixed-effects regression models that included time as a predictor are shown in Fig. 2. The mean estimates from the model (reported to the nearest tens) for fat mass were 560 g, 900 g, 1240 g, and 1580 g at weeks 4, 8, 12, and 16, respectively, while mean estimates for fat-free mass were 3000, 3600, 4100, and 4700 g at the same time points (Table 2). These changes in mass resulted in an increase in the mean estimate of fat percent from 14.3% in week 4–27.6% in week 16. Parameter estimates (slopes) from the models show that infants had a weekly mean increase (95% confidence interval [CI]) in fat percent of 1.1% (0.8%–1.4%), fat mass of 90 g (70–100 g), and fat-free mass of 140 g per week (130–150 g).

Fig. 3 shows individual trajectories of specific growth parameters for the most severely symptomatic infants, defined as those requiring adjuvant pharmacotherapy in addition to morphine

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Table 2. Mean estimates (95% CI[a]) at specific time points from fitted mixed-effects regression models fit to each outcome

Outcome	Week 4	Week 8	Week 12	Week 16
Fat %	14 (12.7–15.7)	19 (16.7–20.5)	23 (21.1–25.3)	28 (24.5–31.3)
Fat mass (kg)	0.5 (0.49–0.63)	0.9 (0.80–1.01)	1.2 (1.10–1.38)	1.6 (1.39–1.77)
Fat-free mass (kg)	3.0 (2.9–3.2)	3.6 (3.4–3.7)	4.1 (3.9–4.3)	4.7 (4.5–4.9)
Length (cm)	52 (51.3–53.6)	56 (54.8–57.1)	59 (58.1–59.8)	62 (61.2–62.9)
Head circumference (cm)	36 (34.9–36.0)	38 (36.9–38.1)	40 (38.8–40.1)	42 (40.9–42.4)
Body mass (kg)	3.6 (3.4–3.8)	4.5 (4.3–4.7)	5.4 (5.1–5.7)	6.3 (6.0–6.7)
Body density (kg/m3)	1.0 (1.03–1.05)	1.0 (1.02–1.04)	1.0 (1.01–1.03)	1.0 (1.00–1.02)

[a]Confidence interval.

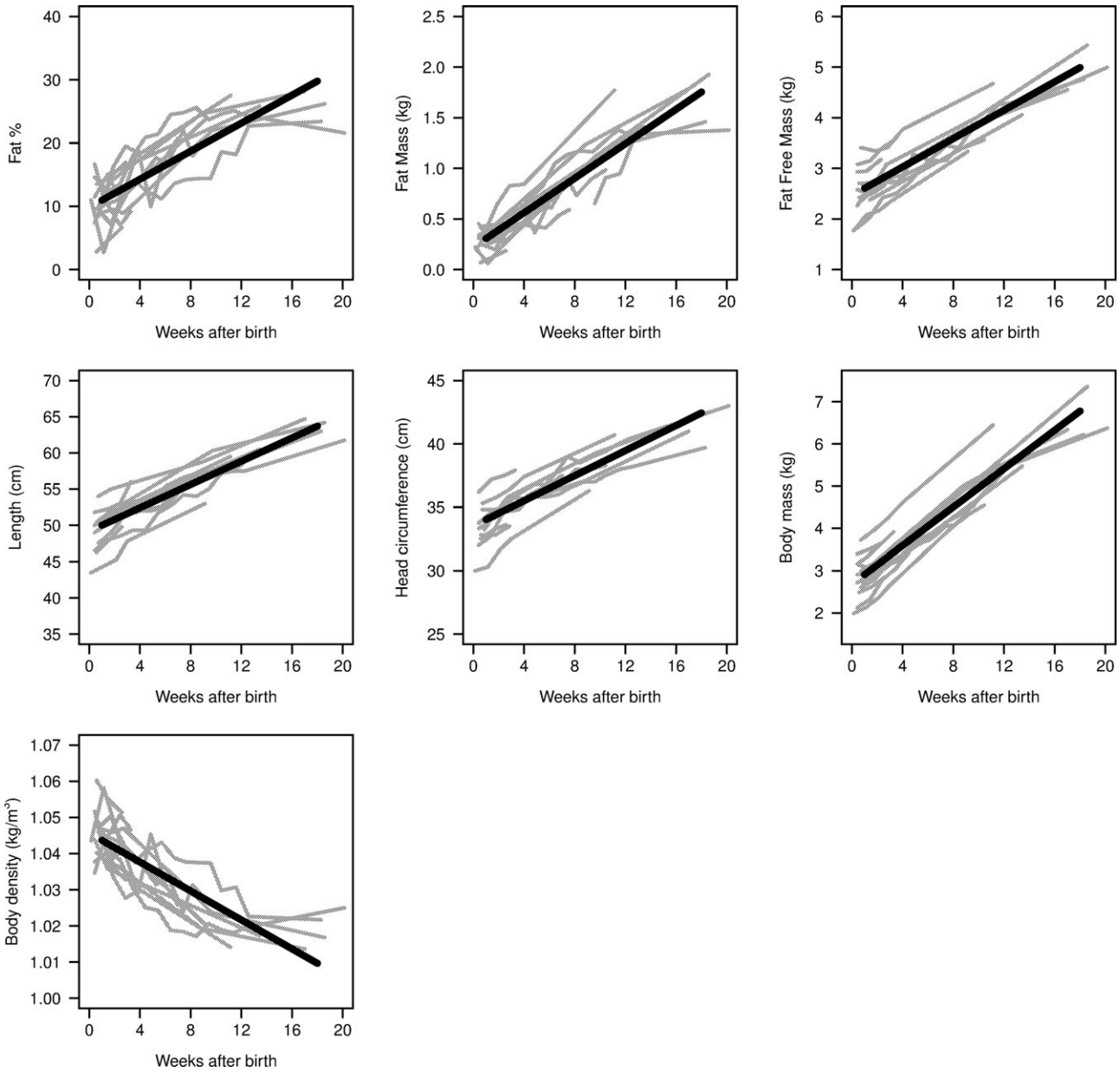

Fig. 2. Individual trajectories (gray lines) of all body composition measurements by weeks after birth. Black overlaid line represents the mean estimate from a fitted regression model.

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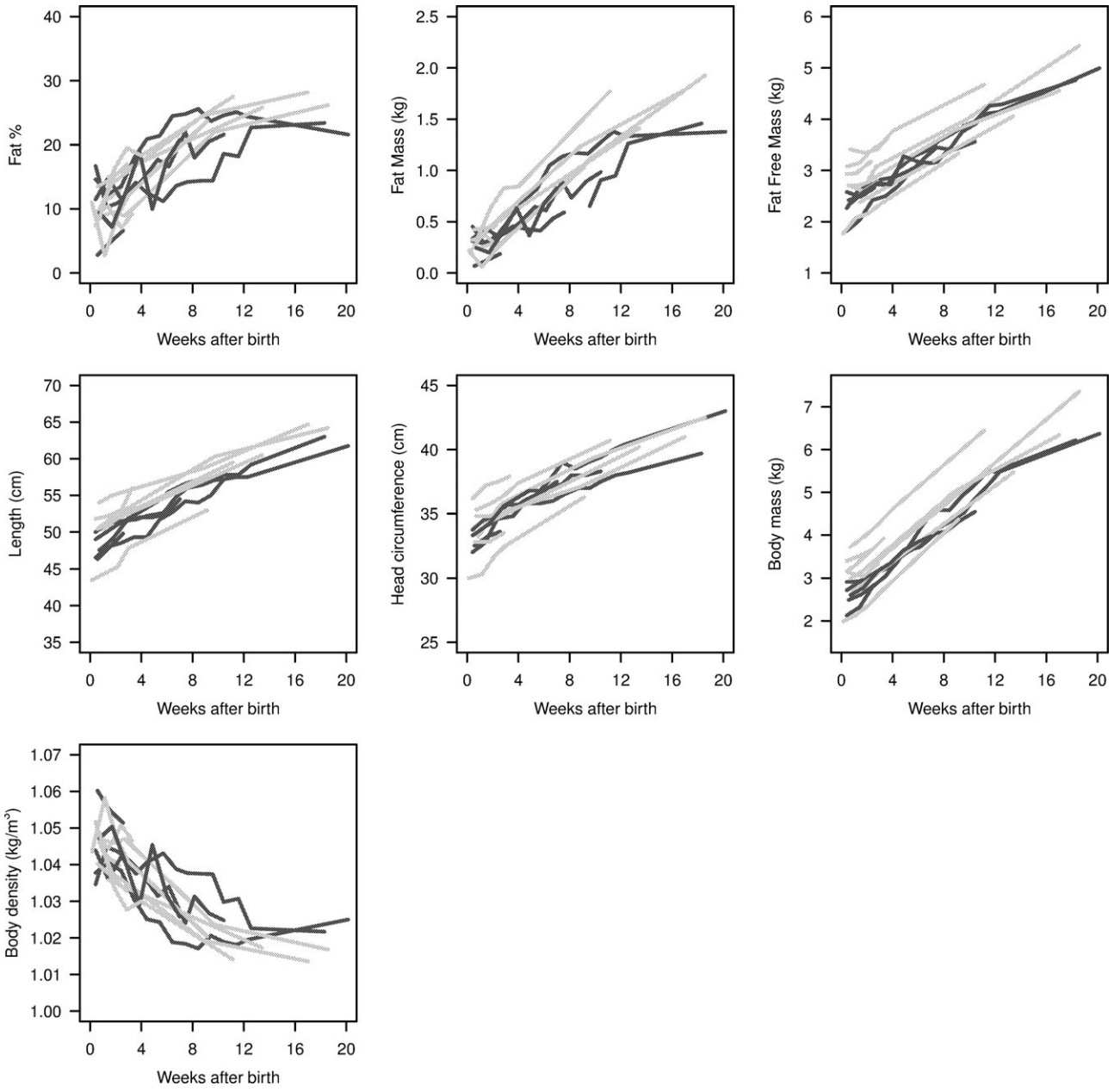

Fig. 3. Individual trajectories for each body composition measurement stratified by pharmacologic treatment received. Black lines indicate patients who received morphine plus and adjuvant medication (clonidine or phenobarbital) and gray lines indicate patients who received morphine only.

for symptom control, compared to less symptomatic infants requiring morphine only. Fig. 4 displays the mean Finnegan scores over time. Infants meeting the definition of severe NAS had, on average, longer lengths of hospital admission for monitoring and treatment of their symptoms (Fig. 4). In a mixed-effects model that included time and pharmacotherapy, infants requiring multi-drug therapy for symptom control had lower mean fat percent (95% CI) of −1.2% (−5.2–2.1%), fat mass (−60 g, −250–130 g), and fat-free mass (−270 g, 610–80 g) across time compared to infants requiring morphine only (Table 3).

Discussion

This pilot study is the first to report serial air displacement plethysmography measurements for infants affected by NAS. We found that infants with NAS had a tendency to be smaller and leaner in the first several weeks compared to other studies evaluating serial body composition measurements in term infants.[22–24] For example, at 4 weeks, Breij demonstrated a mean body mass of 4.3 kg and fat-free mass of 3.6 kg in a cohort of healthy term infants[22] compared to our mean estimates of 3.6 kg and 3.0 kg, respectively. At 12 weeks, our infants again appeared to be slightly smaller than their non-affected counterparts with our mean estimates showing a body mass of 5.4 kg and a fat-free mass of 4.1 kg compared to healthy term equivalent values of 6.0–6.1 kg and 4.5–4.6 kg, respectively.[22,23] However, by 16 weeks, infants with NAS had measurements that were similar to term counterparts in other studies. For example, our mean estimate of body mass was 6.3 kg and fat-free mass 4.7 kg compared to 6.2 kg and 4.7 kg in non-affected term infants.[23] While these values

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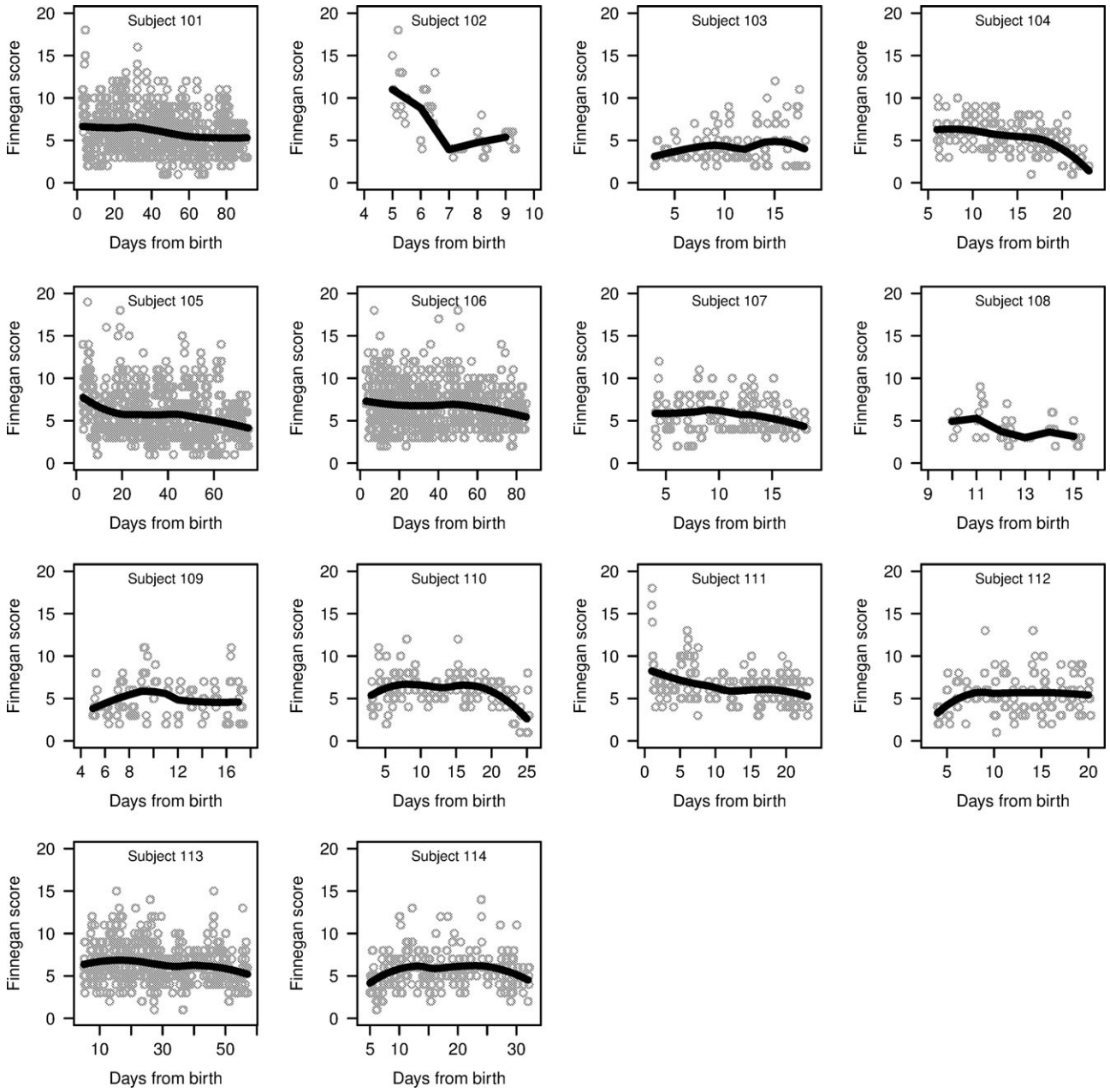

Fig. 4. Finnegan scores for all patients. Black lines show the mean scores over time. Subjects 101, 105, 106, 107, and 113 received adjuvant pharmacotherapy in addition to morphine to control their symptoms. *Note the change in *x*-axis for each patient.

provide direction for contrast, direct comparison is made difficult by variable timing of measurement capture in related studies, which did not always align with our own.

When comparing measurements within our study, we found that infants who required adjuvant mediations to control symptoms of withdrawal had lower mean fat percent, fat mass, and fat-free mass over time compared to less severely affected infants requiring single-agent therapy. These findings require further evaluation as, if confirmed, they raise concerns that this particular subset of infants may be at risk for insufficient or abnormal growth that continues well into the first year after birth.

Our overall results are consistent with our previous study that showed similar weight gain over the first year of life between infants affected by NAS and their matched counterparts.[11] However, this previous study also demonstrated nonsignificantly greater variation in growth with lower 10th and higher 90th percentile estimates in children with NAS, particularly toward the last quarter of the first year. Thus, it is possible differences in body composition exist in infants with NAS that were not captured in the limited 4-month evaluation. Further providing support for this theory is the observation that infants with NAS seem to be smaller and leaner than term equivalents in the literature during the first few weeks of life, but this difference appeared to resolve with time with nearly identical body mass measurements at 4 months of age. This finding may indicate a rapid increase in body mass and crossing of growth percentiles in infants with NAS as time progresses and the hypermetabolic state of withdrawal resolves, a pattern that would place them at risk for obesity if persistent.

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Table 3. Parameter estimates from fitted mixed-effects regression model for time and drug treatment category (morphine alone vs. morphine plus adjuvant drug therapy)

Outcome	Parameter	Estimate (SE[a])	95% CI[b]
Fat %	Time, 1-week increase	1.10 (0.12)	(0.85, −1.43)
	Morphine plus other drugs	−1.20 (1.63)	(−5.17, 2.08)
Fat mass (kg)	Time, 1-week increase	0.09 (0.01)	(0.07, 0.10)
	Morphine plus other drugs	−0.06 (0.07)	(−0.25, 0.13)
Fat-free mass (kg)	Time, 1-week increase	0.14 (0.01)	(0.13, 0.15)
	Morphine plus other drugs	−0.27 (0.18)	(−0.61, 0.08)
Length (cm)	Time, 1-week increase	0.81 (0.03)	(0.75, 0.89)
	Morphine plus other drugs	−1.56 (0.78)	(−3.07, 0.07)
Head circumference (cm)	Time, 1-week increase	0.50 (0.03)	(0.43, 0.57)
	Morphine plus other drugs	−0.34 (0.70)	(−1.71, 1.01)
Body mass (kg)	Time, 1-week increase	0.23 (0.01)	(0.21, 0.25)
	Morphine plus other drugs	−0.40 (0.22)	(−0.85, 0.05)
Body density (kg/m3)	Time, 1-week increase	−0.002 (0.0001)	(−0.003, −0.001)
	Morphine plus other drugs	0.002 (0.003)	(−0.004, 0.009)

[a]Standard error.
[b]Confidence interval.

Growth in childhood is a complicated, multifaceted process shaped by caloric intake, nutrient consumption, genetics, the environment, and overall health. In the newborn period, infants affected by NAS are unique in their nutritional requirements. They are more commonly born growth restricted or small for gestational age, particularly if the pregnancy is complicated by illegal substance use and lack of medication-assisted treatment.[25,26] Early symptoms of withdrawal lead to a hypermetabolic state, which combined with symptoms of poor and uncoordinated feeding, place these infants at risk for excessive weight loss in the days following birth.[7,8] While the newborn may compensate for these conditions by increased intake,[9] our study suggests that infants with more severe NAS may not be able to effectively overcome this challenge. Indeed, differences in growth may continue beyond infancy, affecting the ultimate growth trajectory of the child. Future research, using a larger sample, may clarify whether differences in growth exist between patients most severely affected by NAS and their more-mildly affected counterparts so that potential differences in nutritional requirements and feeding patterns may be appropriately addressed.

The effects of early established feeding habits on long-term degree and quality of growth in infants with NAS is poorly understood. Evidence suggests that early feeding behaviors influence eating habits and weight in childhood,[27,28] and neonatal adiposity has been significantly associated with childhood obesity.[29] Infants have an innate ability to regulate their caloric intake.[13,14] However, this concept may not retain validity in infants affected by NAS given their early, hypermetabolic state and characteristic symptoms related to withdrawal such as excessive or uncoordinated sucking, poor feeding, regurgitation and emesis, and frequent, loose stools. In addition, caregiver feeding practices may also alter intake. Specifically, caregivers may respond to symptoms of excessive irritability and sucking by feeding the infant in an effort to soothe. Because parental feeding practices can modify eating behavior and affect subsequent weight gain and growth,[15] infants most severely affected by NAS may also be at increased risk for abnormal weight gain and obesity into later infancy, particularly as the early symptoms of withdrawal subside. Indeed, our results suggest the presence of inappropriate feeding practices within our study subjects, with parental reports of their infant consuming up to 10 daily bottles and 8 ounces or more at a feed 1week following discharge. These findings along with documentation of parental belief that "crying usually indicates an infant needs to be fed" support the idea that some caregivers may be using feeding as a method to comfort their baby. By confirming the existence of differences in feeding practices and weight gain in this specific population, targeted interventions can be proactively implemented early in infancy to prevent aberrant growth and promote health. Specifically, promotion of maternal breastfeeding, caregiver instruction on correct bottle-feeding behaviors, and parental training in appropriate soothing methods are evidence-based strategies to prevent obesity.[30]

There are several limitations to our study. Because it is a pilot study with a small sample size, the CI are wide and definitive conclusions cannot be drawn. However, the study raises interesting questions about abnormalities in growth in infants most severely affected by NAS and provides preliminary data for a larger, future study. The study is also limited by progressive loss of follow-up with only 44% of the PEA POD measurements occurring beyond 30 days. In future studies, less frequent visits may aid in a caregiver's and infant's ability to take part in serial body composition measurements over time. Additionally, the sample size did not allow the inclusion of other variables such as gestational age in the models. However, 13 of the 14 subjects (93%) were term (37–41 weeks) and the individual slopes over time were generally similar, suggesting that adjustment for gestational age would not substantially affect growth estimates, but this limitation further supports the need for evaluation in a larger study. Finally, the lack of normal controls hinders the ability to make comparisons.

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Conclusion

This study is the first to describe serial body composition measurements in infants with NAS. While values of fat percent, fat mass, and fat-free mass at 4 months were similar to previously reported measurements in term infants, infants with NAS were smaller and leaner than healthy term infants in the literature over the first several weeks of life, and a subset of infants with more severe NAS had lower values over time. These observations indicate infants with NAS may be at risk for abnormalities in longer term growth.

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Conflicts of interest. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation established by the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the Penn State College of Medicine Institutional Review Board.

References

1. Corr TE, Hollenbeak CS. The economic burden of neonatal abstinence syndrome in the United States. *Addiction.* 2017; 112, 1590–1599.
2. Kocherlakota P. Neonatal abstinence syndrome. *Pediatrics.* 2014; 134, e547–e561.
3. Patrick SW, Davis MM, Lehmann CU, Cooper WO. Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012. *J Perinatol.* 2015; 35, 650–655.
4. Winkelman TNA, Villapiano N, Kozhimannil KB, Davis MM, Patrick SW. Incidence and costs of neonatal abstinence syndrome among infants with Medicaid: 2004–2014. *Pediatrics.* 2018; 141, e20173520.
5. Ramphul K, Mejias SG, Joynauth J. An update on the burden of neonatal abstinence syndrome in the United States. *Hosp Pediatr.* 2020; 10, 181–184.
6. Hudak ML, Tan RC. Neonatal drug withdrawal. *Pediatrics.* 2012; 129, e540–e560.
7. Dryden C, Young D, Campbell N, Mactier H. Postnatal weight loss in substitute methadone-exposed infants: implications for the management of breast feeding. *Arch Dis Child Fetal Neonatal Ed.* 2012; 97, F214–F216.
8. Weinberger SM, Kandall SR, Doberczak TM, Thornton JC, Bernstein J. Early weight-change patterns in neonatal abstinence. *Am J Dis Child.* 1986; 140, 829–832.
9. Martinez A, Kastner B, Taeusch HW. Hyperphagia in neonates withdrawing from methadone. *Arch Dis Child Fetal Neonatal Ed.* 1999; 80, F178–F182.
10. Shephard R, Greenough A, Johnson K, Gerada C. Hyperphagia, weight gain and neonatal drug withdrawal. *Acta Paediatr.* 2002; 91, 951–953.
11. Corr TE, Schaefer EW, Paul IM. Growth during the first year in infants affected by neonatal abstinence syndrome. *BMC Pediatr.* 2018; 18, 343–350.
12. Vance JC, Chant DC, Tudehope DI, Gray PH, Hayes AJ. Infants born to narcotic dependent mothers: physical growth patterns in the first 12 months of life. *J Paediatr Child Health.* 1997; 33, 504–508.
13. Cohen RJ, Brown KH, Canahuati J, Rivera LL, Dewey KG. Effects of age of introduction of complementary foods on infant breast milk intake, total energy intake, and growth: a randomised intervention study in Honduras. *Lancet.* 1994; 344, 288–293.
14. Fomon SJ, Filer LJ, Jr., Thomas LN, Rogers RR, Proksch AM. Relationship between formula concentration and rate of growth of normal infants. *J Nutr.* 1969; 98, 241–254.
15. Paul IM, Bartok CJ, Downs DS, Stifter CA, Ventura AK, Birch LL. Opportunities for the primary prevention of obesity during infancy. *Adv Pediatr.* 2009; 56, 107–133.
16. Yao M, Nommsen-Rivers L, Dewey K, Urlando A. Preliminary evaluation of a new pediatric air displacement plethysmograph for body composition assessment in infants. *Acta Diabetol.* 2003; 40(Suppl 1), S55–S58.
17. Ma G, Yao M, Liu Y, *et al.* Validation of a new pediatric air-displacement plethysmograph for assessing body composition in infants. *Am J Clin Nutr.* 2004; 79, 653–660.
18. Ellis KJ, Yao M, Shypailo RJ, Urlando A, Wong WW, Heird WC. Body-composition assessment in infancy: air-displacement plethysmography compared with a reference 4-compartment model. *Am J Clin Nutr.* 2007; 85, 90–95.
19. Stewart DL, Barfield WD. Updates on an at-risk population: late-preterm and early-term infants. *Pediatrics.* 2019; 144, 2760–2769.
20. Patrick SW, Dudley J, Martin PR, *et al.* Prescription opioid epidemic and infant outcomes. *Pediatrics.* 2015; 135, 842–850.
21. Whiteman VE, Salemi JL, Mogos MF, Cain MA, Aliyu MH, Salihu HM. Maternal opioid drug use during pregnancy and its impact on perinatal morbidity, mortality, and the costs of medical care in the United States. *J Pregnancy.* 2014; 2014, 1–8.
22. Breij LM, Kerkhof GF, De Lucia Rolfe E, *et al.* Longitudinal fat mass and visceral fat during the first 6 months after birth in healthy infants: support for a critical window for adiposity in early life. *Pediatr Obes.* 2017; 12, 286–294.
23. Eriksson B, Löf M, Forsum E. Body composition in full-term healthy infants measured with air displacement plethysmography at 1 and 12 weeks of age. *Acta Paediatr.* 2010; 99, 563–568.
24. Ramel SE, Gray HL, Ode KL, Younge N, Georgieff MK, Demerath EW. Body composition changes in preterm infants following hospital discharge: comparison with term infants. *J Pediatr Gastroenterol Nutr.* 2011; 53, 333–338.
25. Buckley V, Razaghi A, Haber P. Predictors of neonatal outcomes amongst a methadone- and/or heroin-dependent population referred to a multidisciplinary Perinatal and Family Drug Health Service. *Aust N Z J Obstet Gynaecol.* 2013; 53, 464–470.
26. Mary Beth Sutter, Sarah Gopman, Lawrence Leeman. Patient-centered care to address barriers for pregnant women with opioid dependence. *Obstet Gynecol Clin North Am.* 2017; 44, 95–107.
27. Davison KK, Birch LL. Childhood overweight: a contextual model and recommendations for future research. *Obes Rev.* 2001; 2, 159–171.
28. Savage JS, Fisher JO, Birch LL. Parental influence on eating behavior: conception to adolescence. *J Law Med Ethics.* 2007; 35, 22–34.
29. Moore BF, Harrall KK, Sauder KA, Glueck DH, Dabelea D. Neonatal adiposity and childhood obesity. *Pediatrics.* 2020; 146, e20200737.
30. Paul IM, Bartok CJ, Downs DS, Stifter CA, Ventura AK, Birch LL. Opportunities for the primary prevention of obesity during infancy. *Adv Pediatr.* 2009; 56, 107–133.