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Anthropometric models to estimate fat mass at 3 days, 15 and 54 weeks

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Summary

Background: Currently available infant body composition measurement methods are impractical for routine clinical use. The study developed anthropometric equations (AEs) to estimate fat mass (FM, kg) during the first year using air displacement plethysmography (PEA POD® Infant Body Composition System) and Infant quantitative magnetic resonance (Infant-QMR) as criterion methods.

Methods: Multi-ethnic full-term infants ($n = 191$) were measured at 3 days, 15 and 54 weeks. Sex, race/ethnicity, gestational age, age (days), weight-kg (W), length-cm (L), head circumferences-cm (HC), skinfold thicknesses mm [triceps (TRI), thigh (THI), subscapular (SCP), and iliac (IL)], and FM by PEA POD® and Infant-QMR were collected. Stepwise linear regression determined the model that best predicted FM.

Results: Weight, length, head circumference, and skinfolds of triceps, thigh, and subscapular, but not iliac, significantly predicted FM throughout infancy in both the Infant-QMR and PEA POD models. Sex had an interaction effect at 3 days and 15 weeks for both the models.

The coefficient of determination [R^2] and root mean square error were 0.87 (66 g) at 3 days, 0.92 (153 g) at 15 weeks, and 0.82 (278 g) at 54 weeks for the Infant-QMR models; 0.77 (80 g) at 3 days and 0.82 (195 g) at 15 weeks for the PEA POD models respectively.

Conclusions: Both PEA POD and Infant-QMR derived models predict FM using skinfolds, weight, head circumference, and length with acceptable R^2 and residual patterns.

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KEYWORDS
body composition, infancy, infant-QMR, pediatrics, PEAPOD

1 | INTRODUCTION

Body composition during infancy and early childhood has relevance in healthcare settings, clinical research, and national surveys and surveillance.[1] The information has potential to screen for current and future health risks, provide anticipatory guidance, monitor therapeutic progress, and tailor treatment as in precision medicine.[2] Longitudinal follow-up of fat mass (FM) through infancy and early childhood can aid in understanding its influence on general growth and development, and the risk for development of diseases in later life.[3,4] Currently validated and routinely used methods to measure FM such as air displacement plethysmography (ADP), dual-energy X-ray absorptiometry (DXA), and infant quantitative magnetic resonance (Infant-QMR) are expensive, often unavailable and, therefore, impractical for use in community and clinical settings, and in large-scale epidemiological field studies. Anthropometric measurements including weight, stature, skinfold thicknesses, and body circumferences can inform on elements of growth related to body composition.[5,6] They provide an easy, inexpensive, portable proxy for infant fat assessments in resource-limited settings, and a combination of these measures can be used to assess subcutaneous fat distribution variation in infants at the group level.[3,7]

FM can be estimated from anthropometric prediction equations developed using accurate body composition methods such as ADP, DXA, and QMR. Several anthropometric prediction equations are available for estimating FM, % fat mass (%FM), or fat-free mass (FFM) in children aged 3–18 years as described in a systematic review[8] with fewer equations during the first year of life and some specific to individual ethnic groups.[9,10] In infants, anthropometric equations have been developed against total body electrical conductivity (TOBEC),[11,12] ADP,[9,13–15] and DXA[16,17] with ADP being the most widely used for body fat prediction equations in the first week of life.

Validation studies by Cauble et al[18] showed poor agreement, accuracy, and precision for four[9,11,13,19] neonatal anthropometric equations using the criterion of ADP at birth and 3 months. Two FM prediction models with ADP as the criterion were developed in 349 infants, aged 1–3 days using weight, length, flank skinfold, and head circumference and compared with existing equations.[15] They reported reasonable accuracy for FM prediction by the Catalano (Lin's concordance correlation coefficient [CCC] 0.84) and Aris equation (Lin's CCC 0.81) at birth. FM prediction models with ADP as the criterion were developed in 278 white European Australian infants and reported poor agreement for %Fat with (1) Lingwood at birth (mean bias −0.32); (2) Aris at 3 (mean bias −3.45) and 6 months (mean bias 0.25 with wide limits of agreement); (3) Lingwood at 3 (mean bias −3.9) and 6 months (mean bias −3.7) against the ADP.[14] These results indicate the lack of a consistent anthropometric equation within the age range (0–3 days) in which the equation(s) were derived, and the lack of applicability of these 0–3-day equations to older aged infants at 3 and 6 months. Such inconsistencies are likely attributable to the rapid changes in FM and hydration during the early months of life, ethnic-specific differences in FM and FFM, and differences in the outcome variable across the anthropometric equations (FM, %FM, FFM). Furthermore, body composition data from multi-ethnic cohorts throughout infancy are lacking in the literature. The reader is referred to Table 1 for a list of published anthropometric equations frequently referenced in this manuscript.

The purpose of the current study was to develop anthropometric models to estimate FM from ADP (PEA POD®) and Infant-QMR (EchoMRI-Infant: Echo Medical Systems, Houston, Texas) in the same cohort with longitudinal assessments at ages 3 days, 15, and 54 weeks. These models, if validated, aim to serve as a research tool for FM assessments in similarly aged populations when more sophisticated body composition measurement methods are unavailable.

2 | METHODS

2.1 | Participants

Participants were offspring of mothers enrolled in the LIFT (Lifestyle Intervention for Two) trial as previously reported[20–22] on whom measures were acquired at three time points (Figure 1). LIFT is part of the LIFE-Moms consortium[23] and was a parallel-group, randomized controlled trial investigating the effects of a behavioural lifestyle intervention in pregnant women. Women were recruited from hospital-affiliated private and clinic practices from February 2013 to October 2015. Eligibility criteria included age ≥ 18 years, a BMI ≥25 at baseline measurement, singleton pregnancy, and gestational age between 9,0 (week, day) and 15,6 confirmed by dating ultrasound. Women diagnosed with seizures, hypertension, or pre-eclampsia were excluded in the LIFT study. The study was approved by the IRBs of St. Luke's-Roosevelt Hospital and Columbia University and registered with ClinicalTrials.gov (NCT01616147; www.ClinicalTrials.gov). A written consent was obtained from a parent prior to participation in the study. Infant race/ethnicity was based on maternal self-report of maternal race/ethnicity. The study was approved by and conducted in accordance with the Institutional Review Boards at St Luke's-Roosevelt Hospital and Columbia University Irving Medical Center. Race included the following categories: White, Black, Asian, other, and multiracial. Ethnicity was classified as Hispanic and non-Hispanic.

TABLE 1 Select published anthropometric equations based on TOBEC, ADP, and DXA

Reference and *N*	Population	BC method and dependent variable	Equation	R^2 and error
Catalano[12] *N* = 194 (D) 65 (V)	Two-thirds White, USA Day 0–72	TOBEC FM	FM = 0·54 657 + 0·39 055 × birth W (kg) − 0·03237 × birth L (cm) + 0·0453 × flank skinfold (mm).	$R^2 = 0.78$
De Bruin[13] *N* = 435 (D) 110 (V)	White, Netherlands Day 21–365	TOBEC FM and FFM	lnFM = −0.358 + 1.499[ln(W*calf circumference)/L] lnFM = −2.219 + 1.176[lnW*calf circumference* sq. root (sum of 3skinfolds/L)] lnFFM = 0.433 + 0.056[sq. root(W*L)]	$R^2 = 0.87$; SE 0.148 kg $R^2 = 0.89$; SE 0.138 kg $R^2 = 0.0.95$; SE 0.044 kg
Schmelzle[18] *N* = 185 (D)	White, Germany Day 10–4 months	DXA FM	FM (newborn) = 68.2 × SigmaSFT([0.0162] × l) − 172.8	$R^2 = 0.94$
Dung[17] *N* = 118 (D)	Preterm infants, at hospital discharge White, Germany	DXA and BIA FFM	Female FFM = $0.04Ht^2/I + 0.71$ W + 0.29 Male FFM = $0.05Ht^2/I + 0.68$ W + 0.40	$R^2 = 0.919$ $R^2 = 0.957$
Deierlein[14] *N* = 128 (D)	Multi-ethnic, USA, New York Term, Day 1–3	ADP FM	FM = −0.012–0.064*sex + 0.024*day of measurement post-delivery − 0.150*w (kg) + 0.055*w $(kg)^2$ + 0.046*ethnicity +0.020*sum of three skinfold thicknesses (triceps, sub scapular, and thigh)	$R^2 = 0.81$, MSE = 0.08 kg.
Aris[10] *N* = 88 (D) 62 (V)	Singaporean Term infants	ADP FM	FM = –0·022 + 0·307 × weight (kg) − 0·077 × (sex) + 0·028 × subscapular skinfold (mm) − 0·019 × gestational age (weeks) Sex: 1 male, 0 female	$R^2 = 0.81$
Lingwood[20] *N* = 77 (birth) *N* = 54 (6 weeks) *N* = 55 (3 months) *N* = 53 (4–5 months)	White, Australia Term, Day 0–4	ADP FFM	FFM (birth) = 0.507 + 0.646*W − 0.089*sex+0.009 L FFM (6 week) = 0.0260 + 0.528*W − 0.125*sex +0.022*L FFM (3 months) = −0.338 + 0.434*W − 0.177*sex +0.041*L FFM (4–5 months) = −0.044 + 0.397*W − 0.427*sex +0.045*L	R^2 (birth) = 94 R^2 (6 week) = 89 R^2 (3 months) = 89 R^2 (4–5 months) = 87
Josefson[16] N = 349 (D) 119 (V)	Multi-ethnic, USA 12–72 h of life	ADP FM	M0 FM = 0.54657 + 0.39055*weight − 0.03237*L M1 FM = 0.24087 + 0.28396*W(kg) − 0.00968*L + 0.06669*flank skinfold M2 FM = 0.40367 + 0.34824*W − 0.01163*L + 0.0625*flank skinfold-0.02168*head circumference (cm)	
Jayasinghe[15] N, Birth = 188 (D) N, 3 months = 92 (D) N, 6 months = 51 (D)	White, Australia Birth (0–2 days, 3 months, and 6 months	ADP %Fat	Birth (%Fat) = 1.287 + 0.439*W − 0.026*L − 0.030*GA + 0.060*G 3 months (%Fat) = 1.053 + 0.045*SS + 0.488*W − 0.052*L + 0.137*G 6 months (%Fat) = 2.537 + 0.679*W − 0.090*L + 0.195*G	$R^2 = 72$; SEE 0.093 $R^2 = 0.64$; SEE 0.249 $R^2 = 0.63$; SEE 0.246

Abbreviations: ADP, air displacement plethysmography; BIA, bioelectrical impedance; D, derivation group; DXA, dual-energy X-ray absorptiometry; G, gender; GA, gestational age; Ht^2/I, impedance index; L, length; ln, log-transformed; M, model; SFT, skinfold thickness; SS, subscapular skinfold; TOBEC, total body electrical conductivity; V, validation group; W, weight.

2.2 | Assessment visits

The first visit was performed prior to hospital discharge, between 1 and 4 days after birth for term infants, or at 37 weeks post-last menstrual period for preterm infants. If preterm infants were discharged prior to 37 weeks, they were measured as close to discharge as possible. The follow-up visits were scheduled to occur between 13,0–15,0 and 48,0–56,6 weeks.

2.3 | Anthropometric measurements

Measurements were not collected on day 0 (<24 hours post-delivery) as data from our laboratory suggest that there is an initial weight loss in infants during this period.[24] Trained and certified study personnel (up to 3) obtained neonatal and infant study weight, length, head circumference (HC), and skinfold thicknesses measures prior to hospital discharge between 1 and 4 days after birth for term infants (or at

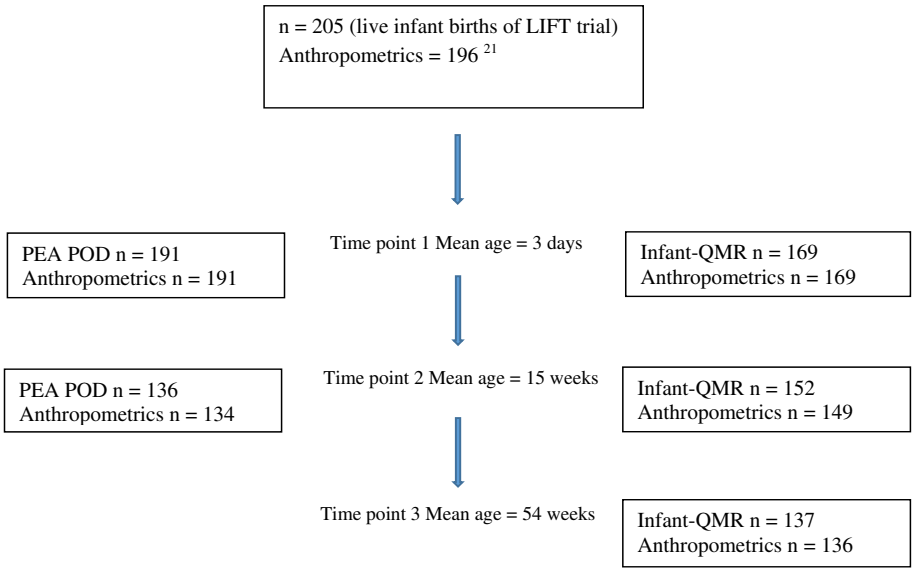

FIGURE 1 Flow diagram of LIFT infants at each follow-up visit

36 weeks post-last menstrual period of preterm infants) and at the two follow-up visits. All measures throughout the study were conducted using the same calibrated instruments. Weight was measured on a calibrated scale (PEA POD, Cosmed), lengths on a length board (Ellard Instrumentation Ltd), and HC using a tape measure with a tensiometer (Gulick II, model 67 020). Small for gestational age (SGA) and large for gestational age (LGA) were determined using WHO guidelines for reference population and ultrasound for gestational age.[15] Birth weight and length were extracted from medical records. Weight, length, and HC were each measured twice, and when >100 g difference in weight or 0.5 cm difference in length and HC were detected, a third measurement was taken and the average of the two closest measurements was used in the analyses. Skinfold thicknesses of the triceps, sub-scapula, iliac crest, and mid-thigh were measured in duplicate using skinfold callipers (Harpenden, model HSB-BI) on the left side of the body. When the results of the duplicate skinfold measures differed by more than 0.5 mm, a third measurement was acquired. The two measurements in closest agreement were averaged and used in analyses. Coefficient of variation (CV) of repeated skinfold measures for triceps (TRI), subscapular (SCP), iliac (I), and thigh (THI) in 23 infants at 3 days were 2.5%, 3.1%, 3.3%, and 2.8%, respectively; in 20 infants at 15 weeks were 2.5%, 2.4%, 3.6%, and 1.4% respectively; and in 45 infants at 54 weeks were 2.0%, 2.5%, 2.2%, and 0.8%, respectively.[22]

2.4 | Body composition assessment

Body composition data for this study were obtained from the LIFT trial,[20] for which the infants were measured by the PEA POD (Cosmed USA, Inc.) and the EchoMRI-Infant (Infant-QMR). A detailed description of the measurement protocol has been published previously.[20,22] PEA POD and Infant-QMR require short measurements times of under 4 minutes and no sedation. PEA POD is among the most widely used research method for FM and FFM in infants with an upper weight limit of 8 kg that corresponds to approximately 6 months. The PEA POD employs a two-compartment model that estimates body fat from body weight and volume using assumed densities for FM and FFM. Specifically, a constant FM density of 0.9007 g/ml[25,26] and varying age- and sex-specific densities of FFM from Fomon[27] (birth to 10 years) or Butte[28] (0.5–24 months). QMR is a non-imaging technique that uses the differences in relaxation times of hydrogen protons in response to radiofrequency pulses of the electromagnetic field to provide independent measures of FM, lean mass, free water, and TBW. Infant-QMR demonstrated high accuracy for TBW against deuterium dilution method in infants at the age of 3 days, and for small changes in FM when simulated fat phantoms using canola oil were added to newborns.[29] In our laboratory, repeated PEA POD tests performed twice on the same day on 29 infants gave CVs of 6.6% for %fat, 6.5% for FM, and 1.1% for FFM; the CVs in 14 newborns measured three times by Infant-QMR with repositioning between scans were 3.27%, 1.83%, and 1.34% for fat mass, lean mass, and total body water (TBW), respectively.[29]

2.5 | Statistical analysis

Stata 15.1 was used for statistical analyses. Descriptive statistics were calculated for all variables. Means and standard deviations were calculated for continuous variables and percentages for discrete variables. Stepwise regression methods were used to identify a minimal subset of independent variables necessary to predict FM with significance level for removal of variables at pr (0.20) and entry of variables at pe (0.1). Dummy variables were created for the categorical variables, biological sex, and race/ethnicity and were used as independent variables in the regression equations. Interaction effects of sex with its significant skinfolds were confirmed in a series of models and subsequently retained as multiplicative terms to ascertain the most parsimonious

TABLE 2 Descriptive characteristics, anthropometric and body composition at 3 days, 15 and 54 weeks

	3 days		15 weeks		54 weeks
	Infant-QMR $N = 169$	PEA POD $N = 191$	Infant-QMR $N = 152$	PEA POD $N = 136$	Infant-QMR $N = 137$
Demographics	Percentage (%)				
Sex					
Female	77 (46%)	87 (46%)	67 (44%)	63 (46%)	63 (45%)
Male	92 (54%)	104 (54%)	85 (56%)	73 (54%)	76 (55%)
Race/ethnicity					
White	43%	44%	47%	45%	45%
Black	20%	19%	20%	21%	22%
Hispanic	16%	17%	16%	15%	15%
Asian	1%	2%	1%	1%	0%
Multiracial/other	20%	18%	16%	18%	18%
	Mean (SD)				
Gestational age (weeks)					
Term ($n = 179$)	37.5 (1.08)				
Preterm ($n = 12$)	34.13 (2.1)				
SGA (<10th %ile) *N*	15 (8%)				
LGA (>10th %ile) *N*	20 (10.5%)				
Age (weeks)	0.45 (0.84)	0.44 (0.83)	15.0 (3.05)	14.79 (2.53)	54.64 (5.27)
Anthropometrics					
Weight (kg)	3.15 (0.52)	3.17 (0.51)	6.16 (0.96)	6.14 (0.91)	9.68 (1.18)
Length (cm)	49.46 (2.38)	49.55 (2.33)	61.34 (2.98)	61.28 (2.99)	75.36 (2.78)
Head circumference (cm)	34.12 (1.50)	34.16 (1.49)	40.84 (1.54)	40.76 (1.48)	46.35 (1.48)
Triceps (mm)	4.66 (1.19)	4.66 (1.24)	9.45 (1.92)	9.58 (1.84)	9.84 (2.49)
Subscapular (mm)	4.38 (1.19)	4.46 (1.22)	7.30 (1.79)	7.3 (1.8)	6.80 (1.69)
Iliac (mm)	3.91 (0.97)	3.95 (0.96)	9.31 (2.53)	9.38 (2.66)	9.06 (2.97)
Thigh (mm)	5.74 (1.70)	5.81 (1.73)	17.85 (4.25)	17.97 (4.29)	16.96 (4.12)
Body composition					
Fat mass (kg)	0.53 (0.18)	0.34 (0.17)	1.77 (0.52)	1.51 (0.45)	2.77 (0.64)
Fat (%)		10.5 (4.1)		24.3 (4.8)	
Lean (kg)	2.27 (0.32)		3.70 (0.47)		5.35 (0.57)
Fat-free mass (kg)		2.83 (0.4)		4.62 (0.61)	

Note: PEA POD output provides fat mass, fat %, and fat-free mass.
Abbreviations: Infant-QMR, quantitative magnetic resonance output provides fat mass, lean mass, and total body water; *N*, number; SD, standard deviation.

model. The initial set of independent variables used to model FM included weight, length, triceps, iliac, subscapular, thigh, head circumference, sex, and the multiplicative terms of sex interactions. The final models included all variables with a p value < 0.05. R-squared and root mean squared errors were used to evaluate the models. A residual analysis of the model obtained was performed, and studentized residuals were tested for assumption of normal distribution using the Shapiro–Wilk's test. The main effect of ethnicity was tested in each model using the F-statistic. Separate models were derived for 3 days, 15 and 54 weeks. Significance was set at two-tailed, $p < 0.05$.

3 | RESULTS

3.1 | Infant characteristics

Births occurred between August 2013 and April 2015. Infant birth characteristics have been previously described.[20] Descriptive characteristics, anthropometric and body composition data (mean ± SD) obtained at 3 days, 15, and 54 weeks are presented in Table 2. Infant-QMR measures were obtained at 3 days ($n = 169$), 15 ($n = 152$), and 54 weeks (n = 137). PEAPOD measures were

TABLE 3 Correlations (*r*) of fat mass with infant anthropometric variables

	Fat mass (kg)				
	3 days		15 weeks		54 weeks
	Infant-QMR $N = 169$	PEA POD $N = 191$	Infant-QMR $N = 152$	PEA POD $N = 136$	Infant-QMR $N = 137$
Weight (kg)	0.84*	0.71*	0.88*	0.80*	0.76*
Length (cm)	0.67*	0.50*	0.64*	0.5*	0.35*
Head circumference (cm)	0.60*	0.48*	0.51*	0.38*	0.27*
Skinfold thickness (mm)					
Triceps	0.72*	0.72*	0.58*	0.61*	0.62*
Thigh	0.78*	0.76*	0.58*	0.58*	0.73*
Sub-scapular	0.71*	0.77*	0.54*	0.50*	0.66*
Iliac	0.72*	0.70*	0.61*	0.62*	0.67*
Sum of skinfolds	0.81*	0.81*	0.64*	0.70*	0.79*

*Significance $p < 0.05$.

TABLE 4 Fat mass prediction models for females (F) and males (M)

Age		Equation	R^2	RMSE
3 days	Infant-QMR	F: Fat (kg) = −0.027 + 0.273*W − 0.016*HC + 0.027*TRI + 0.026*THI	0.87	0.066
		M: Fat (kg) = −0.027 + 0.273*W − 0.016*HC + 0.046*SCP		
	PEA POD	F: Fat (kg) = −0.028 + 0.237*W − 0.013*L + 0.014*THI + 0.049*SCP	0.77	0.080
		M: Fat (kg) = 0.795 + 0.237*W − 0.013*L + 0.014*THI + 0.049*SCP − 0.026*HC		
15 weeks	Infant-QMR	F: Fat (kg) = 0.431 + 0.637*W − 0.067*HC + 0.038*SCP	0.92	0.153
		M: Fat (kg) = 1.196 + 0.467*W − 0.067*HC + 0.036*TRI		
	PEA POD	F: Fat (kg) = 2.600 + 0.586*W − 0.041*L − 0.063*HC + 0.015*THI + 0.026*TRI	0.82	0.195
		M: Fat (kg) = 2.917 + 0.586*W − 0.041*L − 0.063*HC − 0.013*THI + 0.026*TRI		
54 weeks	Infant-QMR	Fat (kg) = 3.728 + 0.413*W − 0.036*L − 0.076*HC + 0.063*SCP + 0.051*THI	0.82	0.278

Note: N (Infant-QMR) = 169 at 3 days, 152 at 15 weeks, and 137 at 54 weeks. N (PEA POD) =191 at 3 days and 136 at 54 weeks.
Abbreviation: Fat, fat mass (kg); HC, head circumference (cm); L, length (cm); SCP skinfolds, subscapular (mm); THI, thigh skinfolds (mm); TRI, triceps skinfolds (mm); W, weight (kg).

obtained at 3 days ($n = 191$) and again at 15 weeks ($n = 136$) in 71.2% of the baseline sample. Variations in sample size across visits were due to attrition.

3.2 | Correlations of anthropometric measures with FM

Significant moderate to strong positive correlations ($r = 0.5$–0.8) between FM (Infant-QMR and PEA POD) with weight and skinfolds were observed at 3 days, 15, and 54 weeks (Table 3). Length and HC showed weak to moderate positive correlations ($r = 0.3$–0.6) with Infant-QMR-FM and PEA POD-FM at all three time points.

3.3 | Fat mass prediction models

Regression models were derived for FM by Infant-QMR at 3 days, 15, and 54 weeks and by PEA POD at 3 days and 15 weeks, as shown in Table 4. There was a significant sex interaction at 3 days and 15 weeks for both Infant-QMR and PEA POD ($p < 0.001$), and multiplicative terms were used in the analysis to derive the models. As the multiplicative terms are treated as independent variables in the current models, model coefficients for male and female are presented separately for clarity in Table 4. No significant sex effect was noted at 54 weeks (Infant-QMR $p = 0.3$). No significant effect for ethnicity was found at 3 days (Infant-QMR $p = 0.5$; PEA POD $p = 0.3$), 15 (Infant-QMR $p = 0.5$, PEA POD $p = 0.2$), or at 54 weeks (Infant-QMR $p = 0.8$).

The studentized residuals were consistent with a normal distribution across all models (3 days Infant-QMR $p = 0.3$ and PEA POD $p = 0.8$; 15 weeks Infant-QMR $p = 0.8$ and PEA POD $p = 0.3$; 52 weeks Infant-QMR $p = 0.2$). Weight was a consistent predictor of FM and was positively associated with FM across all models throughout infancy. Each individual skinfold when present in the model was positively associated with FM, whereas length and HC were negatively associated with FM. Infant-QMR FM and PEA POD-FM were strongly correlated at 3 days ($r = 0.87$) and 15 weeks ($r = 0.94$). Moreover, linear regression of Infant-QMR FM on PEA POD-FM was consistent with a unity slope with a non-constant intercept suggesting that Infant-QMR FM was consistently higher than the PEA POD-FM.

3.4 | 3 days

The model that best explained QMR-FM contained weight, HC, TRI, and THI skinfolds in females ($n = 77$); weight, HC, and SCP skinfold in males ($n = 92$). This model explained 87% of the variance in QMR-FM with a root mean square error (RMSE) of 66 grams (g). The PEA POD-FM model contained weight, length, HC, THI, and SCP skinfolds in females ($n = 87$); and weight, length, THI, and SCP skinfolds in males ($n = 104$). This model explained 77% of the variance in PEAPOD-FM with an RMSE of 80 g.

3.5 | 15 weeks

The model that best explained QMR-FM contained weight, HC, and SCP in females ($n = 67$); and weight, HC, and TRI skinfolds in males ($n = 85$). This model explained 92% of the variance in QMR-FM with an RMSE of 153 g. The PEA POD-FM model contained weight, length, HC, THI, and TRI skinfolds in both females ($n = 63$) and males ($n = 73$). This model explained 82% of the variance in PEA POD-FM with an RMSE of 195 g.

3.6 | 54 weeks

The model that best explained QMR-FM contained weight, length, HC, SCP, and THI skinfolds ($n = 137$). This model explained 82% of the variance in QMR-FM with an RMSE of 278 g. There was no effect of sex in this model.

4 | DISCUSSION

FM prediction models using weight, head circumference, length, and skinfolds were developed in a cohort of infants measured longitudinally at 3 days, 15 and 54 weeks. The Infant-QMR derived models explained 87% (3 days), 92% (15 weeks), and 82% (54 weeks) of the variation in FM, and the PEAPOD derived models explained 77% (3 days) and 82% (15 weeks) of the variation in FM. The Infant-QMR models explained a larger percentage of the variability in FM than the PEA POD models. The Infant-QMR models had an estimated FM standard deviation of 66 gm (12%) at 3 days, 153 gm (8%) at 15 weeks, and 278 gm (10%) at 54 weeks. The PEA POD models had an estimated FM standard deviation of 80 g (23%) at 3 days and 195 gm (13%) at 15 weeks. The RMSE expressed as a percentage of the mean FM was lower for Infant-QMR models (8%–12%) compared with PEA POD models (13%–23%), suggesting greater accuracy for Infant-QMR models. To our knowledge, these are the first FM prediction equations developed in the same cohort across the first year of life using Infant-QMR as a criterion. This effort serves to narrow a gap in the literature related to the paucity of anthropometric FM prediction models at 54 weeks of age.

Due to its high cost, Infant-QMR is available globally in just a few specialized research centres, and the Infant-QMR system allows for measurements up to 12 kg. Infant-QMR presents a unique opportunity to estimate FM longitudinally across infancy to at least 1 year of age, while the PEA POD can accommodate only up to 8 kg (~6 months of age). Furthermore, the PEA POD and Infant-QMR measure different components using distinct approaches. In our study, we applied the Fomon density for FFM, which depends on hydration. The Foman[27] birth constants were derived from infants of several pooled studies but placed in a single category, which may not accurately represent the body composition of 3-day-old infants, due to rapid changes in hydration following birth.[2] Fomon[27] reported lower TBW at birth (~68.6%–69.6%) compared with other studies (74%–78%)[29,30] that are lower than our study (76.5%), which may reflect the assumptions made in methods and calculations as described by Fomon.[31] Lipsmeyer et al[32] reported high accuracy for both PEA POD and QMR (EchoMRI-AH Small version) against a 4C model and a strong correlation between PEA POD and QMR ($r = 0.96$) in infants <8 kg. However, the QMR EchoMRI-AH Small with adjusted FM estimation equation[33] was used, and the individual components of the 4C model were obtained from the methods being compared, which could introduce bias. In our study, there was a significant mean FM difference of 190 gm (6.3% Fat) at 3 days between Infant-QMR and PEA POD and a difference of 260 gm (3.5% Fat) at 15 weeks. The between-method differences in measured FM are likely due to differences in the underlying assumptions and algorithms incorporated[2,29,33,34] and hydration changes with age.

Body composition changes progressively from birth throughout infancy as children grow and mature, reflecting dynamic differences in FM and FFM.[1] It is to be expected that equations developed in one age group would not perform well in other age groups given the rapid changes in body composition throughout infancy.[14,15,18] The newborn has higher hydration of FFM (i.e., TBW/FFM, expressed in percent) than a child at 1 year, approximately 83% versus 78%–79%.[27,28] In our study population, TBW at 3 days was 76.5%[22]which is higher than previously reported by Fomon[27] (~68%) and Butte[28] (~73%), and TBW decreased to 54% at 54 weeks, which is lower than Fomon (~60%) and Butte (~58%). In our study, FM increased from 341 gm (10.5% Fat) by PEAPOD and 530 gm (16%) by Infant-QMR at 3 days to 1510 gm (24.3% Fat) by PEAPOD and 1770 gm (28.7%) by Infant-QMR to 2790 gm (28%) by Infant-QMR at 54 weeks. Additionally, factors affecting fat prediction include differences in body composition methods and

variables in the derived models. Hence, models based on a single-center longitudinal cohort at three time points are a strength of this study.

Consistent with other studies that estimated FM by ADP,[9,13,15] TOBEC,[11] or DXA,[17,35,36] the current study found weight, length, and skinfolds to be predictors of FM. In general, weight and length are known to explain a significant portion of the variance in infant FM[3,9,35] ($R^2 = 0.62–0.84$) but the literature investigating the magnitude of the role of skinfolds in FM prediction is inconclusive. While one study found the sum of skinfolds were correlated more strongly with FM ($r = 0.62$) than FFM ($r = 0.42$) by PEAPOD in a cohort of neonates ($n = 251$, mean age 10 days),[37] other studies found skinfolds to be poor predictors of FM determined by body water dilution technique at varying ages between 4 days and 14 months.[38–40] As shown in Table 1, one to three skinfolds have been included in some of the existing models for FM in the published literature. Our study included three skinfolds (Tri, SCP, and Thi), where each alone or in combinations of two skinfolds were significant predictors of FM across infancy. The inclusion of skinfolds to a base model of weight, length, and sex in our study improved the R^2 on average by 9% for 3 days and 15 weeks and by 23% for the 54-week models. Interestingly, HC was a predictor in all models except in the PEA POD female model at 3 days. Only one other study involving a PEA POD based model[15] included HC as an FM predictor variable with flank (i.e., iliac) skinfold. Small head circumference at birth predicts an early adiposity rebound, which predicts obesity and type 2 diabetes, and coronary heart disease later in life.[41] There is a paucity of data exploring the relationship between head circumference and FM.

Sex differences in FM and FFM are evident from birth throughout childhood, with girls having higher FM values.[27,28,42–44] Up to a 3% difference in %fat between sexes from birth through 12 months was reported by Fomon[27] and Butte.[28] A systematic review of body composition by ADP in infants born at term[45] reported a 2% higher %fat in girls compared with boys within the first 4 days of birth. It is therefore appropriate for sex to be included as a covariate in body composition prediction models beginning at birth.[9,13,14] These sex differences are postulated to be related to the effect of androgenic steroids present in males.[46,47] A sex interaction was observed in the current study at 3 days, indicating the need for development of sex-specific models at later time points. However, no sex interaction was found at 54 weeks, likely due to a smaller sample size. Others have found neonatal FM differences based on ethnicity.[13,45,47,48] While ethnicity was not a predictor of FM in this study, it is acknowledged that maternal self-reported race/ethnicity was applied to the infant without consideration for the father's ethnicity. In such multiracial and multi-ethnic cohorts typical of New York City, it is probable that the role of ethnicity cannot be truly determined.

Higher birth weight and accelerated infant weight gain are consistently associated with later childhood overweight.[49] The first 1000 days refers to the period from conception to age 2 years that presents as a unique window of opportunity when intervention could help shape a child's health trajectory. In the era of precision nutrition medicine, the first 1000 days are gaining recognition for a potential role in chronic disease prevention, and in particular, childhood obesity prevention.[49] The simple FM prediction models presented here may aid towards this goal. Furthermore, this study adds to the literature with models based on Infant-QMR, to further knowledge in this field. Such models, after validation in different cohorts, have the potential to serve as a valuable tool both at the field/population level to collect large group data in studies assessing links between FM in infancy and development of morbidities in the future. The time points of 3 days, 15 and 54 weeks correspond closely to the Bright Futures/American Academy of Paediatrics recommendations for preventative health care visits of 3–5 days, 16 and 52 weeks, which could provide an opportunity for application of these models after validation. While weight, height, and HC are part of routine growth monitoring, the skinfold measures may be collected with additional training.[50] Future application of appropriately validated FM prediction models includes incorporation into electronic medical records that could inform clinicians/pediatricians to initiate discussions at these early life child wellness visits, as it is well established that a large percentage of children with early onset obesity continue to have obesity in later childhood and adulthood.

While many published equations presented in Table 1 do not provide maternal data, maternal data and factors affecting neonatal body composition for this cohort were previously discussed.[20] Small significant differences were reported in mean FM and body fat percent in the first months of life between children born to mothers with overweight or with obesity and those from mothers with normal maternal pre-pregnancy weight, based on a meta-analysis.[51] It is important to note that our cohort involved infants of mothers with overweight or obesity (average BMI 30 kg/m^2), which may affect the generalizability of the models. Feeding practices affect hydration in the first 2 weeks of infancy, and differences in FM and FFM exist between breast- and formula-fed infants.[52] This dataset did not include details of feeding practices or physical activity throughout infancy. Internal and external validation studies are needed to assess the accuracy and agreement of these equations in broader and similar populations. It is acknowledged that skinfolds are prone to measurement errors,[12] which, in this study, were minimized by using trained personnel with annual certification by a master trainer.

5 | CONCLUSIONS

This study presents FM anthropometric prediction models developed using robust criterion methods in early infancy and childhood, which with future validation studies could have potential application in population studies. These could be valuable for assessing disease development and risk on a larger scale in longitudinal studies from birth and into adulthood, with considerations for preventative strategies at a very early stage.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Mahalakshmi Gopalakrishnamoorthy, **Dympna Gallagher**, and **John Thornton** designed this study; **Dympna Gallagher** and **Xavier Pi-Sunyer**

are co-principal investigators of the LIFT trial and were responsible for supervision of data collection; **Jill Johnson**, **Tatiana Toro-Ramos**, **Elizabeth Widen**, **Michelle Horowitz** were responsible for anthropometric outcome measures; **Charles Paley** and **Sonia Gidwani** were responsible for medical supervision; **Michelle Horowitz** was the primary project coordinator; **Susan Lin** was responsible for data management; **John Thornton**, **Kathryn Whyte** were responsible for data analysis; **Dympna Gallagher** had primary responsibility for final content. All authors read and approved the final manuscript.

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