Eating difficulties in children born late and moderately preterm at 2 y of age: a prospective population-based cohort study[1–3]

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ABSTRACT

Background: Very preterm (<32 wk of gestation) infants are at increased risk of eating difficulties compared with their term-born peers. Little is known about the impact of late and moderately preterm (LMPT; 32–36 wk of gestation) birth on eating difficulties in early childhood.

Objectives: The aims were to assess the prevalence of eating difficulties in infants born LMPT at 2 y corrected age and to explore the impact of neonatal and neurodevelopmental factors.

Design: A geographic population-based cohort of 1130 LMPT and 1255 term-born controls was recruited at birth. The parents of 651 (59%) LMPT and 771 (62%) term-born infants completed questionnaires at 2 y corrected age to assess neurodevelopmental outcomes. Parents also completed a validated questionnaire to assess eating behaviors in 4 domains: refusal/picky eating, oral motor problems, oral hypersensitivity, and eating behavior problems. Infants with scores >90th percentile were classified with eating difficulties in each domain. Neonatal data were collected at discharge, and sociodemographic information was collected via maternal interview. Poisson regression was used to assess between-group differences in eating difficulties and to explore associations with neonatal factors and neurodevelopmental outcomes at 2 y of age.

Results: In unadjusted analyses, LMPT infants were at increased risk of refusal/picky eating (RR: 1.53; 95% CI: 1.03, 2.25) and oral motor problems (RR: 1.62; 95% CI: 1.06, 2.47). Prolonged nasogastric feeding >2 wk (RR: 1.87; 95% CI: 1.07, 3.25), behavior problems (RR: 2.95; 95% CI: 1.93, 4.52), and delayed social competence (RR: 2.28; 95% CI: 1.49, 3.48) were independently associated with eating difficulties in multivariable analyses. After adjustment for these factors, there was no excess of eating difficulties in LMPT infants.

Conclusions: Infants born LMPT are at increased risk of oral motor and picky eating problems at 2 y corrected age. However, these are mediated by other neurobehavioral sequelae in this population. This trial was registered on the UK Clinical Research Network Portfolio at http://public.ukcrn.org.uk/search/ as UKCRN Study ID 7441. *Am J Clin Nutr* 2016;103:406–14.

Keywords: eating behavior, gestational age, neurodevelopment, oral motor problems, preterm

INTRODUCTION

Infants born very preterm (<32 wk of gestation) are at high risk of oral feeding difficulties during the neonatal period, including problems coordinating suck-swallow and swallow-respiration reflexes, neurological immaturity, and readiness for oral feeding (1–3). Feeding difficulties may persist throughout childhood, manifesting in delayed feeding skill development, food refusal, difficulties weaning, oral motor dysfunction, oral hypersensitivity, and eating behavior problems (4–7). Prolonged exposure to nasogastric tube feeding and the provision of mechanical ventilation during neonatal care have both been associated with feeding difficulties and oral sensitivity in very preterm survivors (5, 8, 9). Eating difficulties in infancy and middle childhood have also been associated with neurodevelopmental and behavioral sequelae, which are common after preterm birth (10), small-for-gestational-age (SGA)[6] status, male sex, and socioeconomic adversity in children born very preterm or with high neonatal risk (4, 7, 8, 11–13).

Much less is known about the development of eating difficulties in infants born late or moderately preterm (LMPT; 32–36 wk of gestation). Although there is mounting evidence that LMPT infants are at increased risk of health, neurodevelopmental, and behavioral sequelae compared with their term-born peers (14, 15), there is a paucity of research related to eating behaviors in this population. In 1 study, 20 low-risk LMPT infants who received nasogastric feeding exhibited more oral sensitivity, facial defensiveness, and delayed feeding development than

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[3] Supplemental Table 1 is available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

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[6] Abbreviations used: BITSEA, Brief Infant and Toddler Social Emotional Assessment; CP, cerebral palsy; LMPT, late and moderately preterm; NSI, neurosensory impairment; PARCA-R, Parent Report of Children's Abilities–Revised; SES, socioeconomic status; SGA, small for gestational age.

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10 term-born controls at 11–17 mo of corrected age; LMPT infants who received >3 wk of nasogastric feeding had poorer feeding development than did LMPT infants who received nasogastric feeding for <2 wk (16). In 2 further studies, late preterm infants had rates of parent-reported eating difficulties similar to those in very preterm infants over the first year of life (17, 18). These results suggest that, compared with term-born infants, LMPT infants may be at increased risk of eating difficulties in early childhood and that these may be associated with prolonged nasogastric feeding and neurodevelopmental or behavioral sequelae. However, to our knowledge, there have been no population-based studies of the prevalence of eating difficulties in LMPT infants.

Here we report the results of a large, prospective, population-based cohort study in LMPT infants compared with term-born controls. The aims of the study were to determine whether *1*) infants born LMPT are at higher risk of eating difficulties than their term-born peers at 2 y of corrected age, *2*) prolonged exposure to nasogastric feeding and mechanical ventilation are associated with the development of eating difficulties in LMPT infants, and *3*) whether eating difficulties in LMPT infants are mediated by neurodevelopmental sequelae.

METHODS

Participants

All infants born LMPT (32^{+0}–36^{+6} wk) to mothers resident in a geographically defined region of the East Midlands of England from September 2009 through December 2010 were invited to participate in the Late and Moderately Preterm Birth Study. This comprised infants delivered at 4 large maternity centers, a midwifery-led birthing unit, and at home. A random sample of singleton infants born at 37^{+0}–42^{+6} wk was also recruited during the same time period and in the same geographical region to form a control group. These were selected on the basis of random sampling of dates and times of birth of infants in the same area during the previous year from computerized records. Mothers of all multiples born at term during the study period were also invited to participate given the high rate of multiple births in the LMPT population. To examine the effects of preterm birth per se on eating difficulties, infants with major structural or chromosomal congenital anomalies, including cardiovascular malformations, and neurosensory impairment were excluded from the analyses.

Procedure

Informed consent was obtained from mothers and information about mothers' sociodemographic status was obtained via a semistructured postnatal interview conducted by research midwives. Obstetric and neonatal data were collected from mothers' and infants' medical notes, respectively, at discharge from the hospital. Infants were followed up at 2 y corrected age using a parent questionnaire. This questionnaire was mailed to parents 7–10 d before the child turned 2 y corrected age, with instructions to mail the completed questionnaire back to the study center in the prestamped envelope provided. Parents were contacted by telephone when the child reached 2 y corrected age to remind them to complete the questionnaire if they had not yet responded. Parents who did not respond to the postal questionnaire were also offered the option to complete it via a telephone interview or electronically to maximize response rates. The study was approved by the Derbyshire National Health Service Research Ethics Committee (reference: NHS REC 09/H0401/25) and was registered on the UK Clinical Research Network Portfolio (reference: UKCRN Study ID 7441).

Measures

At 2 y corrected age, parents were asked to complete a questionnaire comprising measures to assess infants' eating behavior, cognitive development, behavior and emotional problems, and neurosensory impairment. These measures were as follows:

1) A validated eating behavior questionnaire (4) was used to assess the presence of eating difficulties in the 4 domains of refusal/picky eating (e.g., poor appetite, food refusal, selective eating), oral motor problems (e.g., problems biting, chewing, or swallowing; gagging; or choking on food), oral hypersensitivity (e.g., aversion to being touched around the mouth or having things put in the mouth), and eating behavior problems (e.g., has tantrums or makes a mess during meals) (see **Supplemental Table 1** for a copy of the questionnaire). For each of 17 items, parents were asked to state whether their child exhibited the problem behavior never, occasionally, or often. Each item was scored 0, 1, or 2, respectively, from which a total eating difficulties score was computed (range: 0–34) and 4 subscale scores for refusal/picky eating (7 items; range: 0–14), oral motor problems (5 items; range: 0–10), oral hypersensitivity (2 items; range: 0–4), and eating behavior problems (3 items; range: 0–6); for all scales, higher scores indicate greater problems. Infants with missing data on individual items were excluded from the total feeding score ($n = 64$ infants; 4.6%) and feeding subscales (<2.5% missing data for each subscale). In accordance with previous studies (4), scores >90th percentile of the term control group were used to identify children with clinically significant eating difficulties overall (total eating difficulties score >12) and for each domain (refusal/picky eating score >8, oral motor problems score >2, oral hypersensitivity score >2, and eating behavior problems score >3). The eating behavior questionnaire had good internal consistency (Cronbach's $\alpha = 0.83$) and has previously been used to assess eating difficulties in children born preterm (4).

2) In addition, parents were asked whether they felt their child had an eating problem (yes or no), whether they had sought advice about eating problems from a health professional (yes or no), and whether their child had ever been prescribed medicine for reflux (yes or no).

3) The validated Parent Report of Children's Abilities–Revised (PARCA-R) parental questionnaire was used to assess nonverbal cognitive and language development at 2 y corrected age (19, 20). A total Parent Report Composite score was computed (range: 0–158; higher scores indicate more advanced development) from which scores <35, corresponding with scores <2.5th percentile of the

term control group, were used to identify moderate/severe cognitive impairment (15). In cases in which children had ≤4 missing items on the nonverbal scale, these were substituted with the child's average nonverbal cognition item score and the Parent Report Composite score was computed. Cognitive impairment was not classified for 6 children with substantial missing PARCA-R data. For 20 non–English-speaking children in whom the language section could not be completed, scores <22 for nonverbal cognition, corresponding with nonverbal cognition scores <2.5th percentile of the term control group, were used to classify cognitive impairment (15). PARCA-R scores are strongly correlated with scores on the Bayley Scales of Infant Development, and the questionnaire is widely used to assess neurodevelopmental outcomes in preterm infants in epidemiologic studies and randomized trials (19–23).

4) The Brief Infant and Toddler Social Emotional Assessment (BITSEA) questionnaire was completed by parents to assess behavioral and emotional outcomes at 2 y corrected age (24). This comprises 2 scales to assess problem behaviors (internalizing and externalizing problems, dysregulation, and maladaptive and atypical behaviors) and socioemotional competence (attention, compliance, mastery motivation, peer relations, empathy, imitation/play skills, and social relatedness) from which a total problem score (higher scores indicate greater problems) and a total competence score (lower scores indicate lower competence) were computed, respectively. Missing BITSEA items were scored as "0" in cases in which there were ≤5 missing items on the problem scale and ≤2 missing items on the competence scale. Data from children with additional missing data were excluded (n = 18). Children with clinically significant behavior problems and delayed social competence were identified by using the published norms in which cutoffs corresponded with problem scores >25th percentile and competence scores <15th percentile of the standardization sample (24). The BITSEA has excellent test-retest reliability, interrater reliability, and predictive validity for psychiatric disorders at school age (25).

5) Parents were asked whether their child had a diagnosis of cerebral palsy (CP) and to rate their child's vision, hearing, and gross motor function with the use of forced-choice items corresponding with standard criteria for classifying health status at 2 y (26). Infants with one or more of moderate/severe vision impairment (blind/vision uncorrected with aids), hearing impairment (deaf/hearing requiring aids), or gross motor impairment (nonambulant/requires assistance to walk) were classified with neurosensory impairment (NSI).

To adjust for neonatal factors previously shown to be related to eating difficulties in children born very preterm (5, 7, 9, 11, 13), sex, multiplicity, birth weight, SGA [fetal weight less than the third percentile for sex and gestation with the use of customized antenatal growth charts (27)], days of nasogastric feedings, and use of mechanical ventilation were obtained from infants' medical notes by research midwives at the infant's discharge from the hospital. Prolonged nasogastric feeding was defined as the provision of nasogastric feeding for >2 wk.

To quantify socioeconomic status (SES), mothers' self-report of their occupational status (by using the UK Office for National Statistics Socio-occupational Classification system), highest educational qualification, social support (cohabiting status during pregnancy), income (car ownership), and wealth (home ownership) was obtained during the postnatal maternal interview. These were scored on a 4-point scale (occupational status and educational qualification) or on a 2-point scale for dichotomous variables (social support, income, and wealth) and a total SES index score was computed (range: 0–12), with higher scores indicating greater socioeconomic risk. SES index scores were then used to classify mothers into 3 risk categories: low (scores of 0–2), moderate (scores of 3–5), and high (scores of ≥6) risk. This classification system has been described in detail previously (15).

Statistical analyses

Baseline characteristics are presented for the term and LMPT groups with sampling weights applied to the term infants to account for the oversampling of multiple births in this group. Chi-square tests were used to compare weighted proportions between groups. Poisson regression was used to compare the proportion of LMPT and term-born infants with eating difficulties, again by using sampling weights to account for the oversampling of multiple births in the control group. Interaction terms were fitted to explore group differences between male and female infants. Among LMPT infants, Poisson regression was used to explore factors associated with eating difficulties at 2 y. Between-group differences in total feeding difficulties between term and LMPT infants were then adjusted for the following: *1*) sex, SGA, SES, and prolonged nasogastric tube feeding, and *2*) all of these factors, as well as for behavior problems, delayed social competence, and cognitive impairment at 2 y. Models 1 and 2 were fitted including a missing category for dependent variables with missing data to ensure that all models contained the same infants for estimation. Repeating the analysis on a complete case basis did not alter the conclusions. Cluster sandwich estimators were used to produce variance estimates in all models to account for the correlation between outcomes among multiple births. Because 2 items on the BITSEA problem scale overlapped with items in the eating questionnaire (gags or chokes on food, refuses to eat), sensitivity analyses were performed by recalculating the BITSEA total problem score omitting these 2 items. The presence of behavior problems was identified by using the same percentile cutoffs (i.e., ≥75th percentile) as the standardization sample applied to the term control group. Analyses were then repeated by using the modified BITSEA problem score to explore the effect this had on the results. Statistical analysis was performed by using Stata Statistical Software, version 13.

RESULTS

Population

Of the 1340 LMPT and 1583 term births, 1130 (84%) LMPT and 1255 (79%) term-born infants were recruited (**Figure 1**); these included 47 complete sets of twins and 2 sets of triplets born LMPT and 75 complete sets of twins born at term. Two-year parent questionnaires were received for 651 (59%) LMPT and 771 (62%) term-born infants who were eligible for follow-up at 2 y of age (Figure 1); this equates to 58% and 61% of

LMPT and term-born infants who were recruited to the study at birth. After excluding those with congenital anomalies, CP, and NSI, 628 LMPT infants and 759 controls were included in the final sample (Figure 1).

Infants' characteristics are shown in **Table 1**. LMPT infants were significantly more likely to be born SGA than were term-born controls (10.7% compared with 4.0%) and to have received mechanical ventilation (8.8% compared with 0.7%) and nasogastric feeding (31.8% compared with 1.5%). At 2 y of age, LMPT infants were also at increased risk of cognitive impairment (5.4% compared with 2.6%), behavioral problems (20.4% compared with 17.2%), and delayed social competence (25.6% compared with 17.9%). There were no significant differences between mothers of infants born LMPT and those of infants born at term. We previously reported that mothers who did not respond to follow-up were younger; more likely to be nonwhite, non–English-speaking, single parents; have lower occupational and educational status; to be struggling financially; and to have poorer health than responders (28).

Prevalence of eating difficulties

The prevalence of eating difficulties in LMPT and term-born infants is shown in **Table 2**. Overall, 14.9% of LMPT and 9.5% of term-born infants had eating difficulties at 2 y. In unadjusted analyses, this represented a 57% increased risk of eating difficulties among LMPT infants (RR: 1.57; 95% CI: 1.14, 2.16). However, LMPT infants were at significantly increased risk only for refusal/picky eating problems (RR: 1.53; 95% CI: 1.03, 2.25) and oral motor problems (RR: 1.62; 95% CI: 1.06, 2.47) (Table 2).

There were no significant differences between male and female infants for total eating difficulties ($P = 0.19$), refusal/picky eating ($P = 0.12$), oral motor problems ($P = 0.25$), oral hypersensitivity ($P = 0.26$), and eating behavior problems ($P = 0.41$). Boys born LMPT were at increased risk of total eating difficulties (RR: 1.87; 95% CI: 1.22, 2.87) and refusal/picky eating (RR: 2.11; 95% CI: 1.18, 3.77) compared with term-born boys (Table 2). These differences were not observed in girls. Conversely, girls born LMPT were more likely to have oral motor problems than term-born girls (RR: 2.35; 95% CI: 1.10, 5.02).

There were no significant between-group differences in the proportion of parents who felt that their child had an eating problem (term compared with LMPT: 9.0% compared with 11.9%; RR: 1.33; 95% CI: 0.95, 1.85) or who had sought advice about eating problems (term compared with LMPT: 6.5% compared with 9.0%; RR: 1.39; 95% CI: 0.94, 2.05). However, significantly more LMPT than term-born infants had been prescribed medicine for reflux by 2 y of age (term compared with LMPT: 8.7% compared with 16.8%; RR: 1.94; 95% CI: 1.40, 2.67).

Association of neonatal and neurodevelopmental factors with eating difficulties in LMPT infants

Results from regression analyses of factors identified a priori as potential associates of eating difficulties in LMPT infants are shown in **Table 3**. On univariable analyses, cognitive impairment,

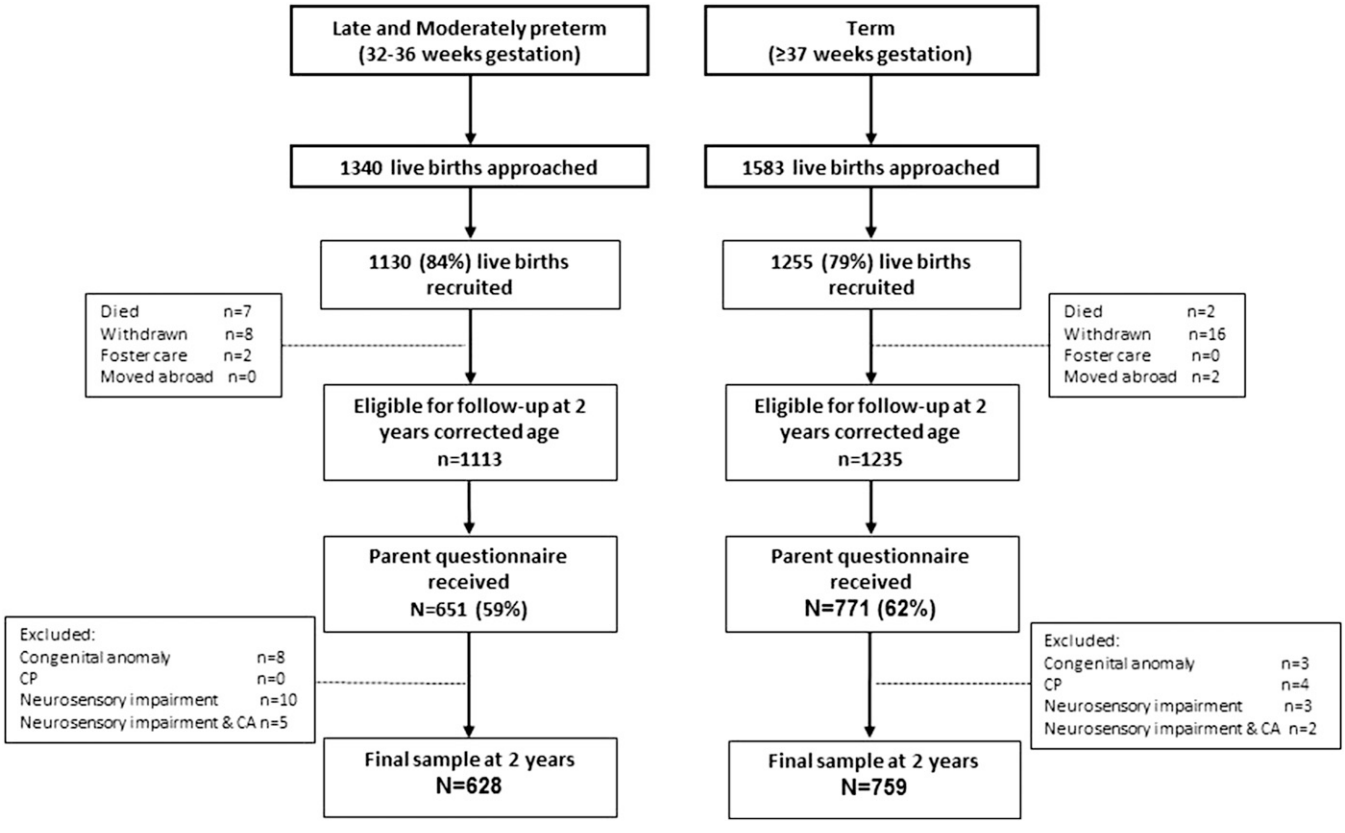

FIGURE 1 Recruitment and follow-up rates at 2 y of corrected age for the Late and Moderately Preterm Birth Study. CA, congenital anomaly; CP, cerebral palsy.

TABLE 1
Demographic characteristics of LMPT (32–36 wk of gestation) and term-born (37–42 wk of gestation) infants assessed at 2 y of corrected age[1]

Variable	Term	Term weighted[2]	LMPT	*P*
Infants, *n*	759		628	
Gestational age, *n* (%)				
32–33 wk	—	—	87 (13.9)	—
34–36 wk	—	—	541 (86.2)	—
37–38 wk	239 (31.5)	(16.4)	—	—
39–40 wk	355 (46.8)	(56.9)	—	—
41–42 wk	165 (21.7)	(26.7)	—	—
Multiple birth, *n* (%)	151 (19.9)	(1.6)	107 (17.0)	<0.001
Birth weight, g	3322.9 ± 535.4[3]	3448.9	2434.0 ± 504.8	—
Birth weight *z* score, *n* (%)				0.002
More than 1 SD below the mean	84 (12.3)	(10.2)	102 (17.7)	—
1 SD below to 1 SD above the mean	476 (70.0)	(70.0)	349 (60.5)	—
More than 1 SD above the mean	124 (18.1)	(19.8)	126 (21.8)	—
SGA,[4] *n* (%)	48 (6.3)	(4.0)	67 (10.7)	<0.001
Male sex, *n* (%)	381 (50.2)	(49.6)	338 (53.8)	0.13
Received mechanical ventilation, *n* (%)	5 (0.7)	(0.7)	55 (8.8)	<0.001
Nasogastric tube fed, *n* (%)	13 (1.7)	(1.5)	198 (31.8)	<0.001
Cognitive impairment,[5] *n* (%)	17 (2.3)	(2.6)	34 (5.4)	0.01
Behavior problems,[6] *n* (%)	135 (17.9)	(17.2)	126 (20.4)	0.15
Delayed social competence,[6] *n* (%)	138 (18.3)	(17.9)	159 (25.6)	0.001
Corrected age, mo	24.6 ± 1.1[3]	24.6	24.6 ± 1.0	—
Mothers, *n*	684		577	
Age, *n* (%)				0.16
<20 y	16 (2.3)	(2.6)	19 (3.3)	—
20–24 y	96 (14.0)	(14.4)	84 (14.6)	—
25–29 y	179 (26.2)	(26.3)	172 (30.0)	—
30–34 y	208 (30.4)	(31.3)	189 (32.8)	—
≥35 y	185 (27.1)	(25.3)	112 (19.4)	—
Ethnic group, *n* (%)				0.16
White	568 (83.0)	(82.8)	453 (78.5)	—
Mixed	6 (0.9)	(0.8)	12 (2.1)	—
Asian or Asian British	74 (10.8)	(11.3)	84 (14.6)	—
Black or Black British	29 (4.2)	(3.7)	21 (3.7)	—
Chinese or other	7 (1.0)	(1.0)	6 (1.0)	—
Unknown	0 (0.0)	(0.0)	1 (0.2)	—
English not first language, *n* (%)	83 (12.3)	(12.6)	82 (14.4)	0.36
SES index,[7] *n* (%)				0.28
Low risk	337 (49.3)	(47.5)	254 (44.0)	—
Medium risk	209 (30.6)	231 (31.1)	178 (30.9)	—
High risk	138 (20.2)	159 (21.5)	145 (25.1)	—

[1]BITSEA, Brief Infant and Toddler Social and Emotional Assessment; LMPT, late and moderately preterm; PARCA-R, Parent Report of Children's Abilities–Revised; SES, socioeconomic status; SGA, small for gestational age.

[2]Weighted for oversampling of multiple births in the term reference group. Chi-square tests were used to compare weighted proportions.

[3]Mean ± SD (all such values).

[4]SGA was classified by using birth weight less than the third percentile for sex and gestation with the use of customized antenatal growth charts.

[5]Cognitive impairment was defined as a PARCA-R Parent Report Composite score <2.5th percentile of the term reference group (Parent Report Composite score <35).

[6]Clinically significant behavior problems and delayed social competence were assessed by using the BITSEA and classified by using the test norms.

[7]SES index refers to socioeconomic risk category derived from a composite measure of 5 indexes of socioeconomic risk (see Methods).

delayed social competence, male sex, SGA, and prolonged nasogastric feeding were all significantly associated with eating difficulties at 2 y (Table 3). In contrast, mechanical ventilation and socioeconomic risk factors were not significantly associated with eating difficulties. On multivariable analyses that included all these factors, nasogastric feeding for >2 wk (RR: 1.87; 95% CI: 1.07, 3.25), behavior problems (RR: 2.95; 95% CI: 1.93, 4.52), and delayed social competence (RR: 2.28; 95% CI: 1.49, 3.48) were significant independent risk factors for eating difficulties at 2 y of corrected age.

TABLE 2
Descriptive statistics for parent-reported eating difficulties in LMPT and term-born infants and between-group differences in the prevalence of clinically significant problems in univariable (unadjusted) analyses[1]

	Term			LMPT			Proportion in the clinical range (LMPT vs. term)[2]	
Eating difficulties	*n*	Median[3] (IQR)	Clinical range,[4] *n* (%)	*n*	Median[3] (IQR)	Clinical range, *n* (%)	RR (95% CI)[5]	*P*
Total eating difficulties	726	6 (3–9)	69 (9.5)	597	7 (4–10)	89 (14.9)	1.57 (1.14, 2.16)	0.005
Boys	362	6 (4–9)	36 (9.9)	320	7 (4–11)	57 (17.8)	1.87 (1.22, 2.87)	0.004
Girls	364	6 (3–9)	33 (9.5)	277	6 (4–10)	32 (11.6)	1.22 (0.75, 1.97)	0.41
Refusal/picky eating	744	3 (1–6)	48 (6.5)	611	4 (2–6)	61 (10.0)	1.53 (1.03, 2.25)	0.03
Boys	370	3 (2–6)	20 (5.2)	330	4 (2–7)	36 (10.9)	2.11 (1.18, 3.77)	0.01
Girls	374	3 (1–6)	28 (7.9)	281	4 (1–6)	25 (9.0)	1.12 (0.65, 1.91)	0.65
Oral motor problems	749	0 (0–1)	41 (5.4)	612	0 (0–1)	53 (8.7)	1.62 (1.06, 2.47)	0.03
Boys	374	0 (0–1)	28 (7.8)	328	0 (0–1)	33 (10.0)	1.29 (0.77, 2.14)	0.32
Girls	375	0 (0–1)	13 (3.0)	284	0 (0–1)	20 (6.9)	2.35 (1.10, 5.02)	0.03
Oral hypersensitivity	756	0 (0–1)	32 (3.8)	619	0 (0–1)	33 (5.3)	1.39 (0.83, 2.33)	0.21
Boys	378	0 (0–1)	16 (4.0)	333	0 (0–1)	24 (7.2)	1.78 (0.91, 3.48)	0.09
Girls	378	0 (0–1)	16 (3.6)	286	0 (0–1)	9 (3.2)	0.87 (0.36, 2.05)	0.74
Eating behavior problems	738	2 (1–2)	45 (6.0)	616	2 (1–2)	42 (6.8)	1.15 (0.73, 1.78)	0.54
Boys	370	2 (1–2)	22 (5.8)	331	2 (1–3)	26 (7.9)	1.35 (0.74, 2.44)	0.32
Girls	368	2 (1–2)	23 (6.1)	285	2 (1–2)	16 (5.6)	0.93 (0.48, 1.78)	0.82

[1]LMPT, late and moderately preterm.
[2]Unadjusted models.
[3]Eating behavior questionnaire scores.
[4]Weighted for oversampling of multiple births in the term group.
[5]Data were analyzed by using Poisson regression models with sampling weights to account for the oversampling of multiple births in the term control group and cluster sandwich estimators to account for the correlation in outcomes among multiple births. There was no significant difference in eating difficulty scores between boys and girls.

Are eating difficulties in LMPT infants mediated by neurodevelopmental sequelae?

To determine whether the increased risk of eating difficulties in LMPT infants could be accounted for by neurodevelopmental sequelae, multivariable models were used to explore between-group differences after adjustment for important neonatal or neurodevelopmental factors (**Table 4**). After adjustment for sex, SES, and >2 wk of nasogastric feeding, the risk of refusal/picky eating problems was no longer significant (model 1). However, there was still an increased risk of oral motor problems (RR: 1.65; 95% CI: 1.05, 2.58) and total eating difficulties (RR: 1.44; 1.01, 2.03) among LMPT infants. After further adjustment for behavior problems, delayed social competence, and cognitive impairment at 2 y (model 2), the risk of both total eating difficulties and oral motor problems in LMPT infants was no longer significant (Table 4). Repeating the analyses with the use of the modified BITSEA problem score excluding the 2 overlapping items did not change the results appreciably and did not alter the conclusions.

DISCUSSION

To our knowledge, this is the first study to explore the prevalence and associates of eating difficulties in LMPT infants. Compared with their term-born peers, we observed that infants born LMPT were at increased risk of oral motor problems, such as chewing, biting, and swallowing, and refusal/picky eating, such as selective eating, eating too little or too slowly, or having a poor appetite at 2 y corrected age. However, these difficulties were mediated by neurodevelopmental sequelae and are thus unlikely to represent a specific functional deficit after LMPT birth.

To date, there are few studies of eating behaviors in LMPT infants and none that have explored the impact of birth at 32–36 wk of gestation compared with birth at term. An exploration of eating difficulties in early childhood is important for providing appropriate parental counseling and anticipatory guidance about postdischarge care because feeding difficulties in infancy show continuity to later life and may affect a child's health, development, and growth (8, 18, 29). Here we observed that LMPT infants were at 1.6 times increased risk of eating difficulties, particularly oral motor problems. However, these were explained by the excess of neurodevelopmental and behavioral sequelae in this population. In a previous study in 6-y-old children born extremely preterm (<26 wk of gestation) that used the same eating behavior questionnaire, the greatest effect size was also observed for oral motor problems compared with eating difficulties in other domains. However, in contrast with the present study, neurodevelopmental factors only partly explained the relation between eating difficulties and extremely preterm birth (4).

In the LMPT population, the impact of eating difficulties should not be overlooked, but it is likely that these co-occur with other neurodevelopmental and behavioral morbidities. Screening for eating difficulties during early childhood may therefore be useful in identifying not just those in whom intervention to support feeding practices might be beneficial but those who may have other behavioral issues or developmental morbidity. These results also point to a common underlying mechanism for oral motor problems and poor developmental outcomes that may be associated with neurological immaturity. Indeed, studies have shown that substantial brain maturation occurs during the third trimester of pregnancy. As such, normal neurodevelopmental processes may be interrupted by LMPT preterm birth, leaving infants at risk of impairments in multiple developmental domains (30, 31).

TABLE 3
Association of neonatal and neurodevelopmental variables with eating difficulties at 2 y corrected age in LMPT infants[1]

	Total eating difficulties, *n* (%)		Univariable analysis		Multivariable analysis (*n* = 584)[2]	
	Problem (*n* = 508)	No problem (*n* = 89)	RR (95% CI)	*P*	RR (95% CI)	*P*
Cognitive impairment[3]						
Not impaired	78 (13.8)	486 (86.2)	1	—	—	—
Impaired	11 (33.3)	22 (66.7)	2.41 (1.41, 4.11)	0.001	—	—
Behavior problems[4]						
No problems	45 (9.5)	428 (90.5)	1	—	1	—
Behavior problems	42 (35.0)	78 (65.0)	3.68 (2.53, 5.34)	<0.001	2.95 (1.93, 4.52)	<0.001
Delayed social competence[4]						
No delay	45 (10.2)	397 (89.8)	1	—	1	
Delayed social competence	44 (28.4)	111 (71.6)	2.79 (1.91, 4.07)	<0.001	2.28 (1.49, 3.48)	<0.001
SES[5]						
Low risk	36 (13.0)	240 (87.0)	1	—	—	—
Medium risk	31 (17.4)	147 (82.6)	1.34 (0.84, 2.10)	0.21	—	—
High risk	22 (15.4)	121 (84.6)	1.18 (0.71, 1.95)	0.52	—	—
Sex						
Female	32 (11.6)	245 (88.5)	1	—	—	—
Male	57 (17.8)	263 (82.2)	1.54 (1.03, 2.31)	0.04	—	—
AGA	74 (13.9)	459 (86.1)	1	—	1	—
SGA[6]	15 (23.4)	49 (76.6)	1.69 (1.02, 2.78)	0.04	1.57 (0.99, 2.49)	0.05
Nasogastric tube feeding						
No nasogastric feedings	54 (13.8)	337 (86.7)	1	—	1	—
<1 wk	8 (11.1)	64 (88.9)	0.80 (0.39, 1.63)	0.54	0.75 (0.35, 1.58)	0.45
1–2 wk	13 (16.7)	65 (83.3)	1.21 (0.68, 2.13)	0.51	1.22 (0.70, 2.11)	0.49
>2 wk	12 (26.1)	34 (73.9)	1.89 (1.08, 3.30)	0.03	1.87 (1.07, 3.25)	0.03
Ventilation						
None/noninvasive respiratory support	79 (14.5)	466 (85.5)	1	—	—	—
Mechanical ventilation	10 (19.2)	42 (80.8)	1.33 (0.73, 2.41)	0.35	—	—

[1]AGA, appropriate for gestational age; BITSEA, Brief Infant and Toddler Social and Emotional Assessment; LMPT, late and moderately preterm; PARCA-R, Parent Report of Children's Abilities–Revised; SES, socioeconomic status; SGA, small for gestational age.

[2]Data were analyzed by using Poisson regression models with cluster sandwich estimators to account for the correlation in outcomes among multiple births. Multivariable analysis included behavior problems, delayed social competence, SGA, and nasogastric tube feeding.

[3]Cognitive impairment was defined as a PARCA-R Parent Report Composite score <2.5th percentile of the term reference group (Parent Report Composite score <35).

[4]Clinically significant behavior problems and delayed social competence were assessed by using the BITSEA and classified by using the test norms.

[5]SES index refers to socioeconomic risk category derived from a composite measure of 5 indexes of socioeconomic risk (see Methods).

[6]SGA was classified by using birth weight less than the third percentile for sex and gestation by using customized antenatal growth charts.

Nasogastric feeding during the neonatal period was more common among LMPT (32%) than term-born (2%) infants, as was mechanical ventilation (9% compared with 1%). In contrast with studies in very preterm infants (<32 wk of gestation) (4, 8), mechanical ventilation was not associated with the development of eating difficulties at 2 y of age, nor was exposure to nasogastric

TABLE 4
RRs for differences in clinically significant eating problems between LMPT and term-born infants after adjustment for neonatal and neurodevelopmental factors[1]

			Unadjusted		Model 1		Model 2	
	Term, *n*	LMPT, *n*	RR (95% CI)	*P*	RR (95% CI)	*P*	RR (95% CI)	*P*
Total feeding problems	726	597	1.57 (1.14, 2.16)	0.005	1.44 (1.01, 2.03)	0.04	1.20 (0.86, 1.66)	0.28
Refusal/picky eating	744	611	1.53 (1.03, 2.25)	0.03	1.30 (0.84, 1.98)	0.23	1.21 (0.80, 1.82)	0.37
Oral motor problems	749	612	1.62 (1.06, 2.47)	0.03	1.65 (1.05, 2.58)	0.03	1.26 (0.80, 1.96)	0.31
Oral hypersensitivity	756	619	1.39 (0.83, 2.33)	0.21	1.22 (0.69, 2.13)	0.49	1.01 (0.58, 1.73)	0.99
Eating behavior problems	738	616	1.15 (0.73, 1.78)	0.54	0.88 (0.53, 1.45)	0.61	0.73 (0.44, 1.20)	0.21

[1]Data were analyzed by using Poisson regression models with sampling weights to account for the oversampling of multiple births in the term control group and cluster sandwich estimators to account for the correlation in outcomes among multiple births. Unadjusted analyses are also shown in Table 2 but are presented again here to allow direct comparison with the results of models 1 and 2. Model 1 adjusted for sex, small for gestational age, socioeconomic status index score, and nasogastric tube feeding >2 wk. Model 2 adjusted additionally for behavioral problems, delayed social competence, and cognitive impairment at 2 y corrected age. LMPT, late and moderately preterm.

feeding per se. However, prolonged nasogastric feeding (>2 wk) was independently associated with later eating difficulties and may partly explain the association between LMPT birth and oral motor problems. The association of eating difficulties with prolonged nasogastric feeding was previously noted in a small study in LMPT infants and supports the present findings (16). We also found that LMPT infants were almost twice as likely as term-born infants to have been prescribed medicine for reflux by 2 y of corrected age, and this may contribute to the excess of oral motor problems observed in the LMPT population. However, it not possible to ascertain from our data whether this represents ongoing problems or prescription of antireflux medication during the neonatal period.

The strengths of this study lie in the collection of prospective geographical population-based data on early childhood outcomes. This is also the first study to our knowledge to assess eating difficulties in LMPT infants compared with term-born controls. However, we acknowledge that a response rate of ~60% may have affected our findings. In particular, infants whose parents did not respond to follow-up were at greater socioeconomic risk and of poorer health. Because these factors are associated with adverse neurodevelopmental outcomes, we may have underestimated the true prevalence of eating difficulties in the LMPT population. In addition, we excluded children with CP and NSI to explore the effect of preterm birth per se, which may underestimate the absolute prevalence of eating difficulties in this population. Outcome data at 2 y were collected by parent report, which was necessary given the size and geographical dispersion of the cohort to be followed up. Although well-validated parent report measures were used to assess outcomes in all domains, we were unable to carry out formal observations of eating behaviors or oral motor skills or to administer formal assessments of infants' cognitive and motor development. These data therefore represent parents' perceptions of their child's language, cognitive development, and eating behavior at 2 y of age rather than diagnoses obtained from clinical consultation or diagnostic tests. Although the measures used in the present study have been shown to have good validity and diagnostic accuracy, parent report questionnaires may result in over-referrals due to relatively low positive-predictive values. As such, future studies should seek to replicate these findings by using formal examiner-administered developmental tests and observations by speech and language therapists. In addition, it would be beneficial to explore early childhood eating behaviors after LMPT birth in association with measures of growth, which were not available in this cohort. Longer-term follow-up of this cohort will enable us to assess the predictive validity of parent-reported eating difficulties at 2 y for eating behaviors and growth in middle childhood.

In summary, infants born LMPT were at increased risk of oral motor problems and picky eating behaviors at 2 y of age compared with infants born at term. These were explained by the excess of neurodevelopmental and behavioral sequelae in this population. LMPT children who are exposed to prolonged nasogastric feeding and those with poor neurodevelopmental outcomes are at greatest risk of eating difficulties. Multidomain developmental screening may be beneficial in this population.

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