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ORIGINAL ARTICLE

Iron status, body size, and growth in the first 2 years of life

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Abstract

Rapid growth in infancy has been shown to adversely affect iron status up to 1 year; however the effect of growth on iron status in the second year of life has been largely unexplored. We aimed to investigate the impact of growth and body size in the first 2 years on iron status at 2 years. In the prospective, maternal-infant Cork BASELINE Birth Cohort Study, infant weight and length were measured at birth, 2, 6, 12, and 24 months and absolute weight (kg) and length (cm) gain from 0 to 2, 0 to 6, 0 to 12, 6 to 12, 12 to 24, and 0 to 24 months were calculated. At 2 years (n = 704), haemoglobin, mean corpuscular volume, and serum ferritin (umbilical cord concentrations also) were measured. At 2 years, 5% had iron deficiency (ferritin < 12 μg/L) and 1% had iron deficiency anaemia (haemoglobin < 110 g/L + ferritin < 12 μg/L). Weight gain from 6 to 12, 0 to 24, and 12 to 24 months were all inversely associated with ferritin concentrations at 2 years but only the association with weight gain from 12 to 24 months was robust after adjustment for potential confounders including cord ferritin (adj. estimate 95% CI: −4.40 [−8.43, −0.37] μg/L, p = .033). Length gain from 0 to 24 months was positively associated with haemoglobin at 2 years (0.42 [0.07, 0.76] g/L, p = .019), only prior to further adjustment for cord ferritin. To conclude, weight gain in the second year was inversely associated with iron stores at 2 years, even after accounting for iron status at birth. Further examinations of iron requirements, dietary intakes, and growth patterns in children in the second year of life in high-resource settings are warranted.

KEYWORDS

birth cohort, body size, iron status, length gain, serum ferritin, weight gain

1 | INTRODUCTION

Iron deficiency is the most common micronutrient deficiency worldwide (World Health Organisation, 2008). Infants and young children are at particular risk of iron deficiency and subsequent anaemia, with iron requirements per kilogram of body weight higher during this period than any other time of life (Domellof et al., 2014). Globally, it is estimated that 25% of preschool-age children have iron deficiency anaemia (McLean, Cogswell, Egli, Wojdyla, & De Benoist, 2009). In Europe, the prevalence of iron deficiency ranges from 3% to 48% and most investigators have reported the prevalence of iron deficiency anaemia below 5% (Eussen, Alles, Uijterschout, Brus, & Van Der Horst-Graat, 2015). Worryingly, iron deficiency with and without anaemia in early childhood has been shown to have long-term consequences for cognitive, motor, and behavioural development (Georgieff, 2011).

Term infants are born with iron reserves that can last for about the first 6 months of life, after which the infant relies heavily on iron intakes to meet the high iron requirements for growth (Agostoni et al., 2008). In the first year of life, a number of dietary factors can influence iron status, including the delayed introduction of appropriate complementary foods beyond 6 months (Agostoni et al., 2008; Chantry, Howard, & Auinger, 2007; Maguire et al., 2013; Wang et al., 2016). While in the second year, consumption of unmodified cows' milk as a beverage and low consumption of iron-fortified products has been associated with an increased risk of low iron status and iron deficiency (Gunnarsson, Thorsdottir, & Palsson, 2004; McCarthy et al., 2016; Uijterschout et al., 2014). The dietary transition, including replacing breast milk or infant formula with unmodified cows' milk as an important beverage, in conjunction with the rapid growth associated with this period, makes the second year of life an especially vulnerable period.

Associations between iron status, body size, and growth in the first year of life have been well documented. In high-resource settings, birth weight was positively associated with iron status at 1 year of age (Persson, Lundstrom, Lonnerdal, & Hernell, 1998; Sherriff, Emond, Hawkins, & Golding, 1999), while weight gain in infancy has been inversely associated with iron status at 1 year (Michaelsen, Milman, & Samuelson, 1995; Morton, Nysenbaum, & Price, 1988; Thorsdottir, Gunnarsson, Atladottir, Michaelsen, & Palsson, 2003). However, apart from a small Icelandic study (Gunnarsson et al., 2004), the relationship between iron status, body size, and growth in the second year of life in healthy children has been largely unexplored. Therefore, the aim of this study was to investigate the influence of body size and growth in the first 2 years of life, with a particular focus on the second year, on iron status at 2 years in apparently healthy children from a prospective birth cohort in Ireland. As iron status at birth has been shown to track through to early childhood (Georgieff, Wewerka, Nelson, & Deregnier, 2002; Hay et al., 2007), a secondary, novel aim of this study was to explore the effect of iron status at birth on associations between iron status, body size, and growth over the first 2 years of life.

Key messages

- The dietary transition, including replacing breast milk/infant formula with unmodified cows' milk as an important beverage, in conjunction with the rapid growth associated with this period, makes the second year of life an especially vulnerable period for iron deficiency.
- In this high-resource setting, weight gain in the second year of life was inversely associated with iron stores at 2 years in healthy children, even after accounting for iron status at birth.
- A specific examination of iron requirements, adequacy of dietary intakes and analysis of growth patterns in children in the second year in high-resource settings is warranted.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

Participants were recruited from the Cork BASELINE (Babies after SCOPE: Evaluating the Longitudinal Impact using Neurological and Nutritional Endpoints) Birth Cohort Study, which followed infants born to mothers in the Screening for Pregnancy Endpoints (SCOPE) Ireland pregnancy cohort. In SCOPE, low-risk, nulliparous women with a singleton pregnancy were recruited before 15-weeks gestation from Cork University Maternity Hospital, as part of an international multicentre pregnancy cohort study aimed at investigating early indicators of pregnancy complications (Kenny et al., 2014).

Written informed consent to the Cork BASELINE Birth Cohort Study was provided by the parents of participants; 1,537 infants recruited from the SCOPE study at 15-weeks gestation and 600 recruited at birth through the postnatal wards of Cork University Maternity Hospital (from 2008 to 2011). Participants were followed prospectively from birth, with assessments at day 2 and at 2, 6, 12, and 24 months. Study assessments at 5 years of age were completed in December 2016. Information was gathered by interviewer-led questionnaires and clinical assessments performed by trained researchers in accordance with the Declaration of Helsinki, with further information on study design and procedures reported previously (O'Donovan et al., 2015). Ethical approval for the Cork BASELINE Birth Cohort Study was granted by the Clinical Research Ethics Committee of the Cork teaching hospitals (ECM 5(9) 01/07/2008) and it is registered at the National Institutes of Health Clinical Trials Registry (www.clinicaltrials.gov NCT01498965).

Detailed dietary information was collected for all participants in assessments at age 2, 6, and 12 months, including information on early-feeding methods and complementary feeding. In this study, predominant breastfeeding refers to breast milk as the main source of nutrition but infants may have received infant formula "top-ups" at some stage (post-delivery awaiting the increase in milk volume or while mothers were on medication). At the 24-month assessment, food and nutrient intake data were collected in the form of a 2-day weighed food diary in a subgroup of the cohort. Parents were instructed to record detailed information about the amount and types of all foods, beverages, and supplements consumed during the diary period. Consumption data were converted to nutrient intake data using the nutritional analysis software Weighed Intake Software Package WISP© (Tinuviel Software, Anglesey, UK), as described (McCarthy et al., 2016).

2.2 | Anthropometric measures

Naked body weight was measured at birth and 2 months to the nearest 0.01 kg and 6, 12, and 24 months to the nearest 0.1 kg using a digital scales (seca 384, seca, Birmingham, United Kingdom). Supine length correct to the nearest 0.1 cm was measured at birth, 2, 6, and 12 months (seca 210) and at 2 years, standing height was measured using a wall-mounted stadiometer (seca 206). Body mass index (BMI) at 2 years was calculated, dividing weight (kg) by height (m) squared. Age- and sex-specific weight, length, and BMI standard deviation scores (SDS) were generated using LMS growth software and the UK-WHO 0 to 4-year growth reference data (Pan & Cole, 2007; Scientific Advisory Committee on Nutrition/Royal College of Paediatrics and Child Health, 2012). Absolute weight (kg) and length (cm) gain from 0 to 2, 0 to 6, 0 to 12, and 0 to 24 months was calculated as the difference between weight/length at each time point and birth weight/length and weight and length gain from 6 to 12 and 12 to 24 months was calculated as the difference between the two time points. Overweight and obesity at 2 years were defined using the UK-WHO age- and sex-specific BMI charts; overweight was defined as a BMI >91st and ≤98th percentile and obesity as a BMI >98th percentile (Scientific Advisory Committee on Nutrition/Royal College of Paediatrics and Child Health, 2012).

2.3 | Biological samples

Umbilical cord blood was collected at birth in infants recruited from the SCOPE pregnancy cohort study and venous blood was collected from all BASELINE Study participants at the 24-month assessment, whose parents provided consent. Ferritin and C-reactive protein (CRP, assessed using a high-sensitivity CRP assay) were analysed in umbilical cord and 24-month serum samples in the laboratory of the Cork Centre for Vitamin D and Nutrition Research, University College Cork, by immunoturbidimetric assay using the RX Monaco Clinical Chemistry Analyser (Randox Laboratories Ltd., Co. Antrim, UK). Haemoglobin and mean corpuscular volume (MCV) were measured in whole blood collected at the 24-month assessment by the Haematology Laboratory of Cork University Hospital on the Sysmex XE 2100 Automated Hematology System (Sysmex America Inc., IL, USA). Participants with potential infections/inflammation as indicated by an elevated CRP (>5 mg/L) were excluded from analyses.

2.4 | Statistical analysis

Data were analysed using IBM SPSS® for Windows™ version 21 (IBM Corp., Armonk, NY, USA). Descriptive statistics were generated and normal distribution of the data was examined by skewness/kurtosis. Comparisons between categorical variables were made using Chi square (χ^2) tests, while independent *t* tests or non-parametric tests were employed for continuous variables, depending on their distribution. Univariate and multivariate adjusted linear regression models were developed to estimate the influence of growth (weight/length gain) and body size (weight/length/BMI) variables on concentrations of haematological indices at 2 years. Factors identified in the univariate models as significant at the 10% ($p < .1$) level were retained in the final multivariate models. Potential confounders included in the final models were infant gender, birth weight, maternal age at delivery, education level, obstetric mode of delivery, duration of (any) breastfeeding (months), and mean daily iron intake (mg/day) at 24 months. As iron intakes were only available for a subgroup ($n = 278$), regression models were first adjusted for potential confounders without iron intakes and then iron intakes were included. Final adjusted results presented are from the models including iron intakes as a potential confounder as the results were similar both including and excluding iron intakes. Other early feeding methods, complementary feeding and maternal health characteristics during pregnancy (obesity/smoking/iron status) were not associated with any of the haematological indices at 2 years. To explore the effect of iron status at birth on associations between body size/growth and iron status at 2 years, final regression models were subsequently adjusted for cord ferritin concentrations, which reflect iron stores at birth (Macphail, Charlton, Bothwell, & Torrance, 1980; Siimes, Addiego, & Dallman, 1974). The residuals of the final models were normally distributed and associations were expressed as unadjusted/adjusted estimates and 95% confidence intervals (CIs); $p < .05$ was considered significant in final models.

3 | RESULTS

3.1 | Participants

Of those initially recruited to the Cork BASELINE Birth Cohort Study, 1,537 children attended the 24-month assessment and 47% ($n = 729$) of those provided a blood sample. Children born premature (<37 week gestation, $n = 25$) were excluded for this analysis, giving a final sample size of 704. The children included in this study (Table 1) did not differ in any principal characteristics from the rest of the BASELINE Study cohort that attended the 24-month assessment but did not provide a blood sample.

The distributions of the haematological indices assessed at birth (only those recruited from the SCOPE Ireland study) and 2 years in study participants are presented in Table 2. Serum ferritin concentrations were positively correlated with MCV at 2 years ($r = .282$, $p < .0001$), but no significant correlations with haemoglobin concentrations were observed. Using World Health Organisation definitions, iron deficiency (ferritin <12 μg/L) was observed in 5% ($n = 31$) of children and five children (1%) had iron deficiency anaemia (haemoglobin < 110 g/L + ferritin < 12 μg/L) at 2 years. Using other commonly used thresholds for serum ferritin, 12 children (2%) had concentrations <10 μg/L (Bates et al., 2014) and 136 (21%)

TABLE 1 Principal characteristics of participants of the Cork BASELINE Birth Cohort Study with haematological indices measured at 2 years ($n = 704$)

	Median [IQR] or %
Maternal[a]	
Caucasian	99
Attended university/third level education	85
Relationship status, single	5
Mode of delivery, vaginal	71
Age at delivery (years)	32.0 [29.0, 34.8]
Child	
Gender, male	54
Birth weight (kg)	3.6 [3.3, 3.8]
Gestational age (weeks)	40.3 [39.3, 41.0]
Predominantly breastfed at hospital discharge	72
Predominantly breastfed at 2 months	32
Started complementary feeding (17–26 weeks)	78
24-month assessment	
Age (years)	2.1 [2.1, 2.2]
Weight (kg)	12.9 [12.0, 13.9]
Height (cm)	88.1 [86.2, 90.3]
BMI (kg/m^2)	16.7 [15.9, 17.6]
Mean daily iron intake (mg/day)[b]	6.2 [4.9, 7.8]
UK-WHO[c]—overweight	15
UK-WHO[c]—obese	7

Notes. BMI = body mass index; IQR = interquartile range; WHO = World Health Organisation.

[a]Maternal data collected at 15-weeks gestation unless otherwise stated.

[b]Data available in 278 participants.

[c]Scientific Advisory Committee on Nutrition/Royal College of Paediatrics and Child Health, 2012.

TABLE 2 Distribution of haematological indices measured at birth and 2 years in participants of the Cork BASELINE Birth Cohort Study

	n	Mean	SD	Median	10th centile	25th centile	75th centile	90th centile
Haemoglobin (g/L)	588	120.4	7.1	120.0	112.0	116.0	125.0	129.0
MCV (fL)	588	76.0	3.9	76.1	72.0	74.1	78.3	79.8
Serum ferritin (μg/L)								
Birth	379	238.8	136.4	187.5	84.6	133.4	387.1	429.3
2 years	647	24.6	16.7	19.9	13.4	15.4	27.2	39.4

Notes. MCV = mean corpuscular volume; SD = standard deviation.

had concentrations <15 μg/L (Capozzi, Russo, Bertocco, Ferrara, & Ferrara, 2010; Hay, Sandstad, Whitelaw, & Borch-Iohnsen, 2004) at 2 years.

3.2 | Body size

There were no significant differences in measures of body size (weight/length/BMI) at any time point between those with and without iron deficiency, iron deficiency anaemia, or with ferritin concentrations <10 or 15 μg/L at 2 years. The unadjusted associations between serum ferritin, haemoglobin, and MCV at 2 years and weight and length SDS from birth to 2 years from the univariate linear regression models are presented in Table 3 (associations with absolute weight and length are presented in Supplemental Table 1). Body size at birth, 2, 6 or 12 months was not associated with any haematological indices at 2 years. Weight and BMI at 2 years were inversely associated with serum ferritin; however, only the association with weight SDS was significant (adjusted estimate 95% CI: −2.84 [−3.58, −0.11] μg/L, p = .041) following adjustment for infant gender, birth weight, maternal age at delivery, education level, obstetric mode of delivery, duration of breastfeeding, and mean daily iron intake at 24 months in the final regression model. Weight and height at 2 years were positively associated with haemoglobin, although only the association with height (0.39 [0.07, 0.72] g/L, p = .018) and height SDS (1.54 [0.45, 2.63] g/L, p = .006) remained significant in the final adjusted models. To account for the effect of iron status at birth on the observed associations with body size measures, the final models were subsequently adjusted for cord ferritin concentrations. After this adjustment, none of the observed associations remained significant.

There were no significant differences in median [IQR] haemoglobin concentrations (120.0 [114.0, 124.0] vs. 120.0 [116.0, 125.0] g/L, p = .187), MCV (75.7 [74.3, 77.8] vs. 76.3 [74.1, 78.4] fL, p = .159) or ferritin concentrations (18.7 [15.1, 25.1] vs. 20.4 [15.5, 27.5] μg/L, p = .077) between those that were overweight or obese (n = 149) at 2 years and those that were not. There were also no significant differences in haematological indices when overweight and obesity were separated into two categories.

3.3 | Growth

Growth was assessed by absolute weight (kg) and length (cm) gain from 0 to 2, 0 to 6, 0 to 12, 0 to 24, 6 to 12, and 12 to 24 months. There were no significant differences in any growth measures between those with and without iron deficiency, iron deficiency anaemia, or with ferritin concentrations <10 or 15 μg/L at 2 years. Associations between serum ferritin, haemoglobin, and MCV at 2 years and growth measures from birth to 2 years from unadjusted linear regression models are depicted in Table 4. Weight gain from 6 to 12, 0 to 24, and 12 to 24 months was inversely associated with ferritin and positively associated with haemoglobin at 2 years. Weight gain from 12 to 24 months was also inversely associated with MCV. Following adjustment for confounding factors (infant gender, birth weight,

TABLE 3 Unadjusted associations between serum ferritin, haemoglobin and mean corpuscular volume (MCV) at 2 years and weight, length and BMI standard deviation scores (SDS) from birth through to 24 months of age

	Serum ferritin (μg/L)		Haemoglobin (g/L)		MCV (fL)	
	Estimate [95% CI]	*p* value	Estimate [95% CI]	*p* value	Estimate [95% CI]	*p* value
Birth weight	−0.25 [−1.50, 1.00]	0.697	−0.46 [−1.02, 0.11]	0.116	0.22 [−0.09, 0.53]	0.165
Birth length	−1.04 [−2.30, 0.23]	0.107	−0.21 [−0.76, 0.33]	0.448	0.28 [−0.02, 0.58]	0.065
2-month weight	0.54 [−0.92, 2.00]	0.468	−0.47 [−1.14, 0.20]	0.170	0.36 [−0.02, 0.73]	0.063
2-month length	0.57 [−0.67, 1.82]	0.365	−0.12 [−0.68, 0.44]	0.673	0.42 [−0.11, 0.57]	0.089
6-month weight	0.28 [−1.07, 1.62]	0.688	−0.23 [−0.84, 0.38]	0.462	0.23 [−0.11, 0.57]	0.181
6-month length	−0.15 [−1.38, 1.09]	0.817	0.14 [−0.41, 0.69]	0.625	0.35 [−0.05, 0.65]	0.122
12-month weight	−0.04 [−1.49, 1.42]	0.959	0.16 [−0.51, 0.82]	0.646	0.16 [−0.21, 0.53]	0.386
12-month length	0.06 [−1.17, 1.28]	0.929	0.21 [−0.35, 0.76]	0.463	0.39 [−0.08, 0.69]	0.113
24-month weight	−1.46 [−2.86, −0.06]	0.041	0.78 [0.14, 1.42]	0.017	−0.09 [−0.45, 0.25]	0.582
24-month length	−0.35 [−1.66, 0.97]	0.605	0.92 [0.34, 1.51]	0.002	0.06 [−0.26, 0.39]	0.703
24-month BMI	−1.33 [−2.74, 0.08]	0.055	0.03 [−0.62, 0.67]	0.933	−0.20 [−0.55, 0.16]	0.280

Note. BMI = body mass index; CI = confidence interval.

Data presented as unadjusted estimates [95% CI] from univariate linear regression analysis where 1 SDS was the unit of change.

TABLE 4 Unadjusted associations between serum ferritin, haemoglobin, and mean corpuscular volume (MCV) at 2 years and weight/length gain from birth to 2 years

	Serum ferritin (μg/L)		Haemoglobin (g/L)		MCV (fL)	
	Estimate [95% CI]	p value	Estimate [95% CI]	p value	Estimate [95% CI]	p value
Weight gain (kg)						
0–2 months	0.38 [−1.92, 2.68]	0.744	0.43 [−0.57, 1.44]	0.397	−0.15 [−0.71, 0.40]	0.592
0–6 months	−0.10 [−1.61, 1.40]	0.894	0.22 [−0.44, 0.88]	0.515	−0.18 [−0.54, 0.18]	0.333
0–12 months	−0.42 [−1.69, 0.84]	0.510	0.58 [0.01, 1.15]	0.049	−0.23 [−0.55, 0.09]	0.154
0–24 months	−1.16 [−2.06, −0.26]	0.011	0.61 [0.19, 1.02]	0.004	−0.22 [−0.44, 0.01]	0.059
6–12 months	−1.53 [−2.71, −0.34]	0.012	1.04 [0.48, 1.59]	<0.0001	−0.25 [−0.55, 0.06]	0.112
12–24 months	−2.92 [−4.62, −1.22]	0.001	1.03 [0.25, 1.80]	0.010	−0.43 [−0.86, −0.01]	0.049
Length gain (cm)						
0–2 months	0.82 [−0.13, 1.50]	0.089	0.15 [−0.15, 0.46]	0.328	0.08 [−0.09, 0.25]	0.351
0–6 months	0.13 [−0.47, 0.73]	0.667	0.22 [−0.05, 0.48]	0.107	−0.02 [−0.16, 0.13]	0.840
0–12 months	0.04 [−0.46, 0.55]	0.873	0.19 [−0.03, 0.41]	0.091	0.02 [−0.10, 0.14]	0.767
0–24 months	0.08 [−0.33, 0.49]	0.698	0.32 [0.14, 0.50]	0.001	−0.03 [−0.14, 0.07]	0.510
6–12 months	−0.19 [−0.88, 0.49]	0.572	0.06 [−0.24, 0.37]	0.692	0.02 [−0.15, 0.19]	0.791
12–24 months	0.15 [−0.51, 0.82]	0.653	0.44 [0.15, 0.74]	0.003	−0.14 [−0.31, 0.02]	0.094

Note. CI = confidence interval.

Data presented as unadjusted estimates [95% CI] from univariate linear regression analysis.

maternal age at delivery, education level, obstetric mode of delivery, duration of breastfeeding, and mean daily iron intake at 24 months), only the inverse association between weight gain from 12 to 24 months and ferritin concentrations remained robust (−4.33 [−7.36, −1.30] μg/L, p = .005). Length gain from 0 to 24 months and 12 to 24 months was positively associated with haemoglobin concentrations at 2 years and the association with length gain from 0 to 24 months remained robust (0.42 [0.07, 0.76] g/L, p = .019) following adjustment. However, after subsequent adjustment for cord ferritin concentrations, only the inverse association between weight gain from 12 to 24 months and ferritin concentrations at 2 years (−4.40 [−8.43, −0.37] μg/L, p = .033) remained significant. Also when the children with serum ferritin concentrations <12 μg/L were excluded, this association remained significant in the children with normal iron stores only (−4.26 [−8.35, −0.18] μg/L, p = .041).

4 | DISCUSSION

This study has described associations between iron status, body size, and growth in the first 2 years of life in a large sample of healthy children from a well-characterised maternal-infant cohort with concomitant dietary, growth, and biomarker data collected prospectively throughout the first 2 years. The influence of growth and body size on iron status in the first year of life has been documented (Sherriff et al., 1999; Thorsdottir et al., 2003); however, explorations in the second year of life have been limited to a small (n = 71) Icelandic study that observed an inverse association between weight gain from birth to 2 years and serum ferritin concentrations at 2 years (Gunnarsson et al., 2004). To our knowledge, our data are the first to highlight the importance of the second year specifically, for iron status, with an inverse association between weight gain from 12 to 24 months and serum ferritin at 2 years observed in this healthy cohort. This observed inverse association is not unanticipated; the high growth rate, often combined with inadequate dietary iron intakes during this period, results in iron being transferred from the storage sites to support erythropoiesis and provide the iron necessary for growth (Domellof et al., 2014; World Health Organisation, 2001).

This is also the first study to show that the inverse association between weight gain in the second year and ferritin concentrations was robust after accounting for iron status at birth. The iron endowment at birth has been suggested to provide the iron necessary for growth in the first months of life; therefore, the larger the iron stores at birth, the greater the protection an infant has from the iron burden associated with growth in infancy and early childhood (Ziegler, Nelson, & Jeter, 2014). Our novel findings suggest that although large-iron stores at birth have a protective effect against low-iron stores in infancy, this protection may not extend into the second year of life. This reduced endogenous protection, in combination with the dietary transition from breast milk or infant formula to unmodified cows' milk as an important beverage, a product known to adversely affect iron status (McCarthy et al., 2016; Uijterschout et al., 2014), further consolidates the importance of closely examining dietary requirements and nutritional status in children in the second year of life. This examination is necessary to ensure that iron requirements in the second year are adequate to avoid deficiency and suboptimal or low iron status, yet not excessive, given the reported adverse consequences of excess iron for growth and infection risk in subgroups of the population (Domellof et al., 2014; Iannotti, Tielsch, Black, & Black, 2006).

We observed positive associations between height at 2 years and length gain in the first 2 years and haemoglobin concentrations at 2 years, prior to accounting for iron status at birth. This association appears to be biologically plausible given that to support the high iron requirements and expanding blood volume during growth in infancy, iron is taken from storage sites and prioritised towards erythropoiesis and the production of haemoglobin (Domellof et al., 2014). This is a potential explanation for the contrast in the positive associations with haemoglobin compared to the inverse associations with ferritin observed in this study; however, further research is required to fully clarify the relationship with haemoglobin concentrations. Associations between height/linear growth and iron status have been reported, with iron deficiency implicated as a cause of stunting in children in low-resource settings (Bougle, Laroche, & Bureau, 2000). Adults with hereditary hemochromatosis, an autosomal recessive iron-overload disorder (Pietrangelo, 2004), have been reported to be taller than the healthy population, with some authors suggesting that people with the condition may benefit in their first 2 decades from constantly enhanced iron absorption, providing a sufficient supply of iron for linear growth (Cippà & Krayenbuehl, 2013).

Weight status has been shown to influence iron status, with overweight children almost twice as likely to be iron deficient than children that were not overweight (Brotanek, Gosz, Weitzman, & Flores, 2007; Nead, Halterman, Kaczorowski, Auinger, & Weitzman, 2004). Potential explanations for this have included genetic influences, an inadequate diet, or physical inactivity, although animal studies have suggested altered iron metabolism and tissue distribution in overweight and obesity (Failla, Kennedy, & Chen, 1988; Nead et al., 2004). In contrast to studies in older children and adolescents, we observed no significant differences in concentrations of haematological indices at 2 years in those overweight or obese at 2 years. However, given the rising prevalence of overweight and obesity in young children worldwide, the potential adverse effects of overweight and obesity on iron status in early childhood warrant further investigation.

The prospective, longitudinal design of the Cork BASELINE Birth Cohort Study, with multiple anthropometric measurements throughout infancy and early childhood, has enabled this detailed exploration of associations between iron status, body size, and growth in early childhood. The generalisability of our results may be limited, given the region-based recruitment of the cohort; however, findings are generalisable to other healthy, low-risk maternal-infant populations. Exploration of associations between iron deficiency anaemia and body size and growth were somewhat limited by the small number of children with iron deficiency anaemia, however in this high-resource setting, our purpose was to investigate associations between individual haematological indices and growth indicators, as opposed to investigating malnutrition *per se*.

To conclude, in this low-risk, high-resource setting, weight gain in the second year of life was inversely associated with iron stores at 2 years in apparently healthy children, even after accounting for iron status at birth. This novel finding suggests that although large iron stores at birth have a protective effect against low iron stores later in infancy, this effect does not extend beyond the first year of life. Therefore, public health policies and dietary strategies aimed at preventing iron deficiency, and also suboptimal or low iron status in the second year of life are highly pertinent. Furthermore, a specific examination of iron requirements, adequacy of dietary intakes, and analysis of growth patterns in children in the second year of life in high-resource settings is warranted.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTIONS

EKM carried out data collection, database construction, and data analysis. EKM and MEK designed the study and drafted the manuscript. CníC carried out data collection. DMM is the overall principal investigator (PI) of the Cork BASELINE Birth Cohort Study, and JOBH, LCK, ADI, and MEK are co-PIs and specialist leads. LCK is the PI of the SCOPE Ireland pregnancy cohort study. All authors reviewed and approved the final submission.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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