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Infant fat mass and later child and adolescent health outcomes: a systematic review

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ABSTRACT

Objective Obesity and excess adiposity are leading causes of metabolic and cardiovascular morbidity and mortality. Early identification of individuals at risk is key for preventive strategies. We examined the relationship between infant body composition (0–2 years of age) and later (>2 years) health outcomes using a systematic review.

Design We preregistered the study on PROSPERO (ID 288013) and searched Embase, PubMed and Cochrane databases for English language publications using the Medical Subject Headings (MeSH) terms 'infant' and 'body composition' and 'risk' between January 1946 and February 2022. We included studies which assessed infant body composition using predetermined in vivo methods other than body mass index (BMI).

Results We identified 6015 articles. After abstract screening to assess eligibility, we reviewed 130 full text publications. 30 were included in the final assessment and narrative synthesis. Meta-analysis was not possible due to heterogeneity of results. All 30 studies were of high quality and reported associations between infant body composition and 19 different health outcomes after 2 years of age. Outcome measurements ranged from 2 years to 16 years. The strongest associations were found between infant fat mass and later fat mass (7 studies), and later BMI (5 studies). For 11 of the outcomes assessed, there was no relationship to infant adiposity detected.

Conclusions Current evidence, from a small number of studies, suggests a positive association between infant adiposity and future adiposity or BMI, but the validity of infant body composition as a biomarker of future health remains inconclusive. Carefully designed, standardised studies are required to identify the value of infant body composition for predicting later health.

Trial registration PROSPERO: 288013

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The association between infant body composition and later health outcomes is unclear.
⇒ Early identification of individuals at risk of later disease is key for preventive strategies to reduce mortality and morbidity.

WHAT THIS STUDY ADDS

⇒ The strongest associations were found between infant fat mass and later fat mass (seven studies), and later body mass index (five studies).
⇒ There are limited studies which assess other health outcomes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Carefully designed, standardised studies are required to identify the value of infant body composition for predicting later health.

INTRODUCTION

The importance of a child's first 1000 days, from conception to their second birthday, to long-term health outcomes such as non-communicable diseases (NCDs) has been widely discussed.[1 2] The Global Disease Burden report highlights that mortality and morbidity are highly attributable to NCDs, with both undernutrition and overnutrition playing fundamental roles.[3] The top four NCDs of global public health interest are cardiovascular disease, cancer, chronic respiratory disease and metabolic disease (type 2 diabetes and obesity). These account for about 74% of all NCD mortality and are associated with suboptimal early life conditions.[3 4]

It is of relevance to global public health to be able to identify groups or individuals at risk of developing NCDs, to allow for early detection and appropriate interventions to reduce risk of future disease, before ill-health is established. One of the measures used as a physiological marker of interest for adverse prenatal and early life exposures is infant adiposity, measured as the balance between accurate measures of fat-free mass (FFM) and fat mass (FM) (table 1). After infancy, FM is positively associated with risk of NCD and negatively associated with cognitive function in children.[5] In contrast, low FM, such as in growth-restricted infants is associated with poorer short-term outcomes, which especially, if followed by a period of compensatory rapid weight gain in infancy, can predispose to excessive visceral adiposity and associated adverse health outcomes.[6 7] Fetal (eg, gestational age, birth weight for gestational age, intrauterine environment), maternal (eg, diet, gestational diabetes, smoking status, placental function) and infant feeding (eg, type of milk feeding, complimentary food quality) factors can affect infant body composition.[8–11] As reviewed elsewhere, these factors are also associated with increased risk of cardiometabolic disease in adulthood.[12 13]

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Table 1 Predetermined in vivo techniques for measuring body composition included

	Description
Whole body adiposity measures	
Dual energy X-ray absorption (DXA)	Measures bone mineral mass calculated from the differential absorption of two different energy X-rays
Air displacement plethysmography (ADP)	Two-component model assessing mass and volume to estimate body density
Isotope dilution (hydrometry)	Assesses water distribution to estimate body composition (provides an estimate of fat-free mass)
Whole body MRI	Direct imaging technique to measure volume of adipose tissue
Bioelectrical impedance analysis (BIA)	Assesses electrical conductivity to estimate body fat percentage
Regional adiposity measures	
Regional DXA	As described above—provides regional estimates of abdominal adipose tissue
Regional MRI	As described above—abdominal MRI most commonly performed at level of L2/L3 to give an indication of abdominal adipose tissue
Abdominal ultrasound	Sound wave imaging technique to assess central adiposity—can give estimate of abdominal subcutaneous adipose tissue
Skinfold thickness	Measurement of regional subcutaneous fat
Abdominal circumference	Measurement of abdominal circumference—indication of abdominal adipose tissue

Adult body composition is strongly associated with many risk factors,[14] however, the association between infant body composition and later health outcomes is unknown. A systematic review by Bander *et al*[15] assessed the association between body composition in the first 5 years of life and later cardiometabolic diseases.[15] They found that low body mass index (BMI) in infancy and higher BMI in childhood seems to be associated with non-communicable disease in adulthood, however few studies measured body composition using validated methods, and instead used BMI.[16]

We hypothesise that actual infant body composition before a child's second birthday, measured by validated methods of body composition, is associated with later health outcomes. Adiposity in early life and its impact on later health outcomes are not straightforward to assess. FM accretion is sensitive to in utero and early life exposures, and changes with age and sex.[17] Human babies are born with much more adipose tissue compared with other mammals and infant body composition is complex. Previous work has reviewed the challenges in measuring infant body composition, with considerable variability between groups according to gestational birth age, length, weight and mode of feeding.[18]

The aim of this review was to evaluate the evidence of associations between infant body composition and later health outcomes, and identify gaps in the literature to help direct future research.

METHODS

This systematic review included studies that reported the association between infant body composition and subsequent health outcomes. This study was registered with PROSPERO (ID 288013).

Eligible studies were human studies published in English from January 1946 to February 2022, focused on measuring infant body composition using a predetermined in vivo method (table 1) and reported at least one health outcome after 2 years of age. Retrospective and prospective observational studies were included. Studies that focused on BMI as a measure of body composition in infancy, conference abstracts and other review studies were excluded. BMI was included as an outcome.

A comprehensive search of published articles in the Embase, PubMed and Cochrane (via Imperial OVID Medline) databases was performed. This study was conducted aligning with the PRISMA guidelines. The search used the following MEDLINE Medical Subject Headings terms: (((Infant) OR (Neonat*)) AND ((Body Composition) OR (fat mass)) AND ((Risk) OR (Predict*))). Search filters used were humans and abstracts available. We manually searched the bibliographies for pertinent studies.

Data extraction and quality assessment

Three independent investigators (LM, EP and FA) evaluated the studies for eligibility. Publications were double screened based on title and abstract screening then based on assessment of the full text using systematic review software Covidence under Imperial College London license.

Study data were extracted including general information, surname of the first author, the year of publication, study population, type of outcome and definition, study design timing of outcome evaluation, statistical method, and adjusted ORs or mean differences between the study groups by FA and LM. When adjusted ORs or risk ratios were not reported by the studies included, odds, risk or other measure of outcome were extracted for analysis.

Two researchers independently reviewed each article for methodological quality using the validated Joanna Briggs Institute (JBI) quality checklist for observational studies.[19] This tool was used to assess four domains with seven questions. Each study was rated as low (0–2), moderate[3–5] or high quality (>5). Inconsistencies in study inclusion, data extraction or quality assessment were resolved by discussion and consensus among the three researchers.

Data synthesis and analysis

A narrative synthesis of the findings from the included studies alongside summaries of exposure effects for each study with risk (for dichotomous outcomes) or standardised mean differences (for continuous outcomes) is presented. The impact of infant adiposity on reported outcomes is described for each paper and a table summarising the effects of infant body composition on each outcome created for an overview of the evidence.

RESULTS

Figure 1 presents a flow chart of the search. Initially, the search strategy resulted in 6014 articles. A further study was added through manual searching. Forty-three studies were excluded as they measured body composition using BMI, or they did not measure it in infancy. Thirty-four were removed due to incorrect study design (eg, narrative reviews, cross-sectional analyses and protocols). After abstract screening, 130 full-text publications were reviewed for eligibility and 30 were selected for inclusion.

A meta-analysis was not possible due to the heterogeneity of reporting. The studies often included multiple measures of exposures and multiple outcomes, making the clear grouping of change in OR based on infant adiposity difficult. Infant body composition, although measured in all the studies, was not always clearly linked to outcome in the analyses.

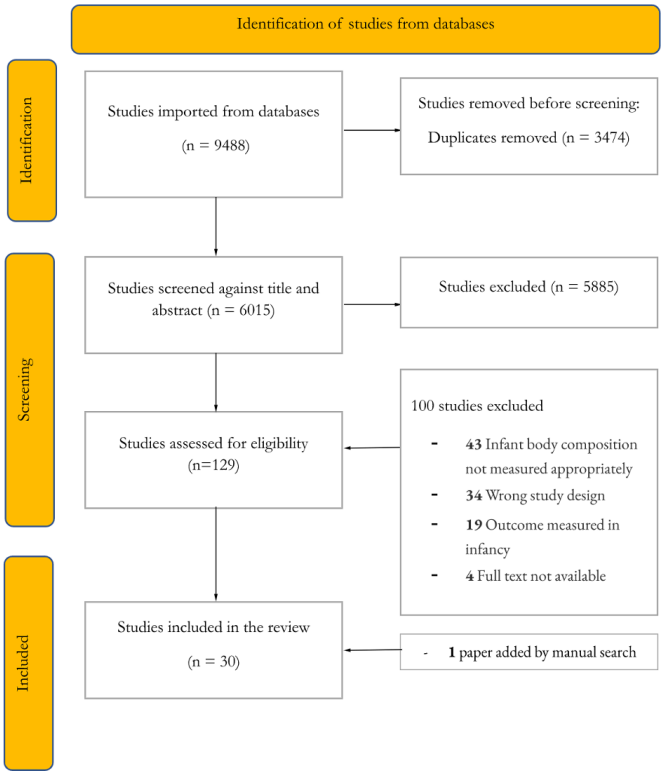

Figure 1 Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) flow diagram of study identification, screening and inclusion.

Since running the search, a study has been published on the topic which does report infant body composition and outcomes in a standardised way.[20] We have therefore taken this study into consideration in the discussion.

Identified studies

All studies were reported as being of high quality in the quality assessment (>5 score out of 7), making them low risk of bias. The number of included infants per study ranged from n=34 to n=9876, with a total n=20 975 infants included in the review. Most of the studies (24 out of the 30) measured infant body composition within the first 3 months of age. The age of outcome measurement spanned from 2 years to 16 years of age. Most of the studies were prospective cohort designs. There was heterogeneity in the methods used to measure infant body composition, and in the reporting of outcomes; for example, for body composition some studies reported FM at a specific timepoint, others reported FM accretion. Many of the studies investigated the association of several parameters with several outcomes. For example, Catalano *et al* reported on over 15 different outcomes.[21] Studies separately assessed male and female infants and mostly recruited healthy infants. The complete data extraction table can be found as web only data (see online supplemental table).

Despite the heterogeneity and complexity of the studies, some themes emerged (table 2). There was a relationship between increased infant adiposity and future anthropometry. From the nine studies that assessed the relationship between FM in infancy and later in life, six found a solely significant positive relationship and one found no significant relationship. Duncan *et al* found a mixed result; infant FM correlated with FM at 3 years, but not at 2 years.[22] Wibaek *et al* found no link with FM at birth but did find a link with FM accretion from 0 months to 3 months and later FM.[23] Santos *et al* also found that the association was dependent on age, with FM at 24 months but not 1.5 months associated with FM at 6 years.[24] There was a relatively consistent association between infant FM and later BMI, with higher FM in infancy associated with higher BMI in later life in five studies.

FM in infancy had some association with blood pressure; of the six studies that assessed blood pressure as an outcome, none showed a clear association other than Krishnaveni *et al*[25] Pfister *et al*'s[26] findings supported these but only when body composition was measured before 4 months.[27] Most of the other reported outcomes had no association with FM in infancy (table 2), although the number of studies assessing each outcome was even more limited.

Table 2 Overview of the associations between infant fat mass and later health outcomes and health biomarkers

Health outcomes	Fat mass/adiposity in infancy		
Outcome Variable	**Increase**	**No relationship**	**Decrease**
FM	7[35 22* 36 37 38 26 39]	3[22** 6† 40]	
FFM	1[6]	2[37 35]	
BMI	5[41 36‡ 26 42 40§]	3[36‡ 43 40§]	
Blood pressure	2[25 27]	5[44 25 24 6 27¶]	
T1DM		1[45]	
Adiponectin		1[22]	
Resistin		1[22]	
Leptin	1[22]		
Fasting glucose	1[25]	2[6 26]	1[37]
Insulin	1[25]	3[25 6 24]	
HDL	1[6]	1[24 26]	1[37]
C-peptide		1[6]	
HbA1c		1[6]	
LDL	1[6]	1[26]	1[24**]
Triglycerides		4[25 26 6 24]	
Total cholesterol	2[25 6]	1[26 24]	
HOMA-IR (insulin resistance)	1[25]	2[26 6]	
Lung function and asthma		1[46]	
Cognitive function/ processing speed		1[26 27]	
P100 Latency		1[27]	

*subscapular skin fold positively correlated with subscapular skin fold at 3 years, but not at 2 years of age.
†FM accretion in 0–3 months and 3–6 months were associated with higher FM at 5 years.
‡FM associated with BMI in girls but not boys.
§Subcutaneous FM was not associated with BMI at 6 years in boys but not in girls.
¶Associated with an increase in blood pressure until 4 months, thereafter no association.
**Although an increase in adiposity during infancy led to higher levels of LDL.
BMI, body mass index; BP, blood pressure; FFM, fat-free mass; FM, fat mass; HDL, high density lipoprotein; HOMA-IR, homoeostatic model assessment for insulin resistance; LDL, low density lipoprotein; T1DM, type 1 diabetes mellitus.

DISCUSSION

Higher FM in infancy was associated with higher FM and BMI at later ages in seven studies, but was not predictive of hypertension, hypertriglyceridaemia, cognitive function, or other cardiometabolic outcomes between ages 2 years and 16 years. No studies followed up cohorts longer than this. The interpretation of the results was limited by the heterogeneity of results, limited number of studies for each outcome, and lack of consistent reporting for infant FM and the health outcomes, which

precluded a meta-analysis. Carefully designed, standardised studies are required to confirm or refute the predictive value of infant adiposity for defined health measures, particularly into adulthood.

Bander *et al*'s systematic review on the association between early childhood body composition and long-term health outcomes also concluded similar findings, despite differing from ours in that it assessed body composition in the first 5 years of life.[15] They found a lack of studies with standardised measures of childhood body composition and adult health outcomes. They found that low BMI at birth and higher BMI in later childhood could be associated with poorer health outcomes in adulthood, aligning with the principles of the capacity-load model, which suggests that accelerated fat accretion is a factor to be further investigated.[28]

Infant FM and later body composition

Our findings suggest that infants with a higher FM at birth could be at higher risk of later high FM and obesity. Studies which measured FM at several time points from birth to second birthday show that body composition after 4 months may be a good indicator of later FM. Most studies show raised BMI is associated with increased FM in infancy. In future studies, it will be useful to differentiate visceral from subcutaneous FM as a marker of later health since the former is known to be associated with more unfavourable health.[29] In addition, the speed at which FM is gained seems to play an important role in later FM, so measuring FM accretion in the first months of life could be a more useful measure than a single cross-sectional measure.

The low number of included studies means there is insufficient evidence to draw conclusions about other cardiometabolic outcomes. Future studies that assess FM distribution and speed of FM accretion may look to address whether there is a difference in cardiometabolic outcomes for children who rapidly accumulate excess visceral fat from birth to second birthday, as a group who may be more at risk when considering the Developmental Origins of Health and Disease principles.[30–32]

Some strength and limitations are to be addressed. We conducted a comprehensive search strategy with 30 included studies and over 20 000 children with a diverse study population and high overall study quality. The studies reported on a variety of cardiometabolic health outcomes of interest for later health.

Several factors precluded a meta-analysis. The types of outcomes and the way the outcomes were measured differed between studies. We had 21 outcomes and of the similar reported outcomes, such as BMI, different papers used different measures including correlation, BMI z-score and BMI. Most of the studies did not include infant body composition as their primary exposure. This limits publication bias but made interpreting the association complicated. All the studies followed up cohorts to 16 years or younger.

Knowledge gaps and future work

Studies designed to assess the relationship between infant body composition and later health are needed, with a standardised approach in terms of exposures, outcomes and timeframes and consideration of potential interactions with sex.

There is a need to define ideal time points to measure infant adiposity as infant feeding, complementary feeding and catch-up growth results in body composition variations.[33 34] A baseline between birth and 4 months of age would coincide with immunisation visits when weight is already commonly measured, and would mean that environmental factors have not compounded the association. A second measurement at around 1 year of age would allow assessment of fat accretion. Once standardised body composition measures during infancy are in place, additional efforts to assess FM and FFM up to 2 years of age would be of value to assess their predictive value for future health outcomes. We suggest using skinfold thickness until other methods are more accessible, as this is currently the most accessible measurement method which can be more easily repeated to track changes over time.

Currently, no studies have followed infants across the life course. Therefore, it is unknown whether there is any association sustained into adulthood. Similarly, the association between infant body composition and outcomes that typically present in adulthood (eg, type 2 diabetes) have not been assessed. Modern technologies that accurately measure body composition in infants are only recently widely available. As other technological advances in assessing metabolic outcomes develop, our ability to address these knowledge gaps will increase.

Our review found higher FM in infancy was frequently associated with higher FM and BMI between ages 2 years and 16 years, but no evidence of other associations within this age cohort. We identify several gaps in the current literature, including the limited evidence on FM in infancy and later health outcomes, FM accretion in infancy and health outcomes, and certain body composition measurements. These findings highlight the need to standardise body composition measurements in infancy, track body composition over regular time periods and follow-up health outcomes into adulthood. Further understanding of the interplay between infant body composition and later health outcomes is needed to identify at-risk individuals, implement interventions and optimise health outcomes.

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