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## Review Article

# Systematic review of randomised controlled trials of interventions that aim to reduce the risk, either directly or indirectly, of overweight and obesity in infancy and early childhood

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## Abstract

The risk factors for childhood overweight and obesity are known and can be identified antenatally or during infancy, however, the majority of effective interventions are designed for older children. This review identified interventions designed to reduce the risk of overweight/obesity that were delivered antenatally or during the first 2 years of life, with outcomes reported from birth to 7 years of age. Six electronic databases were searched for papers reporting randomised controlled trials of interventions published from January 1990 to September 2013. A total of 35 eligible studies were identified, describing 27 unique trials of which 24 were behavioural and three were non-behavioural. The 24 behavioural trials were categorised by type of intervention: (1) nutritional and/or responsive feeding interventions targeted at parents of infants, which improved feeding practices and had some impact on child weight ( $n = 12$ ); (2) breastfeeding promotion and lactation support for mothers, which had a positive effect on breastfeeding but not child weight ( $n = 5$ ); (3) parenting and family lifestyle ( $n = 4$ ); and (4) maternal health ( $n = 3$ ) interventions that had some impact on feeding practices but not child weight. The non-behavioural trials comprised interventions manipulating formula milk composition ( $n = 3$ ). Of these, lower/hydrolysed protein formula milk had a positive effect on weight outcomes. Interventions that aim to improve diet and parental responsiveness to infant cues showed most promise in terms of self-reported behavioural change. Despite the known risk factors, there were very few intervention studies for pregnant women that continue during infancy which should be a priority for future research.

**Keywords:** infancy, prevention, obesity, overweight, intervention.

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## Introduction

Worldwide, more than 40 million children under the age of 5 were overweight or obese in 2011 (World Health Organization 2013). Over a fifth (22.6%) of UK children aged 4–5 years who were measured in 2012/2013 were either overweight or obese (Health and Social Care Information Centre 2013), with the highest rates found in children living in economically deprived areas and children from Black or Black British, Asian or Asian British ethnic groups (Health

and Social Care Information Centre 2013). As a child's weight at 5 years of age is a good indicator of future health (Gardner *et al.* 2009) and risk of obesity in adulthood (Dietz 1998), there is a strong case for early intervention that prevents or reduces the risk (National Institute for Health and Clinical Excellence 2006; Darzi 2008). The risk factors for childhood overweight and obesity are known and can be identified antenatally or during infancy. A systematic review identified significant associations between childhood overweight and maternal pre-pregnancy overweight,

smoking during pregnancy, high infant birthweight and rapid weight gain (Weng *et al.* 2012). Estimates vary, but between 25% (Ekelund *et al.* 2006) and 33% (Hui *et al.* 2008) of infants gain weight more rapidly than is desirable during the first 6 months of life and this is a strong risk factor for the development of childhood obesity (Baird *et al.* 2005; Monteiro & Victora 2005; Ong & Loos 2006). From the infant perspective, rapid weight gain may be modifiable with interventions targeting parental feeding practices. For example, a meta-analysis found breastfeeding decreased the odds of childhood overweight by 15% (Weng *et al.* 2012). There is no systematic review evidence regarding the protective effects of later introduction of solid foods and longer durations of breastfeeding on childhood overweight (Weng *et al.* 2012). However, single studies have found significant associations between early introduction of solid foods (Sloan *et al.* 2008; Hawkins *et al.* 2009; Huh *et al.* 2011), shorter breastfeeding duration (Weyermann *et al.* 2006), higher energy intake (Ong *et al.* 2006), shorter sleep duration (Taveras *et al.* 2008), high maternal control over feeding (Farrow & Blissett 2006), sedentary lifestyle (Brophy *et al.* 2009) and the risk of childhood obesity. Responsive feeding (DiSantis *et al.* 2011) may be protective against childhood obesity.

Despite the epidemiological evidence and calls for prevention strategies targeting multiple risk factors that begin at birth (Dattilo *et al.* 2012), the majority of effective interventions are designed for older children (Waters *et al.* 2011). Hesketh & Campbell (2010) conducted a systematic review of obesity prevention

interventions for children under 5 years of age. They identified five interventions for children under 2 years, all of which reported limited positive impact on feeding practices but not weight outcomes (Hesketh & Campbell 2010). This finding may be at least partially attributed to the focus of the review, which excluded some interventions that potentially modify rapid weight gain such as breastfeeding. It is clinically important to explore whether interventions exist that directly or indirectly address known risk factors (Weng *et al.* 2012) and to examine the impact of these interventions on the development of childhood overweight or obesity. This systematic review includes studies describing randomised controlled trials (RCTs) of interventions that aim to address the risk factors for childhood overweight and obesity identified in an earlier review by the authors (Weng *et al.* 2012). Interventions that commenced antenatally or during the first 2 years of life with outcomes reported from birth to 7 years of age are the subject of this review.

## Methods

### Inclusion/exclusion criteria

The inclusion criteria were:

#### Study design

Prospective studies that identified themselves as RCTs were considered for inclusion. No restriction was placed on geographical location or setting of the intervention programme.

### Key messages

- The most promising obesity prevention interventions for children under 2 years of age are those that focus on diet and responsive feeding.
- Although the number of published studies on obesity prevention interventions for children under 2 years of age has risen exponentially since 2010, interventions for pregnant women with follow-up during early life are rare. This should be a priority for future research.
- Future interventions for obesity prevention in children under 2 years of age should consider the option of advising some families to offer lower protein formula milk together with behavioural change components.
- Future intervention development should explore the most appropriate behaviour change theory to use with parents of young children.

### Participants

The participants were pregnant mothers, parents (carers, guardians) of infants <2 years old and healthy infants <2 years old.

### Intervention

Behavioural and non-behavioural interventions were included in this review.

### Comparison

Studies with any type of comparison group were eligible for inclusion.

### Primary outcomes

The primary outcomes were infant/child body mass index (BMI), weight, weight gain velocity, weight-for-length and weight-for-age from birth to 7 years of age.

### Secondary outcomes

Secondary outcomes were breastfeeding uptake and duration, timing of introduction of solid food, diet intake and quality, responsive feeding practices and physical activity from birth to 7 years of age.

Studies were excluded if the intervention commenced when the infant was 2+ years of age. Studies of interventions which aimed to increase the weight of infants (e.g. in malnourished infants or low-birthweight infants) were excluded. Studies that selectively recruited infants with specific conditions or diseases at the time of the study (e.g. chronic diarrhoea, diabetes, sustained high-blood pressure) were also excluded.

### Search strategy

A full electronic search was carried out in August 2012 and updated in September 2013. Six electronic databases (PubMed, Medline, CINAHL, PsychINFO, Cochrane, EMBASE and the Cochrane Library) were identified and searched for articles published from

#### Box 1. Search terms for review

1. child OR children OR infant OR newborn OR pediatric OR pre-school OR nursery OR nurseries or parent OR caregivers/education
2. 'body mass index' OR BMI OR 'weight gain' OR overweight OR obesity OR 'body fat' OR adiposity OR ponderal OR anthropometric OR growth OR 'child development' OR 'body height' OR 'body weight' OR weight-for-age OR weight-for-length
3. nutrition OR 'complementary feeding' OR baby-led OR 'feeding interaction' OR 'formula feeding' OR 'formula fed' OR 'infant food' OR 'nutritional requirements' OR 'energy intake' OR diet OR 'diet therapy' OR 'feeding behavior' OR 'food preferences' OR 'breast feeding' OR weaning OR parenting OR 'health education' OR 'health facilities' OR 'health promotion' OR 'physical activity' OR exercise OR sedentary OR 'tummy time' OR sleep
4. prevention OR intervention
5. 'randomized controlled trial' OR RCT OR random OR 'control group'
6. [1 AND 2 AND 3 AND 4 AND 5]

1990 onwards. This was chosen as a cut-off because a scoping search could not identify trials of obesity prevention interventions in early childhood prior to this date. Full search terms are provided in Box 1.

Reference lists of articles identified using this strategy and of currently published systematic reviews were scanned to identify potential studies for inclusion in the review that may have otherwise been missed.

Two databases for the registration of clinical trials (<http://www.clinicaltrials.gov/> and <http://www.controlled-trials.com/>) were searched to identify any ongoing or unpublished research trials. An advertisement was distributed to members of the Association for the Study of Obesity (UK) to identify ongoing and/or unpublished studies or those published in the grey literature.

### Data extraction and synthesis

Two reviewers extracted the data from the included studies (SR and BE). Details collected included study characteristics, participants, intervention details, outcomes and quality assessment. The data extraction sheet is available as Supporting Information Table S1.

## Quality assessment

The Jadad scale (Jadad *et al.* 1996) was used to assess the quality of published clinical trials based on the description and appropriateness of random assignment, blinding and the flow of patients.

### Random assignment

Two points were awarded if assignment was explicitly stated as randomised (including the use of words such as randomly, random and randomisation) and the method to generate the sequence of randomisation was described and appropriate (table of random numbers, computer generated, concealed allocation, etc.). Otherwise, the trial scored zero points.

### Blinding

Non-behavioural trials were awarded two points if they were double-blinded where neither the person doing the assessments nor the study participant could identify the intervention being assessed, or if in the absence of such a statement the use of 'active placebos', 'identical placebos' or 'dummies' were mentioned. Behavioural trials were awarded one point if single-blinded (as behavioural trials are not possible to double-blind) where the person(s) collecting and/or assessing outcome data were blind to participants' group allocation, and the study assessed whether blinding had been a success. In all other cases, the trial scored zero points.

### Flow of participants

One point was awarded if the number and reasons for withdrawal in each group were stated. If there was no statement on withdrawals or the description of withdrawals was incomplete, the trial was awarded zero points.

In addition, internal validity (i.e. was the intervention delivered as planned) and external validity (i.e. how generalisable is the delivery of the intervention to other settings) were examined in accordance with the evidence-based behavioural medicine (EBBM) guidelines (Davidson *et al.* 2003) for studies on behav-

ioural interventions. Data were collected on whether trials on behavioural interventions reported (1) training of treatment providers; (2) supervision of treatment providers; (3) preferred treatment of choice of those investigating, providing and receiving the intervention; (4) treatment integrity; and (5) assessment of participants' adherence to study treatment. Studies scored one point for each of these criteria.

## Results

Figure 1 shows the flow diagram of the review process. Electronic searches identified 1784 titles and a further 27 were identified through other searches (see Fig. 1). Of these, 605 duplicate studies were removed. Two reviewers (BE and SR) screened 1206 titles and abstracts; of which, 1064 did not meet the eligibility criteria. The remaining 142 abstracts were eligible for full-text review. One full text study was translated from German to English (Jungmann *et al.* 2010). The 142 full-text studies were examined by at least two authors; of these, 107 did not meet inclusion criteria. The most common reason for exclusion was that the intervention was designed and delivered to a child older than 2 years of age. There were also a number of studies that met the inclusion criteria but on closer inspection it was revealed that the focus was on malnourished, underweight or low-birthweight infants rather than those with the potential to be overweight or obese. These studies were also excluded from the review. A total of 35 eligible studies were identified, describing 27 unique trials of interventions (24 behavioural and 3 non-behavioural).

Details of the main findings in relation to feeding and weight outcomes can be found in Supporting Information Table S2.

The interventions identified were heterogeneous and did not all directly target obesity risk during infancy. Interventions that met the inclusion criteria included those that tackled known risk factors, such as breastfeeding, but did not specifically focus on obesity prevention. Specific obesity prevention interventions and parenting interventions were identified and included in the review. The two reviewers proposed categorising the studies to reflect their intended outcomes. The proposed categories were discussed

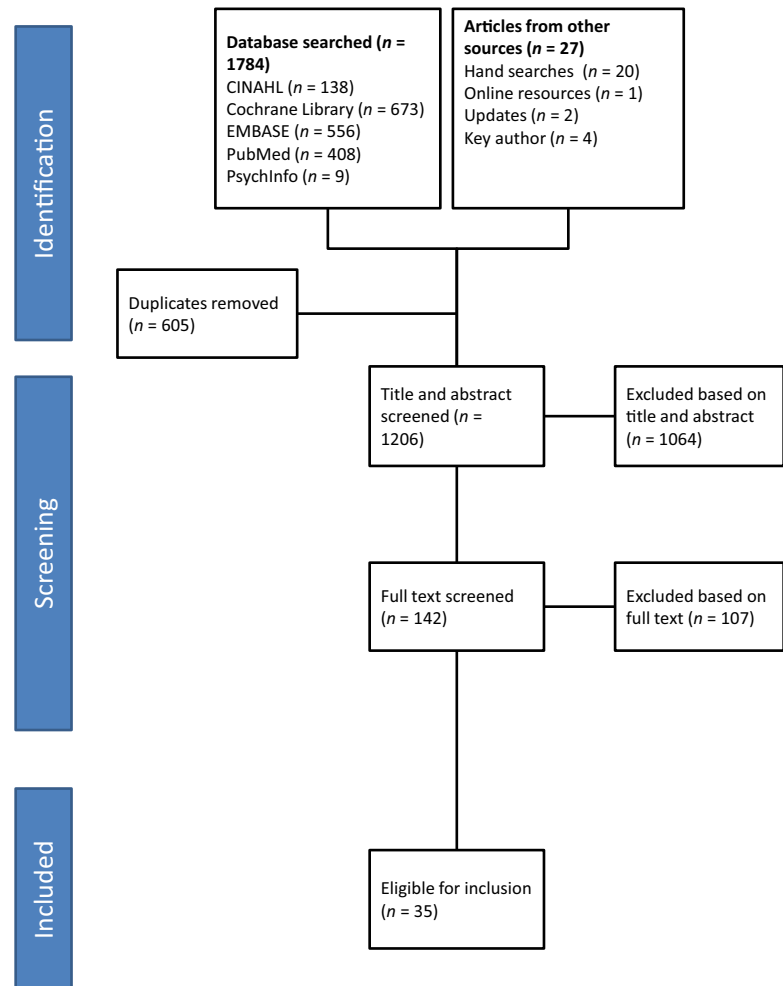


Fig. 1. Flow diagram of review process.

during a full team meeting, amended and agreed by all authors.

Trials of interventions that specifically addressed breastfeeding and lactation support were grouped separately from the diet and/or responsive feeding interventions. The reason for this was that these interventions emphasised improving uptake and duration of breastfeeding not obesity prevention. The diet and/or responsive feeding interventions included breastfeeding as a component but additionally addressed other aspects of infant feeding with outcomes focused on aspects of obesity prevention such as weight and parental feeding practices. The diet and/or responsive feeding interventions were considered distinct from the interventions that addressed

general parenting and lifestyle. These interventions had some outcomes associated with obesity prevention, such as infant weight, but mainly measured aspects of parenting. Specific interventions addressing maternal health with outcomes reported during infancy were grouped separately. The non-behavioural studies reported weight but not feeding outcomes and were therefore assigned to a separate category.

#### Nutritional and/or responsive feeding interventions

Sixteen studies reported the findings of 12 trials of diet, nutrition and/or feeding behaviour

interventions. These interventions were heterogeneous consisting of multiple components designed to improve energy intake and output and diet quality and/or feeding responsiveness. Four trials reported that the intervention had a significant impact on weight outcomes in the desired direction (Paul *et al.* 2011; Daniels *et al.* 2012; Wen *et al.* 2012; Verbestel *et al.* 2013). The most effective trials were either driven by behavioural change theory (Verbestel *et al.* 2013) or included diet, nutrition and parental responsiveness components (Paul *et al.* 2011; Daniels *et al.* 2012; Wen *et al.* 2012).

Seven interventions focused on parent education around diet and feeding practices (Lapinleimu *et al.* 1994, 1995; Watt *et al.* 2009; Scheiwe *et al.* 2010a; Wen *et al.* 2011, 2012; French *et al.* 2012; Jonsdottir *et al.* 2012; Campbell *et al.* 2013; Verbestel *et al.* 2013). In addition, these interventions included components to improve early physical activity (Wen *et al.* 2011, 2012) and reduce sedentary behaviours (Campbell *et al.* 2013; Verbestel *et al.* 2013). Only one of these interventions (Healthy Beginnings) was successful at improving the duration of breastfeeding (Wen *et al.* 2011, 2012), whereas most of the specific breastfeeding interventions reported this as a successful outcome (Morrow *et al.* 1999; Kramer *et al.* 2001, 2002, 2007; Bhandari *et al.* 2003; Agrasada *et al.* 2005; Bonuck *et al.* 2005; Agrasada & Kylberg 2009). The Healthy Beginnings home-visiting trial reported positive intervention effects on children's fruit and vegetable intake, along with others (Watt *et al.* 2009; Scheiwe *et al.* 2010a; French *et al.* 2012), and an increase in an aspect of physical activity known as tummy time (supervised infant laid prone on mat) (Wen *et al.* 2011, 2012). The Healthy Beginnings trial also reported that parents delayed the introduction to solid food following their intervention (Wen *et al.* 2011, 2012). The Melbourne Infant trial reported reductions in television watching (Campbell *et al.* 2013) and a trial by Verbestel reported reductions in screen time following their intervention (Verbestel *et al.* 2013). The Melbourne Infant trial reported a reduction in sweet snack intake (Campbell *et al.* 2013) and a trial by French reported a reduction in juice intake (French *et al.* 2012). Healthy Beginnings included an educational component around parent-

child interaction and the authors report a significant reduction in parents giving food as a reward (Wen *et al.* 2011, 2012).

Three of these studies report outcomes in contrast to the desired direction. Watt *et al.* (Watt *et al.* 2009; Scheiwe *et al.* 2010a) reported that the intervention group infants were heavier when compared with controls at follow-up. Although Verbestel *et al.* (2013) reported that their intervention had a positive impact on weight outcomes, dietary-related behaviours became less healthy in both groups over the study period.

Three interventions included components to help parents understand about responsiveness to infant cues as well as teaching them about diet and feeding. Infants receiving the NOURISH intervention (Daniels *et al.* 2012, 2013) had a significantly lower BMI-for-age z-score than those in the control group (intervention,  $0.23 \pm 0.93$ ; control,  $0.42 \pm 0.85$ ) at 9 months of age. The control group was also more likely to show rapid weight gain from birth to 9 months of age [odds ratio (OR) = 1.6, 95% confidence interval (CI) = 1.1 to 2.4]. Mothers in the control group were more likely to use non-responsive feeding practices that overrode child satiety signals ( $P < 0.001$ ). Although there were no significant differences in anthropometric measures between the groups at aged 2, the intervention group mothers had significantly fewer controlling feeding practices and exhibited more instrumental feeding and parental encouragement to eat (Daniels *et al.* 2013).

Black *et al.* (2001) also provided education around (1) recognition of infants' cues; (2) non-food strategies for managing infant behaviour; and (3) mother-grandmother negotiation strategies. Mothers in the intervention group were nearly four times more likely to adhere to the American Academy of Paediatrics guidelines on infant feeding (OR 3.8: 1.6–9.1) compared with mothers who did not receive the intervention. Kavanagh *et al.* (2008) delivered a behavioural intervention to formula-feeding caregivers in the Special Supplemental Nutrition Programme for Women, Infants and Children. The intervention, comprised information about infant satiety cues and formula milk preparation, only had a positive impact on parents' knowledge about feeding. Infants' growth

in the intervention group was greater than in the control group.

The SLIMTIME intervention (Paul *et al.* 2011) was delivered to 160 first-time mothers who intended to breastfeed. This intervention focused on responsive feeding rather than diet. A significantly slower rate of weight gain was reported for infants receiving 'soothe/sleep' intervention suggesting that educating parents of infants about responsive feeding may be more beneficial than dietary advice alone.

Finally, a unique study by Fewtrell *et al.* (2012) compared the weights of infants receiving one of two different types of bottle design with a breastfed reference group and found no significant differences in anthropometry at 2, 3 and 4 months post-partum.

#### **Breastfeeding promotion and lactation support interventions**

Seven studies reported the findings of five trials of breastfeeding promotion and lactation support interventions (Morrow *et al.* 1999; Kramer *et al.* 2001, 2002, 2007; Albernaz *et al.* 2003; Bonuck *et al.* 2005; Chapman *et al.* 2013). The majority of interventions demonstrated highly significant improvements in the outcomes assessed, which included uptake, duration and exclusivity of breastfeeding (Morrow *et al.* 1999; Kramer *et al.* 2001, 2002, 2007; Bhandari *et al.* 2003; Agrasada *et al.* 2005; Bonuck *et al.* 2005; Agrasada & Kylberg 2009), with two studies reporting significant improvements only in some of the outcomes assessed (Albernaz *et al.* 2003; Chapman *et al.* 2013). The PROBIT (Kramer *et al.* 2001, 2002, 2007) trial reported that infants in the intervention sites weighed significantly more at 1 month of age but this difference was not significant by the age of 12 months.

#### **Parenting and lifestyle interventions**

Four trials were identified that delivered broad parenting and health interventions, with infant feeding components, via home visiting. These interventions had a significant impact on feeding behaviours but overall, this type of intervention reported fewer improvements than those focusing exclusively on diet feeding. Johnson *et al.* (1993) provided peer mentoring for first-

time mothers via home visiting. Cow's milk was introduced significantly later to infants in the intervention group and they consumed significantly fewer inappropriate foods. The Miller Early Childhood Sustained Home-Visiting (MECSH) intervention also provided sustained and structured nurse home-visiting to improve parenting and family health (Kemp *et al.* 2011). Intervention infants were breastfed for significantly longer duration than controls. The MOMENTS trial (Cupples *et al.* 2011) delivered a home-visit intervention which aimed to reduce health inequalities for women living in socio-economically deprived communities of Northern Ireland. The intervention did not have an impact on breastfeeding or weight outcomes. PROKIND (Jungmann *et al.* 2010) found no effect of a home-visiting intervention to improve maternal mental health and child health on infant weight at 12 months of age.

#### **Maternal health interventions**

Three trials were identified where an intervention was delivered to a woman either antenatally or post-natally with outcomes that potentially had an impact on the infant. However, none of these interventions led to significant improvements in the infant's weight in the desired direction. Dewey *et al.* (1994) delivered an aerobic exercise intervention to breastfeeding women which had no impact on the volume or content of breast milk or on infant weight at 12 weeks. The INFAT trial (Hauner *et al.* 2012) found that the intervention resulted in prolonged gestation and that infants in the intervention group had higher birthweight ( $P = 0.019$ ), weight-for-length ( $P < 0.01$ ) and BMI ( $P < 0.01$ ) than infants in the control group. However, no differences in body weight were found at 6 weeks of age. Laitinen *et al.* (2009) evaluated an intervention starting in the first trimester of pregnancy which focused on counselling around a balanced healthy diet containing plant stanol ester products (e.g. soft margarine). There was no effect on infant weight at birth or over the first 12 months of life.

#### **Formula milk interventions (non-behavioural)**

Three studies (one trial; Koletzko *et al.* 2009; Socha *et al.* 2011; Escribano *et al.* 2012) investigated the



effects of providing infants follow-on cow's milk formula with lower or higher protein contents on weight gain. Weight gain velocity was significantly greater in the infants fed higher protein milk from birth to 6 months. Group differences were greatest at 12 months of age; infants fed with lower protein content formula had a significantly lower mean weight-for-age z-score, mean weight-for-length z-score and mean BMI z-score than infants who received higher protein content formula. At 24 months of age, infants who received formula with lower protein content had a weight-for-length z-score 0.2 lower (95% CI 0.06 to 0.34) than infants who received formula with higher protein content.

Two further trials investigated the impact of infant formula containing hydrolysed protein on growth (Rzehak *et al.* 2009; Mennella *et al.* 2011). Both found infants grew more slowly when fed hydrolysed protein formula. Infants who received the extensively hydrolysed casein formula in the GINI trial had significantly slower sex-adjusted BMI gains from 8 to 48 weeks of age, but not beyond (Rzehak *et al.* 2009). Mennella reported that infants fed with hydrolysate formula had significantly lower weight-for-age z scores from 3.5 to 7.5 months and significantly lower weight-for-length z scores from 2.5 to 7.5 months. The weight-gain velocity of infants fed with hydrolysed protein formula conformed to the World Health Organization (WHO) norms, whereas the weight gain velocity of infants consuming the cow's milk formula exceeded the WHO growth norms over the study period. This study was predominantly non-behavioural but some behavioural aspects were reported. In particular, infants fed with protein hydrolysate formula were satiated with less formula than those fed cow's milk (Mennella *et al.* 2011).

### Quality assessment

Quality assessment was undertaken by two reviewers (SR and BE). Each reviewer initially scored the papers separately and then they met to agree the ratings. Where there was disagreement, the two reviewers re-read the paper and justified their rating

to each other. The final ratings were agreed through further discussion. Full details about the quality assessment ratings can be found in Supporting Information Table S3.

Unsurprisingly, non-behavioural interventions scored higher on the Jadad scale than behavioural studies; but clearly, it is not possible to conduct double-blind behavioural studies. Thirteen trials were considered to have used an appropriate method of randomisation for the allocation of participants to experimental groups. Of the remaining trials, the method of randomisation was not described in enough detail in the study protocol or associated research articles to determine whether the method of randomisation was appropriate. Five trials were considered to have used an appropriate method of blinding and, where appropriate, had evaluated the success of blinding. All of these trials were of non-behavioural interventions. Behavioural interventions trials usually did not report if the blinding process had been evaluated, nor if it had been successful. Thirteen trials reported participants flow adequately. The remaining studies failed to provide adequate descriptions for study attrition. Quality problems were inconsistent between papers and the majority of trials had some limitations.

Internal and external validity of 24 behavioural intervention trials was assessed using the EBBM criteria. Descriptions of the training received by intervention providers in the delivery of the intervention varied considerably in the trials reviewed. Five trials (Kramer *et al.* 2001, 2002, 2007; Albernaz *et al.* 2003; Jungmann *et al.* 2010; French *et al.* 2012; Campbell *et al.* 2013) reported that the intervention was delivered by health care professionals (HCPs) (e.g. nurses, dietitians, consultants) who received additional training in intervention delivery. Two trials (Watt *et al.* 2009; Scheiwe *et al.* 2010b; Cupples *et al.* 2011) stated that the intervention was led by peer supporters or other voluntary workers after receiving training in the intervention. The intervention was delivered by HCPs without further training in four trials (Lapinleimu *et al.* 1994, 1995; Wen *et al.* 2011, 2012; Daniels *et al.* 2012, 2013; Jonsdottir *et al.* 2012). Two trials reported intervention delivery by trained personnel, but offered no details of their training or professional

status (Kavanagh *et al.* 2008; Hauner *et al.* 2012). Three trials did not state if treatment providers had been trained (Dewey *et al.* 1994; Laitinen *et al.* 2009; Paul *et al.* 2011).

Two trials (Albernaz *et al.* 2003; Cupples *et al.* 2011) reported on the level of supervision received throughout the study period by staff delivering the interventions. Intervention provider or participant preference for allocation to the intervention or control group was not specified explicitly in any of the trials reviewed. Dewey *et al.* (1994), however, reported the number of women who declined participation to avoid being assigned to the control group.

Adherence (i.e. whether or not the intervention was received by participants) was reported in 11 trials (Dewey *et al.* 1994; Lapinleimu *et al.* 1994, 1995; Kramer *et al.* 2001, 2002, 2007; Albernaz *et al.* 2003; Watt *et al.* 2009; Jungmann *et al.* 2010; Scheiwe *et al.* 2010b; Cupples *et al.* 2011; Paul *et al.* 2011; Wen *et al.* 2011; Daniels *et al.* 2012, 2013; Campbell *et al.* 2013). Adherence was typically monitored by recording the number of classes attended or home visits received. Five trials (Kavanagh *et al.* 2008; Watt *et al.* 2009; Scheiwe *et al.* 2010b; Cupples *et al.* 2011; Daniels *et al.* 2012, 2013; Campbell *et al.* 2013) indicated that attempts had been made to monitor whether the intervention had been delivered as planned. The majority of behavioural interventions lacked theoretical underpinnings and where theory was used this tended to focus on individual behaviour change rather than change at the environmental or system level. One trial used social learning theory (Black *et al.* 2001); one used social support (Watt *et al.* 2009; Scheiwe *et al.* 2010a); one used the health belief model (Wen *et al.* 2011, 2012); one used Kolb's experiential learning cycle (Kavanagh *et al.* 2008) and one used an information-processing, elaboration-likelihood, precaution-adoption process model (Verbestel *et al.* 2013).

## Discussion

### Main findings

This review identified interventions designed to reduce the risk of overweight and obesity from birth

to 7 years of age which included those that commenced antenatally and/or during the first 2 years of life. A wide range of heterogeneous interventions were identified, the majority of which were multi-component. Behavioural ( $n = 24$ ) and non-behavioural ( $n = 4$ ) interventions were tested in 27 trials and reported in 35 articles dating from 1994 to 2013. Twenty of these articles were published since Hesketh and Campbell's review in 2010 (Hesketh & Campbell 2010).

The finding that specific interventions that promote breastfeeding and lactation support were effective in improving the uptake and duration of breastfeeding has been previously established. There is strong evidence from systematic reviews that any antenatal breastfeeding education (peer counselling, lactation counselling and formal breastfeeding education) can increase uptake of breastfeeding and duration (Morrow *et al.* 1999; Lumbiganon *et al.* 2011). Epidemiological evidence suggests that any breastfeeding may be protective against the risk of childhood obesity (Weng *et al.* 2012) but none of the breastfeeding trials identified in this review reported a positive effect of the intervention on infant weight in the first 2 years of life. Nevertheless, breastfeeding-support interventions should be available to all women, particularly those whose infants may be at greater risk, e.g. those mothers who are overweight/obese.

The majority of multi-component interventions showed positive effects in relation to an aspect of infant diet or responsive feeding behaviours (Black *et al.* 2001; Paul *et al.* 2011; Wen *et al.* 2011; French *et al.* 2012; Campbell *et al.* 2013; Daniels *et al.* 2013). However, the NOURISH (Daniels *et al.* 2012, 2013) and Healthy Beginnings trials (Wen *et al.* 2011, 2012) appear to be more effective than the Melbourne Infant Trial (Campbell *et al.* 2013) and other trials that focused on diet and dietary practices (Lapinleimu *et al.* 1994, 1995; Watt *et al.* 2009; Scheiwe *et al.* 2010a; French *et al.* 2012; Jonsdottir *et al.* 2012; Verbestel *et al.* 2013). It is possible that the inclusion of components around parent interaction and responsiveness and adherence to behavioural change theory enhanced the positive impact for these trials. Future intervention developers may

wish to place more emphasis on these aspects particularly because the experimental psychology literature reports strong associations between maternal responsiveness and control over infant feeding in the development of childhood obesity (Farrow & Blissett 2006). Interventions specifically designed to build maternal self-efficacy around infant feeding, which combine behavioural components, such as responsive feeding and soothing strategies with specific dietary advice and anticipatory guidance around feeding behaviours, may lead to more sustainable changes. Further work is needed around the theory of behavioural change that might underpin the development of educational interventions for parents in this area.

Four trials reported that the intervention had a significant impact on weight outcomes in the desired direction (Paul *et al.* 2011; Daniels *et al.* 2012; Wen *et al.* 2012; Verbestel *et al.* 2013) but this effect was not present at later follow-up for one trial (Daniels *et al.* 2013). These small intervention effects may be due to sampling strategy rather than sample size. All the trials randomised groups of parents or prospective parents, whose infants may or may not have been at risk of developing childhood obesity, to preventative interventions. The consequence of this is that intervention effects may not translate to demonstrable changes in anthropometry in samples where many infants have a low risk of obesity.

Three non-behavioural interventions were identified which tested different types of formula milk. One trial reported that infants given higher protein cow's milk formula feed grew more rapidly, when compared with infants fed lower protein formula (Koletzko *et al.* 2009; Socha *et al.* 2011; Escribano *et al.* 2012). The authors have subsequently published a further paper which, although outside the remit of this review, demonstrates that infants fed with lower protein formula maintain their lower BMIs at school age (Weber *et al.* 2014). Although the formulas used in this trial were all within the normal prescribed formulation range, the higher protein formula milk was at the upper end of an infant's requirements. Two further trials reported slower infant weight gain in infants fed hydrolysed formula (Rzehak *et al.* 2009; Mennella *et al.* 2011). One trial reported infants had better

satiation with less formula when fed hydrolysed protein (Mennella *et al.* 2011).

All of the non-behavioural trials were all high quality and blinded both researchers and participants (parents) to intervention group. However, the issue of 'blinding' parents to different types of infant formula, where there is evidence that consumption could lead to higher or lower risk of obesity, is ethically questionable. Parents, as health care consumers, have a right to information about risk, however small, to enable them to make an informed choice about their infant's diet (Have *et al.* 2013).

### Clinical implications

There have been a number of calls for early prevention of childhood overweight and obesity (Institute of Medicine 2011; Laws *et al.* 2014). The findings of this review could potentially support the development of an early childhood obesity prevention strategy. The review identified a number of interventions some of which contained successful components. These components could form the basis of a multifaceted approach to obesity risk which has the potential to be individually tailored by the health professional and parent.

The findings of the non-behavioural trials suggest that there is merit in further exploring the option of recommending lower protein formula milk. However, the formula milks used for these trials are not the standard milks that are available for parents to purchase over the counter. Of those that are available to parents, 'follow-on' formula milks tend to have higher protein content than first-stage milks. Raising parents' awareness of the different constituents of formula milk and advising them to refrain from upgrading their infants onto follow-on or toddler milks may be prudent interventions in terms of reducing obesity risk. Although the evidence suggests that recommending hydrolysed protein may be beneficial for infants at risk of rapid weight gain, caution is needed. The authors of this review suggest that using formula derived from hydrolysed protein in the absence of medical need may have adverse implications, i.e. allergies. Furthermore, hydrolysed protein formula has a different taste from normal formula

and unless there is a medical need, parents may not wish to expose their infant to this.

Focusing support for obesity prevention on vulnerable families at greatest risk is another option. However, health professionals may find this difficult as they may perceive it to be stigmatising and fear it may jeopardise their relationship with parents (Redsell *et al.* 2010, 2013c). A debate is needed about the feasibility and acceptability of targeted vs. generic parental behaviour change interventions. Several tools are available that can identify infant obesity risk (Santorelli *et al.* 2013; Weng *et al.*; Weng *et al.* 2013), although these require feasibility testing prior to implementation in clinical practice. The team has developed the Infant Risk of Obesity Checklist (IROC) (Weng *et al.* 2013a) which, together with the findings from this review, has been incorporated into clinical guidelines for Public Health Nurses (UK health visitors) (Redsell *et al.* 2013a,b). The IROC tool and intervention strategies have been developed into an interactive, education programme for UK health visitors to use to facilitate discussions about obesity prevention with parents during routine home visits. The Proactive Assessment of Obesity Risk during Infancy (ProAsk) programme is delivered via digital technology and is currently being subjected to a feasibility trial, the results of which will be delivered in late 2016. Funding for this has been awarded by the UK Medical Research Council Public Health Intervention Development Scheme (MRC-PHIND PH01/14-15).

### Limitations

The majority of behavioural interventions were not underpinned by a theory of change and where a theory was applied, this tended to be social-cognitive in nature targeting the individual and/or family rather than the environment or health system. This approach is appropriate where individuals might be at higher risk but this was not the case for the majority of studies which recruited general samples. Trial quality (Jadad *et al.* 1996) was an issue for the behavioural interventions and whilst lack of blinding is inevitable for this type of intervention, it was disappointing that many studies failed to adequately describe their

randomisation method or attrition rates. Davidson *et al.* described five categories (training, supervision, preference, adherence and integrity) for assessing internal and external validity of trials of behavioural interventions (Davidson *et al.* 2003). Furthermore, although the interventions have been delivered by both trained volunteers and health practitioners, the majority of studies lacked sufficient detail to make valid conclusions about which might be most effective (Davidson *et al.* 2003). Reporting of participant adherence and fidelity of intervention delivery was variable and problems in these areas might explain the small effect sizes. Although not part of the EBBM criteria, this review also examined the application of behaviour change theory in the trials identified; for most interventions, this was underexplored and/or underreported. Intervention development for behavioural change in this area could benefit from greater attention to theory, supported by a robust trial design that includes the use of a checklist to ensure internal and external validity.

Two high-quality, systematic reviews of obesity prevention interventions delivered during early years have been published (Hesketh & Campbell 2010; Laws *et al.* 2014), one fairly recently (Laws *et al.* 2014). Both reviews broadly concluded that further research in this area is urgently needed. Although our review can only report the findings of completed intervention studies, there were a number of protocols of interest, e.g. Brambilla *et al.* (2010). Thirty-two ongoing RCTs that appear to have fitted the inclusion criteria were identified via the clinical trials registers (see Supporting Information Table S4). The findings of these studies may better inform strategies to prevent childhood obesity during infancy.

### Conclusion

This systematic review was broad in range in order to identify any important interventions which have the potential to prevent childhood obesity. Interventions that aim to improve parental feeding practices, including infant diet and parental responsiveness to infant cues, showed most promise in relation to behaviour change but not weight. The option of advising some

families to offer lower protein formula milk is worthy of further exploration if imbedded into a multi-component intervention together with behavioural change components. Despite the known risk factors for child obesity, there were very few intervention studies for pregnant women that continued during infancy. Further research by the team will explore the feasibility of intervention to prevent obesity during infancy.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

## Contributions

SR (Reviewer 2) led the study, drafted the original protocol, screened 1206 abstracts, read the full-text papers, checked the Jadad and EBBM scores, identified the ongoing trials and drafted the paper. BE (Reviewer 1) refined the original protocol, undertook the searches, screened 1206 abstracts, read the full-text papers, undertook data entry, checked the Jadad and EBBM scores, drafted the Supporting Information tables and drafted the results. SW advised the team about review procedures and helped with data presentation. JAS, CG, DN and ANS refined the protocol, screened abstracts where there was disagreement between the two reviewers, read the full-text papers and co-wrote the paper.

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## Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

**Table S1.** Data extraction sheet.

**Table S2.** Main findings in relation to weight and feeding outcomes.

**Table S3.** Quality assessment and process evaluation.

**Table S4.** Ongoing registered trials.