Physical activity interventions in early life aimed at reducing later risk of obesity and related non-communicable diseases: A rapid review of systematic reviews

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Abstract

Objective: To identify useful components of interventions aimed at prevention of childhood obesity and related non-communicable disease (NCD) which included physical activity, and which targeted any or all of four life-course stages: peri-conception; pregnancy; infancy and toddlerhood (0-23 months); early childhood (24-59 months).

Design & Methods: In May 2016, WHO Geneva searched the Cochrane Library and Pubmed for systematic reviews of interventions including physical activity to prevent childhood obesity or risk factors for obesity-related NCDs. Using a narrative synthesis, the efficacy of randomised controlled trials (RCTs) to alter energy balance outcomes (measures of weight status or body fatness) was characterised by life-course stage, study characteristics, intervention functions (as defined in the Behaviour Change Wheel) and level of the socio-ecological model (SEM) targeted. The quality of included systematic reviews was assessed.

Results: We retrieved 82 reviews from the WHO search, of which 23 were eligible for the present synthesis. The number of eligible studies by life-course stage was: 0 (peri-conception); 0 (pregnancy); 8 (infancy and toddlerhood, age 0-23 months; 7 RCTs; age); 37 (early childhood, age 24-59 months 30 RCTs;). Thus, there was a lack of evidence for physical activity interventions during peri-conception and pregnancy. Almost all relevant studies in the 0-23 month and 24-59 month life-course stages were multicomponent interventions (i.e. targeted physical activity, dietary and/or sedentary behaviours). Interventions with evidence of efficacy tended to target multiple levels of the SEM, with emphasis on parents; and extend over long periods. Effective intervention elements for early life obesity prevention included classes on parenting skills, alteration of the kindergarten playground, and financial incentives. Evidence from low-and middle-income countries was scarce and evidence for intervention effect on obesity-related NCDs was missing.

Conclusions: Future physical activity interventions in toddlerhood and early childhood aimed at prevention of obesity should adopt the characteristics typical of effective interventions identified by the present synthesis. There is an urgent need for more evidence on physical activity interventions set in low-and middle-income countries, and which target the peri-conception and pregnancy periods.

Introduction

There is increasing recognition of the opportunities for prevention of obesity which exist in early life (1,2). Emphasis on physical activity is also increasing, culminating in the landmark recommendations in the World Health Organization (WHO) Report on Ending Childhood Obesity (ECHO) in 2016 (1) that modifying physical activity and sedentary behaviour in early life should be central to obesity prevention and prevention of non-communicable diseases (NCDs). Higher maternal levels of physical activity before or during pregnancy, or higher infant and child levels of physical activity, might reduce later obesity risk either by a programming effect, and/or by the accumulation of effects across multiple stages of the life-course (2). The obvious potential mechanism for physical activity in obesity prevention is via energy expenditure and hence energy balance (2). Other less direct effects of physical activity on obesity risk have also been suggested. These indirect mechanisms include possible effects on: appetite regulation (3); later physical activity (due to associations between physical activity level across the life-course, or effects of physical activity on fundamental movement skill development, which might in turn influence later physical activity; 4); cognitive abilities relevant to energy imbalance (e.g. aspects of executive function such as impulse control which could influence energy intake; 5).

Despite the increasing emphasis on early obesity prevention using physical activity interventions, including the rapidly increasing number of randomised controlled trials (RCTs,2, 6) there is uncertainty over what policy and research interventions should actually consist of. For example, how to operationalise the WHO ECHO recommendation to promote physical activity in early life to prevent obesity is unclear. One reason for this lack of clarity is that the elements required for efficacious interventions have not been identified explicitly. The primary aim of the present study was therefore to conduct a rapid review of systematic reviews in order to identify elements of physical activity interventions in early life (peri-conception; pregnancy, infancy and toddlerhood, early childhood) with evidence of efficacy in childhood obesity prevention for incorporation into subsequent Healthy Life Trajectory Initiative (HeLTI) interventions (7), and potentially into any

future physical activity interventions aimed at obesity prevention which targeted early life. Specific research questions addressed by the present review were as follows:

1. Which 'intervention functions' (as defined in the Behaviour Change Wheel, **Table 1; 8)** were used in interventions with evidence of efficacy?
2. Which levels of the socio-ecological model were targeted?
3. What was the intervention duration?
4. What is the likely generalisability of these interventions?

Can useful models or 'case studies' be identified which would be particularly informative for development of the HeLTI interventions ?

Methods

Literature search and study selection

A literature search for systematic reviews of interventions to prevent overweight/obesity and risk factors for NCDs in children was conducted in the Cochrane Library and Pubmed by the WHO in May 2016. The search conducted by the WHO in Pubmed is provided in**Table 2** The WHO provided the present authors with a list of titles and abstracts of potentially eligible systematic reviews which focused on four stages of the life-course: females during peri-conception; pregnant women; children aged 0-23 months (referred to here as infants and toddlers); children aged 24-59 months (referred to here as early childhood). We obtained the full-text articles of 82 systematic reviews which included studies that contained a physical activity intervention component. We then assessed the eligibility of those systematic reviews.

Systematic reviews and primary studies were considered eligible for the present rapid review if they

- targeted one of the four life-course stages listed above,
- included physical activity modification in the intervention,

- compared the intervention with no treatment, active/alternative control, usual care, waiting list, attention control,
- used an outcome measure of infant or child adiposity (or a proxy for adiposity such as the BMI z-score), an NCD, or NCD risk factor from 6 months of age onwards. The rationale for this was to focus the present synthesis on interventions which had demonstrable effects on energy balance, since the primary aim was to inform obesity prevention interventions.

All study designs were considered eligible for the synthesis, but RCT evidence was regarded as the most informative. Exclusion criteria were as follows:

- Non-systematic reviews, i.e. reviews without a systematic search strategy, pre-defined study methodology and/or quality appraisal,
- Wrong population (for example, the general adult population and not women of reproductive age),
- Intervention focus was on treatment, rather than prevention (exercise for weight reduction in an already-overweight or obese population, or bariatric surgery),
- Reviews focusing on only pre-eclampsia, asthma, pharmacological interventions;
- Reviews of observational studies (e.g. prevalence studies);
- Reviews that focused on rare conditions, physical deformities, neurological defects or genetics only,
- Reviews where obesity/overweight was examined as a side effect or outcome of another condition or if it was examined as a contributing factor to other diseases;
- Reviews without primary studies reporting suitable child outcomes.

Data extraction and analysis

Three reviewers (AH, JG, SM) extracted data from primary studies from the evidence tables included in eligible systematic reviews. Data extraction from the original primary studies would have been preferred, but was not possible within the time/resource available, a problem common to many rapid reviews of systematic reviews . The inclusion/exclusion criteria described above were developed so as

to ensure a high degree of similarity in aims/focus between the questions addressed by the present rapid review and those addressed by the systematic reviews. A standardised data extraction template was developed and used by all reviewers. Extracted data were cross-checked by another reviewer (AM). Where primary studies were included in multiple systematic reviews, we used all sources for compiling relevant data of primary studies.

For the conduct of this narrative synthesis we followed the guidance by Popey et al (9). The synthesis process is summarised in **Figure 1**. By using the two synthesis tools 'moderator and subgroup analysis' and 'qualitative case description' (**Figure 1),** we sought to answer our five research questions. Systematic reviews considered eligible for the present study were synthesised separately for each of the four life-course stages: peri-conception; pregnancy; infants and toddlers (up to 23 months); young children (up to age 59 months). Two behavioural frameworks were used to guide the narrative synthesis process: the Behaviour Change Wheel and the Socio-Ecological Model. The Behaviour Change Wheel, developed by Michie et al 2009 (8) ''forms the basis for a systematic analysis of how to make the selection of interventions. Having selected the intervention function or functions most likely to be effective in changing a target behaviour, these can then be linked to more fine-grained specific behaviour change techniques (e.g. goal setting, self-monitoring)". The Socio-Ecological Model focuses on the interrelationships between individuals and the social, physical and policy environment (10). We applied this data synthesis strategy to RCTs to base the synthesis on evidence from the highest-quality study design.

Assessment of relevance and quality of evidence

We assessed the robustness of the narrative synthesis in three ways. First, two reviewers independently assessed the quality of the most highly relevant systematic reviews using the ROBIS tool (11). ROBIS was used first to provide a formal test of whether the eligible systematic reviews were highly relevant to the questions being asked in the present study, and then used to assess the quality of the highly relevant systematic reviews. Since the present rapid review was based so heavily on eligible systematic reviews, it was desirable to establish the quality and relevance of these reviews. Second, we assessed

the quality of outcomes using the GRADE tool (12). Finally, we reflected critically on the synthesis process as a whole (10).

Developing intervention recommendations based on the synthesis

Recommendations for HeLTI intervention development were made which focused on the specific research questions listed in the Introduction above, taking the quality of evidence into consideration, and the likely generalisability of interventions to low-middle income settings as these are crucial to the HeLTI initiative (7). Components of interventions associated with some evidence of efficacy are provided here, but further details, e.g. of extracted data, are available from the corresponding author. In addition, further details of case studies (see below) are available from the corresponding author on request.

Finally, a number of primary intervention studies emerged as being particularly informative for the intervention development process in HeLTI. These were identified as HeLTI 'case studies' if they had any or all of the following characteristics: were set in low-and middle-income countries (LMICs; hence might have highest generalisability to the HeLTI interventions); had evidence of efficacy on energy balance outcomes; included intervention elements which we found were associated with intervention efficacy (hence would be particularly important to HeLTI); described their intervention development process in great detail (hence would contain useful lessons for intervention development in HeLTI).

Results

Systematic review assessment

From the list of titles and abstracts of systematic reviews, provided by WHO, we identified and screened 82 potentially relevant full-text review articles. Of these, 23 were deemed eligible for inclusion in our present rapid review and we extracted primary studies and relevant data from these reviews.

Quality assessment of the 23 eligible systematic reviews indicated that only nine systematic reviews (13-21) were judged to be of highest relevance to the research questions of the present study, based on the formal assessment of relevance using the assessment tool within ROBIS (11).In summary, these nine reviews had research questions/aims with a high degree of similarity to the research questions of the current overview study. Despite the high relevance, all nine of these highly relevant systematic reviews were rated as being of high risk of bias, with frequent and consistent weaknesses across all four quality domains within the ROBIS tool **(**Supplement Table 1) and in order to widen the evidence synthesis we decided to consider evidence from all 23 of the systematic reviews identified as eligible, rather than just the 9 rated as 'highly relevant'.

Descriptive synthesis by life-course stage

Peri-conception. None of the systematic reviews met the inclusion criteria for the peri-conception stage, and so no primary study was available for data synthesis.

Pregnancy. No reviews and original studies reported data on infant (from 6 months) or child weight status or body composition outcomes.

Infancy and toddlerhood. Eleven eligible systematic reviews (including three highly relevant reviews) provided data on five cluster-RCTs (22-26), three RCTs (27-29), and one before-after trial (30). All of the eligible studies were multicomponent lifestyle interventions, i.e. the interventions targeted physical activity plus other behaviours (e.g. diet, sedentary behaviour). The outcomes reported by the primary

studies were BMI Z-score (22, 23, 25-27), obesity prevalence (28,29), BMI (28) and infant weight (24). None of the studies reported NCD risk factors, other than the measures or indices of adiposity mentioned above. Details of study characteristics are available in Table S2 of the Online Supporting Information.

Early childhood. Nineteen eligible systematic reviews provided data on 37 separate eligible primary intervention studies. Thirty-one primary studies (84%) were reported in the nine systematic reviews assessed to be of high relevance to the research question of the present study. Of the 36 primary studies, 20 were cluster-RCTs (31-50), 10 were RCTs (51-60), four were quasi-experimental controlled trials (61-64), and three before-after trials (65-67). Two studies were single-component physical activity interventions (31, 50), on targeted sedentary behaviour only (53). The remaining studies were multicomponent interventions. Eligible outcomes reported in RCTs were BMI z-score (31-41, 51, 53-57, 59), obesity prevalence (42, 51), BMI percentiles (42-44, 58), body fatness (35-37, 44, 45, 52), and BMI (46-49, 60). None of the studies reported NCD risk factors other than the measures or indices of adiposity mentioned above. Details of study characteristics are available in Table S3 (Online Supplementary Information).

Interpretative synthesis by life-course stage

Infancy and toddlerhood. There was no evidence that intervention functions that were educational and involved modelling components were associated with intervention efficacy for preventing an increase in BMI z-scores (**Table 3).** That is, both interventions with evidence of efficacy and those without evidence of efficacy included educational and modelling intervention functions. A commonly employed education strategy was the delivery of an "active parenting curriculum" on physical activity and diet. However, out of the four RCTs providing data on BMI z-scores, one effective study (25) included elements of training, enablement, and persuasion in addition to education and modelling functions **(Figure 2**). Mustilla et al. (25) included physical activity sessions with the child and parent (training), provided the option to attend exercise classes (enablement) and counselled on benefits of

physical activity and diet for health (persuasion). Besides the differences in intervention functions, inconsistencies in efficacy between studies can be explained by the marked differences in 'intervention dose' with longer counselling about lifestyle behaviour being more evident in the more effective compared to the less-effective interventions.

Early childhood. More intervention functions were employed in interventions targeting early childhood compared to interventions which targeted infancy/toddlerhood. There was moderate quality evidence of no beneficial intervention effect in 11 out of 16 studies for preventing an increase in BMI-z-scores compared to the control condition (**Table 4, Figure 3**). Non-effective studies appeared to employ more intervention functions compared to effective studies; thus, an increasing number of intervention functions was not obviously related to efficacy of the intervention. An intervention function used by non-effective studies only was 'enablement'; an intervention function to increase the means or reduce the barriers to behaviour change, targeting family and home environment level of the socio-ecological model. (**Figure 3**). For example, non-effective studies provided equipment or offered motivational interviewing.

It became evident though, that the link between efficacy and intervention function depends on how the intervention function is put into practice: **Table 5** provides examples of the same intervention function with difference practice examples in effective versus non-effective studies.

Both studies reporting findings on obesity prevalence (based on BMI) showed moderate quality evidence of beneficial intervention effects in favour of the intervention group (**Table 4).** In three out of five studies, there was evidence of beneficial effects of multicomponent interventions on *body fat* favouring the intervention. This might relate to the greater sensitivity of body fatness as an outcome rather than the content of the intervention (2). Overall, the quality of evidence for change in body fat was low (**Table 4**).

Case studies

In order to highlight characteristics of interventions which should be considered for inclusion in HeLTI physical activity interventions it was decided at the outset of the project to identify specific examples of interventions, referred to here as 'case studies' as noted above. No quantitative thesis of these case studies was possible or necessary here, and so a brief narrative synthesis, focusing on the relevance to the HeLTI interventions, is provided.

Two interventions addressed obesity prevention in infants/toddlers, both in high-income countries: the mother-infant intervention in Finland by Mustila et al (25) and the Childcare Centre-based intervention in Belgium by Verbestel et al (26). Both studies had evidence of intervention efficacy (improved BMI Z score relative to control groups) which is very difficult to achieve (as discussed below) and suggests they should be regarded as promising. The Finnish mother-infant intervention (25) is also of note because the intervention ran for a relatively long period (most of the infant's first year), and was relatively simple (see Supplement Table S2), so could potentially be adapted for use in at least some low-middle income countries. The Belgian intervention (26) was of interest because: it targeted both increased physical activity and reduced screen time; had parental involvement as well as being childcare centre based; was also a lengthy intervention; used an exemplary theory and evidence-based approach to intervention development which is described in great detail in the study publications and so could be used to develop HeLTI interventions.

Two interventions addressed obesity prevention in early childhood, both in childcare settings in high-income countries: Hip Hop to Health Junior (32,33) in the USA and Tooty Fruity Veggie in Australia (36,37). Both are noteworthy as case studies because: they have somewhat rare evidence of efficacy; were relatively long-term interventions, used interventions which could potentially be incorporated sustainably into childcare/early education settings in at least some low-middle income countries. The Tooty Fruity Veggie intervention was of note because it targeted improved fundamental movement skills as a way of mediating increased physical activity, and was based on an exemplary theoretically and empirically- based approach to intervention development described in some detail in study publications. The Hip-Hop-to Health Junior intervention is also of particular note because the

intervention was efficacious when set in kindergartens populated largely by families from one ethnic group, but not efficacious when used in kindergartens populated largely by another ethnic group (34), highlighting the importance of not taking intervention generalisability for granted across populations in HeLTI interventions and other future interventions.

Two intervention case studies were identified for LMICs, particularly important and novel because of likely generalisability to the HeLTI interventions and globally, and of interest because of the two distinct settings (in kindergarten; in health clinics). Hu et al (55) set their interventions in kindergartens in China, with 4-6 year olds. This intervention was noteworthy because it was particularly lengthy, and may be generalizable to kindergarten settings across much of the world. Martinez-Andrade et al (40) described a clinic based Mexican study of 2-5 year olds and their families which was valuable in that it focused on both physical activity and screen time , and that it demonstrated the importance of devoting intervention resource to ensuring a high degree of adherence to the intervention: efficacy was related to degree of family adherence to the intervention, and this has lessons for HeLTI and other future interventions.

Further details of the case study interventions are provided in Online Supplement **Tables S2, S3 .**

Discussion

Summary of findings and study implications

The present narrative synthesis provided little evidence which could be used to support the development of specific physical activity interventions for the life-course stages: peri-conception and pregnancy. Obesity prevention interventions might gain a great deal from targeting pre-conception and pregnancy, and targeting these periods for physical activity interventions should have important co-benefits, beyond obesity prevention (e.g. managing gestational weight gain and pregnancy and delivery related complications which are related to it; 2). We therefore suggest that this research gap be addressed as a matter of urgency. In fact, at least 14 intervention trials which targeted physical activity during pre-pregnancy and pregnancy were registered at the time of the present review (6), but had not reported on outcomes. The evidence base should therefore improve quite rapidly, though most of these registered trials were in high-income countries, in very high-risk study participants (overweight and/or obese pregnant women), and in many interventions physical activity was targeted along with other behaviours including diet.

Other papers in this HeLTI series provide some guidance on interventions which might usefully target those life-course stages, though focusing on behaviours other than physical activity. In addition, the general principles of intervention development which have been identified for the other life-course stages included in the present review should also apply to peri-conception and pregnancy, e.g. the importance of targeting multiple stages in the socio-ecological model, the importance of both involving parents in the intervention as well as targeting them for intervention , of ensuring adherence to interventions, and the likely benefit from interventions of longer-duration, lasting for around a year or more. In addition, very few interventions have targeted the policy/cultural/organisational environment to date . Our five research questions could only be answered in relation to two of the life-course stages we considered: infancy-toddlerhood and early childhood. No studies reported on the intervention effect of other NCD risk factors.

One important conclusion from our overview is that, despite an increasingly gloomy literature on the prospects for childhood obesity prevention interventions (68-70), our rapid review in fact found many published interventions with evidence of efficacy, though interventions effects were often modest and short-term. Multiple previous studies with promising outcome data could be considered to be useful models for HeLTI and other future interventions, notably the case study interventions trials highlighted in our overview. Our rapid review also found that interventions with evidence of efficacy tended to take place over lengthy periods of time, presumably because any intervention effects on energy balance were relatively modest (at least as measured by changes in crude proxies for energy balance such as BMI-for-age; 2), and required time to become manifest as body-weight related changes. Maximising the gains from interventions for early life obesity prevention may require that such interventions obtain a cumulative benefit by extending across multiple life-course stages, perhaps over all four stages of the life-course, which we set out to consider in the present study (2). One of the unique and major advantages of the HeLTI interventions over other early life intervention studies directed at obesity and NCD prevention is the intention to extend interventions over multiple stages of the life-course (HeLTI paper 1 in this series; 7). Future childhood obesity prevention interventions other than HeLTI, including future policy interventions as well as research interventions, might usefully consider such a long-term, multiple life-course stage approach, with interventions at each stage of the life course being part of an integrated approach to obesity prevention in early life (2). As noted in our previous critique of early childhood obesity prevention interventions (2) all of the interventions which would be considered for obesity prevention would be considered as good for other aspects of child health and development, with co-benefits, and so should be part of comprehensive systems of health promotion aimed at early life.

We found that the intervention functions which seem important to target in infancy-toddlerhood are training, enablement, and persuasion in addition to education and modelling, and in early childhood are education (classes on parenting skills), environmental restructuring (alteration of the playground), and

incentivisation (financial incentives). Individual level (child) interventions were most effective when the family (parents) were included as targets of the intervention and where the higher organisational/environmental level of the socio-ecological model (e.g. childcare centre) was also involved.

The generalisability of the intervention evidence to LMICs for which the HeLTI initiative is largely intended may be limited because the present synthesis was based on evidence largely from high-income, western, nations. The general principles of behaviour change interventions aimed at obesity prevention are probably at least broadly applicable to LMICs (71), but the specific content and delivery of intervention would need to be tailored to the circumstances in each individual setting. The lack of evidence from LMICs was not specific to this overview, and is a more general problem (2), but there is little evidence from recent registered intervention trials that the evidence base from LMICs will increase substantially in the near future (2) , despite the rapid increases in childhood obesity prevalence in many LMICs (1).

Comparisons with other evidence

By synthesising evidence on physical activity interventions, the present review was intended to complement the other reviews in the present series of HeLTI papers, specifically to support the intervention development in the HeLTI initiative by informing the physical activity content of future HeLTI interventions. Other reviews in the series had a focus on diet and multicomponent interventions. All of the various HeLTI reviews support recommendations made elsewhere, e.g. in the WHO Ending Childhood Obesity Initiative (1,73), that interventions should be multi-component The authors of the various HeLTI reviews worked independently and it is of note that they have reached some similar conclusions, e.g. in relation to the benefits of interventions which target a range of behaviours e.g. changes in physical activity, sedentary behaviour (notably screen time) and dietary behaviours, rather than just single behavioural targets. The HeLTI reviews on dietary interventions also concluded, as we did, that intervention effects are likely to be maximised when extended over a long period of time (73),

ideally over multiple stages of the life-course, with multiple small-medium effects hopefully producing larger cumulative effects (2).

In a previous critique of childhood obesity interventions during the 'first thousand days' we noted that in many previous intervention trials there was evidence of efficacy, usually in the form of small-modest effects, but these effects often attenuated over time once the interventions had ended (2). This evidence provides an additional argument for maintaining interventions over as long a period as possible, and extending them over multiple life-course stages in early life. Longer-term interventions should provide a greater buffer against the obesogenic environment which extends over the entire period of early life (2).

Our previous critique of obesity prevention intervention during the 'first thousand days' also found that in the vast majority of intervention trials crude proxies for energy balance/ body composition were being used as primary outcome measures, e.g. the BMI-for-age. While such proxies are simple, and practical, there is a great deal of evidence that more direct measures of body fat and fat-free mass are much more informative. In paediatric clinical trials for example, it has long been clear that interventions aiming to modify growth or body composition are much more likely to demonstrate effects if they have body composition outcomes, which are far more sensitive to changes in energy balance than crude proxies for body composition (74). The fact that a number of interventions considered in the present overview, including the case studies identified, found intervention effects despite using crude proxies as outcomes suggests that they were having real and possibly quite substantial effects on energy balance of children in the intervention groups. While body composition measurement may add complexity and cost to trials, the increased sensitivity to change is more informative and can permit the useful trade-off of permitting trials with smaller sample sizes (2). Studies of the aetiology of obesity in childhood also demonstrate the substantially increased sensitivity of body composition to detect effects not detectable with crude proxies for body fatness (75,76). One advantage of HeLTI intervention trials over previous literature is the intention to include measurement of body composition where possible, and this

advantage could also be considered by the wider obesity prevention research community beyond HeLTI.

Review and evidence strengths and weaknesses

Strengths of the present review included the fact that it was based on systematic reviews and the evidence base was tested formally for relevance and quality using the ROBIS tool (11). Moreover, we used a formal framework for the narrative synthesis considering intervention functions as well as the socio-economic model for intervention implementation (10,11), which has not been used widely to date in obesity prevention research.

The main limitation of the present synthesis was that resource limitations meant that we were unable to refer to the original study publications and were restricted to extracting data from systematic reviews This problem is common in overviews of systematic reviews (77) particularly when these have to be conducted rapidly and/or with limited resource. The presented evidence is limited in that the evidence base consisted largely of multicomponent interventions (i.e. interventions which target physical activity and other behaviours). This means that the extent to which efficacy can be attributed to the physical activity component of interventions is uncertain, similar to the other HeLTI reviews in particular the diet intervention reviews (73). Identifying the effects of modifying individual behaviours/components in multi-component interventions is a major methodological and logistical challenge, but has been achieved in some obesity prevention interventions previously (e.g. Planet Health; 78), and HeLTI and other future obesity prevention interventions might usefully consider identifying which behavioural components are most and least responsible for any changes in energy balance induced by the intervention, in order to inform obesity prevention in the longer-term..

A further limitation in the present study is the extent to which the evidence base considered at the time the overview was being carried out reflects the evidence base today. The present study started with a

literature search in 2016 and our rapid review had to be carried out rapidly in the second half of 2016 in order to inform the intervention content of international HeLTI studies in early 2017. One issue is therefore whether or not newer intervention evidence might have arisen since 2016, and this might be particularly important for the evidence gaps identified by the present overview (interventions targeting peri-conception and pregnancy As noted above, many interventions which targeted these lifecourse – stages were underway (or at least registered) at the time of the present rapid review, but had not reported outcomes. While the evidence base inevitably goes out of date to some extent over time, one of the strengths of the present study is that it described the basis of the subsequent HeLTI interventions, and an understanding of the foundations of the HeLTI interventions should be of great value when, in future, the HeLTI outcomes are known.

One further limitation is recent changes not just in the evidence base, but in the paradigms used for obesity prevention. A paradigm shift towards the importance of early life in obesity prevention took place with the publication of the WHO ECHO and ECHO Implementation Reports in 2016 and 2017 (1,72). This shift was in part responsible for the HeLTI initiative, but the paradigm in physical activity specifically has undergone a further and even more recent shift beyond thinking of 'just' physical activity to thinking of the whole 24 hour period and time spent in the entire range of movement behaviours (sitting, screen time, standing, sleeping, moving around; 79) . New evidence based guidance for the 24-hour movement behaviours in the under 5s was published in Canada and Australia at the end of 2017, and by the end of 2018 the WHO should produce global guidance for these behaviours for the under 5s, largely as a response to the ECHO initiative. Modifying the 24-hour movement behaviours in early life is now seen as crucial to early life prevention of obesity (79), but this thinking was not well established at the time the interventions included in the present overview were being developed, and too recent to be influential on the intervention trials which are ongoing. This means that modification of some of the behaviours of importance to obesity prevention -notably sleep- has been neglected in the intervention evidence to date, and there has been little or no emphasis on the development and evaluation of interventions intended to shift the composition of the 24 hour day to a less obesogenic alternative. Future studies should begin to incorporate these paradigm shifts into their interventions.

Conclusions

The present study suggests that adherence to principles and practices of multi-level behaviour change should be helpful in the design of future research or policy interventions aimed at the early life prevention of obesity. Such interventions should: target multiple levels of the socio-ecological model, with a particular emphasis on parents and policy/organisational levels of the socio-ecological model; extend over long periods, ideally across several (all) stages of the early life-course; target physical activity in combination with diet and sedentary behaviour; use multiple intervention functions.

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Table and Figure Legend

Table 1: Intervention functions and their definitions, as defined by Michie et al (adapted from 8).

Table 2: Literature search strategy in PubMed

Table 3: Quality of evidence of the reported outcomes for interventions targeting infants and toddlers (0-23 months)

Table 4: Quality of evidence of the reported outcomes for interventions targeting early childhood (24-59 months)

Table 5: Examples of intervention functions in effective and non-effective interventions, Outcome: change in BMI z-score

Figure 1: Narrative Synthesis Framework Adapted from Popay et al (9)

Figure 2: Proportion (%) of intervention functions used in interventions targeting infants and toddlers (0-23 months) for effective (n=3) and non-effective (n=1) studies for changing BMI z-scores by level of socio-ecological influence.

Figure 3: Proportion (%) of intervention functions used in interventions targeting young children (24-59 months) for effective (n=5) and non-effective (n=11) studies for changing BMI z-scores by level of socio-ecological influence.

Table 1. Intervention functions and their definitions, as defined by Michie et al (adapted from 8).

Table 2: Literature search strategy in PubMed

systematic [sb]

AND

"Infant, Newborn"[Mesh] OR "Infant"[Mesh] OR "Child"[Mesh] OR "Child, Preschool"[Mesh] OR child [tiab] OR children [tiab] OR childhood [tiab] OR pediatric [tiab] OR paediatric [tiab] OR infantile [tiab] or infant [tiab] OR adolescent [tiab] OR adolescence [tiab] OR youth [tiab] OR youths [tiab])

AND

"Pediatric Obesity"[Mesh] OR pediatric obesity [tiab] OR paediatric obesity [tiab] OR adolescent obesity [tiab] OR obesity in adolescence [tiab] OR infantile obesity [tiab] OR child obesity [tiab] OR childhood onset obesity [tiab] OR obesity in childhood [tiab] OR infant obesity [tiab] OR childhood obesity [tiab]) OR ("Overweight"[Mesh] OR overweight [tiab]) AND ("Infant, Newborn"[Mesh] OR "Infant"[Mesh] OR "Child"[Mesh] OR "Child, Preschool"[Mesh] OR child [tiab] OR children [tiab] OR childhood [tiab] OR pediatric [tiab] OR paediatric [tiab] OR infantile [tiab] or infant [tiab] OR adolescent [tiab] OR adolescence [tiab] OR youth [tiab] OR youths [tiab]) OR ("Infant, Newborn"[Mesh] OR "Infant"[Mesh] OR "Child"[Mesh] OR "Child, Preschool"[Mesh] OR child [tiab] OR children [tiab] OR childhood [tiab] OR pediatric [tiab] OR paediatric [tiab] OR infantile [tiab] or infant [tiab] OR adolescent [tiab] OR adolescence [tiab] OR youth [tiab] OR youths [tiab])

AND

("Metabolic Syndrome X"[Mesh] OR insulin resistance syndrome x [tiab] OR metabolic x syndrome [tiab] OR metabolic syndrome x [tiab] OR dysmetabolic syndrome x [tiab] OR reaven syndrome x [tiab] OR metabolic cardiovascular syndrome [tiab] OR metabolic cardiovascular syndromes [tiab]) OR (("Diabetes Mellitus, Type 2"[Mesh] OR NIDDM [tiab] OR Maturity-Onset Diabetes [tiab] OR Maturity Onset Diabetes Mellitus [tiab] OR Noninsulin-Dependent Diabetes Mellitus [tiab] OR Non Insulin Dependent Diabetes Mellitus [tiab] OR Non-Insulin-Dependent Diabetes Mellitus [tiab] OR Non-Insulin-Dependent Diabetes Mellitus [tiab] OR Noninsulin Dependent Diabetes Mellitus [tiab] OR Adult-Onset Diabetes Mellitus [tiab] OR Adult Onset Diabetes Mellitus [tiab] OR Ketosis Resistant Diabetes Mellitus [tiab] OR Ketosis-Resistant Diabetes Mellitus [tiab] OR Slow-Onset Diabetes Mellitus [tiab] OR Slow Onset Diabetes Mellitus [tiab] OR Stable Diabetes Mellitus [tiab] OR Type II Diabetes Mellitus [tiab] OR MODY [tiab] OR Type 2 Diabetes Mellitus [tiab])

Table 3: Quality of evidence of the reported outcomes for interventions targeting infants and toddlers (0-23 months)

Quality assessment		Summary of findings
№ of participants (studies)	Overall quality of evidence	Impact
BMI z-score (follow-up: range 4 - 12 months)		
799 **(4 RCTs)**	⊕⊕◯◯ LOW	Both effective and non-effective studies included an educational element on infant feeding and physical activity as well as modelling strategies (Figure 2). Adding elements of training, enablement and persuasion resulted in lower BMI z-scores in the intervention group compared to control.
Obesity prevalence (follow-up: range 2 - 10 years)		
1729 **(2 RCTs)**	⊕⊕◯◯ LOW	The 2 studies reporting on post-intervention group differences of obesity prevalence appeared to be similar in their intervention approach and content. Based on the available data, it is not possible to determine the reason for the inconsistency in findings.

Table 4: Quality of evidence of the reported outcomes for interventions targeting early childhood (24-59 months)

Quality assessment		Summary of findings
№ of participants (studies)	Overall quality of evidence	Impact
BMI z-score (multicomponent studies) (follow up: mean 8 months)		
6910 (14 RCTs)	⊕⊕⊕◯ MODERATE	No evidence of a beneficial intervention effect in 11 out of 16 studies. No clear pattern of differences in intervention functions. Environmental restructuring to facilitate behaviour change was only effective in 1 of 4 studies. There was no evidence that studies including enablement strategies resulted in a reduced BMI z-score (Figure 3).
BMI z-score (physical activity-only studies) (follow up: range 6 to 8 months)		
855 (2 RCTs)	⊕⊕⊕◯ MODERATE	A beneficial intervention effect was associated with an intervention strategy that included aspects of coercion linked to physical activity sessions (training, Figure 3).
Obesity prevalence (follow up: range 8 to 12 months)		
1105 (2 RCTs)	⊕⊕⊕◯ MODERATE	Beneficial intervention effects can be achieved with physical activity-only interventions (with mandatory sessions) and interventions combining physical activity sessions with nutrition education for children and parents. The common variables between the interventions were: group physical activity delivered by childcare staff and an intervention duration >6 months.
BMI percentiles (follow up: range 4 to 12 months)		

499 **(3 RCTs)**	⊕⊕◯◯ LOW	There was evidence that multicomponent interventions employing different intervention functions and with different length in duration and setting can yield beneficial effects on change in BMI percentiles.
Body fat (follow up: mean 8 months; assessed with: skin folds and/or waist circumference, other)		
1608 **(5 RCTs)**	⊕⊕◯◯ LOW	There was evidence of beneficial effects of multicomponent interventions in 3/5 studies. Reasons for inconsistency are most likely due to the different assessment tools used. All effective interventions included a group approach to deliver general information about physical activity.

Table 5: Examples of intervention functions in effective and non-effective interventions, Outcome: change in BMI z-score

Intervention function	Effective	Non-effective
Incentivisation	Financial incentives for taking part in the study	Reward charts, physical activity equipment, pedometers
Environmental restructuring	Alteration of the playground	Changes in the child care policy to increase physical activity participant to 60 min/day
		Provision of PA equipment
Education	Classes on parenting skills	Text messages
	Monthly newsletters on physical activity and diet to the parents	Education curriculum on physical acttivity, diet and obesity targeting the child