YHEC

York Health Economics Consortium

ACADEMY OF MEDICAL SCIENCES

Targeted Review of the Economic Impact of Interventions that Aim to Improve Child Mental and Physical Health

Final Report

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Executive Summary

1. INTRODUCTION

Pre-birth and early childhood (up to five years) are crucial stages for physical, cognitive and emotional development. The environment experienced during this period can have long-term consequences for the mental and physical health of both individuals and society. Public sector resources can be directed towards interventions to improve the early years environment or to mitigate the impact of adverse experiences. Important considerations when selecting which interventions to fund are the cost-effectiveness and potential return on investment that the intervention achieves, which can be evidenced through economic evaluation. Given this, the Academy of Medical Sciences commissioned York Health Economics Consortium (YHEC) to undertake a targeted literature review of economic evaluations of interventions during pregnancy and in children up to five years of age that aim to improve their mental and physical health both in the short and long-term. A particular emphasis of the review was on interventions that may also address health inequalities.

2. METHODOLOGY

The potential scope of the literature review based on the review question was very large. As such, a highly targeted MEDLINE search strategy was developed that identified published economic evaluations in the UK, USA, Canada or Australia since 2013 of mental or physical health interventions that could benefit children under five years of age (including through interventions that take place during the prenatal period). Interventions could either be delivered directly to the child or could be delivered to parents provided the impact on children formed part of the evaluation. Any type of economic evaluation (cost-utility, cost-effectiveness, cost-benefit, cost minimisation or cost consequence) was eligible for inclusion. Grey literature was searched through the PEDE database, which includes citations from unpublished reports and working papers.

Twenty of the identified studies were selected to have key information extracted on the intervention evaluated and potential economic impact (e.g. through economic evaluation) based on the following criteria:

- How widely applicable the given intervention was at a whole population level; wider applicability was prioritised.
- Whether the intervention was already being implemented; those that were not already implemented were prioritised.
- The location of the study; UK based studies were prioritised.
- Whether the intervention studied had a negative impact on the target population; those with a negative impact were not prioritised.
- The purpose of the study; studies which compared an intervention against lack of or different intervention were prioritised, whilst those studies which compared two methods of delivering the same intervention were not prioritised.

3. RESULTS

The literature search identified 2,406 studies, of which 343 were considered eligible for inclusion in the review based upon an assessment of the abstract.

Fewer than ten of the included studies explicitly mentioned health inequalities or were explicitly in a low income or disadvantaged population.

The twenty prioritised studies (reported in 21 publications) were selected to have key information extracted related to interventions that increased rates of breastfeeding (n=3), improved dental health (n=2), reduced parental/carer smoking rates (n=3), improved antenatal and birth outcomes (n=2), improved outcomes for children in families facing challenges (n=3), reduced the risk of obesity (n=2) or supported children or parents with mental ill health (n=5). A summary of the interventions and the study evaluated and the reported return on investment is provided below (Table 1.1).

Table 1.1: Included studies interventions and return on investment

Study	Intervention	Return on investment
Interventions to increase rates of breastfeeding		
Anokye, 2020 [11]	A financial incentive (up to £200) over the first six months of a child's life to encourage breastfeeding (Nourishing Start for Health (NOSH)). The study did not undertake explicit analysis of the benefits of breastfeeding.	The intervention increased breastfeeding rates at 6-8 weeks and has the potential to be cost effective if this increase in breastfeeding rates results in health gains for the infant and/or mother. However, the cost-effectiveness or return on investment was not estimated by the authors.
Camacho, 2020 [1]	Interventions were identified in a review: ▪ Group education and antenatal and postnatal home visits in South Africa (trial based economic evaluation). ▪ Staff promotion of breastfeeding in a neonatal unit with low birth weight (LBW) babies in the UK and Spain (model based on a meta-analysis). ▪ Community based breastfeeding promotion and peer counselling in Uganda (trial based economic evaluation).	The neonatal interventions with mothers of LBW babies in the UK and Spain were likely to cost less with better outcomes than no intervention and so have positive returns on investment. For the other interventions it is unclear whether they would generate a return on investment.
Pokhrel, 2015 [2]	No specific intervention. It considered benefits for women who are exclusively breastfeeding at one week to continue to four months and the benefits of doubling breastfeeding rates for 7 to 18 months.	No intervention costs were discussed. Instead, the modelling shows the potential economic benefits (from reduced infections in infants and risk of breast cancer in women) of increasing breastfeeding rates.
Dental interventions		
Anopa, 2015 [3]	Supervised nursery toothbrushing programme (became Childsmile in 2006).	Supported toothbrushing generated a substantial return on investment.
Anopa, 2022 [4]	Fluoride varnish applied at six monthly intervals in addition to the Childsmile programme to prevent dental caries.	Six monthly fluoride varnish was found to cost more with worse outcomes than treatment as usual (TAU) (the Childsmile programme minus fluoride varnish) and so would not provide a positive return on investment.
Smoking interventions		
Jones, 2019 [5]	MiQuit - self-help smoking cessation support as a 12-week programme of tailored text messages in addition to normal NHS smoking cessation support.	Text message support to stop smoking was likely to be highly cost-effective and generate a positive return on investment.
McMeekin, 2023 [6]	Financial incentives for pregnant women to stop smoking. £400 in shopping vouchers in total: £50 for engaging with stop smoking services and setting a quit date, £50 if carbon monoxide certified as quit at 4 weeks, £100 at 12 weeks and £200 in late pregnancy.	The use of financial incentives to stop smoking was effective in the short term but was only likely to have a substantial return on investment if the impact on mother and infant was projected over a lifetime.
Renwick, 2018 [7]	An intervention to stop smoking in carers (the Smoke Free Home Trial). Participants were recruited from Sure Start Centres. The intervention was based around a smoke free homes advisor who undertook home visits to provide behavioural support and give feedback on air quality in the home. Participants were also provided with nicotine replacement patches.	The intervention was found to reduce tobacco related harm to children, but the return on investment is dependent on the WtP for incremental improvements in air quality or per quitter. There is no consideration of the economic or health consequences of these improvements nor whether the improvements were maintained.
Antenatal interventions		
Bailey, 2022 [8]	Four broad categories of lifestyle interventions in pregnancy: diet, diet with physical activity, physical activity and "mixed" (lacking structured diet or physical activity components).	Diet and physical activity interventions in pregnancy, provided they are structured, are likely to have minimal incremental costs or to save money and reduce complications and so therefore are likely to provide a positive return on investment.

Study	Intervention	Return on investment
Giorgakoudi, 2018 [9]	Vaccination for group B streptococcus (GBS).	It is unlikely there are savings with vaccination but the QALYs generated from vaccination meant that the authors concluded that vaccination could be a cost-effective investment at £54 per dose which the authors considered to be a reasonable price for vaccination in the UK.
Early childhood interventions to families facing challenges		
Barlow, 2019 [10]	Parents under Pressure, an intervention underpinned by the Integrated Theoretical Framework, developed for complex families with multiple adversities. The aim of the programme, delivered through 12 modules, was to enable parents to better regulate their emotions through mindfulness strategies. The intervention was delivered in family homes by fourteen practitioners. Outcomes were reduction in risk of child abuse and parental emotional regulation.	The incremental cost-effectiveness ratio I(CER) per quality-adjusted life-year (QALY) gained was above the threshold normally considered cost-effective by NICE. However, the results only considered parental quality of life (QoL) and it is likely if the reduction in harm to children was taken into account the cost-effectiveness (and therefore return on investment) of the intervention would improve.
Cannon, 2018 [11]	Interventions fell into four categories: ▪ Early care and education: support to children in group settings. ▪ Home visiting: individualised services delivered in homes to promote parent skills and knowledge. ▪ Parent education: individualised services delivered outside of homes to promote parent skills and knowledge. ▪ Transfers: cash or in-kind benefits direct to families.	The review highlighted the following key findings about economic return: ▪ Higher returns are associated with low cost programmes and resource intensive interventions with long term follow up. ▪ Targeted and universal approaches can show positive returns. ▪ Monetary benefits arise from multiple domains but are often highest for income and reductions in crime. ▪ Government benefits (i.e. to the payer of the intervention) rarely outweigh programme cost. ▪ Benefits to children can take years or decades to unfold. ▪ Not all outcomes can have an economic value assigned to them.
Hajizadeh, 2017 [12]	ParentCorps, a family-centred enhancement to pre- kindergarten programming promoting family engagement and safe, nurturing and predictable environments at home and at school.	Potential for high return on investment but this is dependent on effectiveness seen being maintained effectively for life.
Obesity interventions		
Brown, 2019 [13]	Childhood obesity interventions commencing before six months of age.	The study highlighted there is potential for substantial return on investment, but the level of return is dependent on the length of time the effect on BMI from intervention is maintained.
Tran, 2022 [14]	Romp and Chomp, a universal obesity prevention intervention that involved community capacity building, policy changes and the cultural and physical environments of early years settings. The intervention had four key messages: daily active play, daily water and fewer sweet drinks, daily fruit and vegetables, less screen time.	The authors considered that the intervention has a fair probability of being cost-effective, although the QALY gains are small (based on a small average BMI increase) and the total costs of the intervention very high.
Child or parental mental health interventions		
Bee, 2014 [15]	The systematic review looked for any community based interventions that improved the QoL of children with parents with serious mental illness. Only one study was identified that was of a specialist psychiatric parent and baby day unit for treatment of postnatal depression.	The return on investment is unclear from the one study identified.

Study	Intervention	Return on investment
Hodgson, 2022 [16]	Early intensive applied behaviour analysis (ABA) based interventions that impact a child's development by shifting a child's developmental trajectory through early interventions. They are typically delivered to young autistic children for several years on a one-to-one basis, for between 20 to 50 hours per week.	With current evidence, ABAs are unlikely to provide a sufficient return on investment to justify investment.
Mihalopoulos, 2015 [17]	Children were screened for inhibition (a risk factor for anxiety disorders) in the preschool setting with questionnaires being sent home for parents to complete. The questionnaires were primarily assessed by psychologists. Parents of positively screened children were offered a six-session parenting course.	The return on investment was dependent on the value placed on the DALYs averted.
Sonuga-Barke, 2018 [18]	Two interventions were considered compared to TAU: ▪ The New Forest Parenting Programme (NFPP) was a 12-week individual, home-delivered ADHD parent training programme. It included education about ADHD, communication strategies, play based activities and attention training. ▪ Incredible Years Toddler (IY) was a 12-week group-based programme comprising a series of developmentally based interventions for parents, children and teachers. It included problem-solving, videotape modelling and role playing.	The return on investment is unclear as both NFPP and IY cost several thousand pounds per family and the improvement in outcomes over usual care is unclear. However, IY, recommended by NICE, seems to be more costly than NFPP.
Varshney, 2022 [19]	Chicago Child-Parent Centres (CPC). The centres provide continuous education and family support to economically disadvantaged children through to third grade (age 8 or 9). The programme had five key features: ▪ Early education no later than 4 years. ▪ Structured learning for language and basic skills. ▪ Increased parent involvement in home and school (at least half a day per week). ▪ Provision of health and social care services. ▪ Programme continuity between pre-school and elementary school. The programme was for 3 hours daily for 5 days a week with a child-to-staff ratio of 17:2. Promotion of health and good nutrition was also a component of the programme.	The return on investment was estimated to be between $1.35 and $3.66 per dollar spent and could be higher if crime reduction, welfare and earnings were taken into account.

Key: ABA - applied behaviour analysis; ADHD – attention deficit/hyperactivity disorder; BMI – body mass index; CPC – Child Parent Centre; DA – disability adjusted life years; EE – economic evaluation; GBS – group B streptococcus; ICER – incremental cost-effectiveness ratio; IY – Incredible Years; LBW – low birth weight; NFPP – New Forest Parenting Programme; NICE – National Institute for Health and Care Excellence; NOSH – Nourishing Start for Health; QALY – quality-adjusted life year; QoL – quality of life; TAU – treatment as usual; WtP – willingness-to-pay.

4. DISCUSSION

The extracted studies highlight that there are a range of interventions that can be, or are being, implemented often at a national level that potentially generate significant returns on investment. These include interventions to improve dental health, reduce smoking rates in parents, increase breast feeding rates and prevent obesity. Positive returns on investment are easiest to show where interventions can prevent poor short-term outcomes. However, this review also identified interventions that were shown to be cost effective even when positive outcomes from an intervention may not be fully realised for many years after the intervention.

Looking specifically at health inequalities, whilst there were studies of interventions in low income areas because of high levels of need in those areas [7, 19], no studies extracted (or identified) explicitly looked at interventions designed to reduce specific inequalities and only one of the extracted studies showed results by deprivation levels [3]. The searches in total only identified fewer than 10 studies that were explicitly in low income or disadvantaged groups.

This is not to say that any of the interventions identified in the review could not be used to address health inequalities if they were targeted at disadvantaged groups, but that studies in the literature that were identified in the searches have, on the whole, had not looked at interventions in children under five as an explicit means of addressing health inequalities. It should be noted that the targeted searches included one grey literature resource and it is possible that a number of evaluations of interventions funded by central and local government as well as by charities have been undertaken and are available but have not been published in peer-review journals or PEDE and so would not have been picked up in the searches.

The findings of the review should be considered within the context of a number of limitations that came about due to the highly pragmatic nature of the project. The limitations of the searches are outlined in detail in section 2.2.1. Notably, the search strategy was highly targeted. It was not designed to be exhaustive but aimed to target studies likely to be relevant to the research question, whilst retrieving a volume of records manageable within the timescales and resources of the project. Therefore, not all interventions are captured, nor are studies in the EU or lower income countries.

In summary, this targeted review has highlighted interventions targeted towards children under five that could generate positive returns on investment and be considered alongside other evidence to improve health in the early years, and as a result, have the potential to improve health across the life course.

Acknowledgements

We thank the Academy of Medical Sciences for their input into this review throughout. In particular, we are grateful to the steering group for the Academy's work on child health, co-chaired by Professor Helen Minnis FMedSci and Professor Sir Andrew Pollard FMedSci, and supported by the Academy's secretariat: Dr Hannah Chance, Angel Yiangou and Dr Claire Cope [20].

Abbreviations

ABA	Applied behaviour analysis
ADHD	Attention deficit/hyperactivity disorder
BMI	Body mass index
CHU9D	Child Health Utility Instrument
CO	Carbon monoxide
CPC	Child-parent centre
CRE-Obesity	Centre of Research Excellence in Obesity
CRD	Centre for Reviews and Dissemination
DALY	Disability adjusted life years
ECEC	Early childhood education and care
EED	Economic Evaluation Database
EPOCH	Early Prevention of Obesity in Childhood
EQ-5D	EuroQol-5 dimensions
FV	Fluoride varnish
GBP	Gross British Pound
GBS	Group B streptococcus
HALY	Health-adjusted life years
HRQoL	Health-related quality of life
HSUV	Health state utility value
HTA	Health technology Assessment
ICER	Incremental cost-effectiveness ratio
ISD	Information Services Division
IY	Incredible Years
LBW	Low birth weight
LMIC	Lower- and middle- income countries
LRTI	Lower respiratory tract infection
NA	Not applicable
NFPP	New Forest Parenting Programme
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NICU	Neonatal intensive care unit
NOSH	Nourishing Start for Health
NR	Not reported
PEDE	Paediatric Economic Database Evaluation
PM	Particulate matter
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
QALY	Quality-adjusted life year
QoL	Quality of life
RCT	Randomised controlled trial
SR	Systematic review
TAU	Treatment as usual
UK	United Kingdom
USA	United States of America
WTP	Willingness-to-pay
YHEC	York Health Economics Consortium

1 Introduction

The Academy of Medical Sciences commissioned York Health Economics Consortium (YHEC) to undertake a targeted literature review of the economic impact of interventions that aim to improve child mental and physical health.

1.1 Context

Children's health and wellbeing are influenced by many overlapping factors. Pre-birth and early childhood (up to five years) are crucial stages for physical, cognitive and emotional development. The environment experienced during this period can have long-term consequences for the mental and physical health of both individuals and society [21].

Early intervention strategies, aimed at improving long-term outcomes in children and young people, are well recognised in many countries [22-24]. These interventions are delivered in various forms and can be used to identify and support children and their families to help mitigate problems in later life. Early interventions can take many different forms including home visits for vulnerable parents, activities to support early language development, family therapy and programmes based in early childhood education and care (ECEC) settings that develop social and emotional skills. They are associated with a wide range of benefits, including improved mental and physical health, reduced inequality, and a greater capacity for parents and caregivers to support child development [25, 26]. These interventions may also be associated with reduced public spending and increased economic productivity; however, this is difficult to assess [25].

1.2 Objectives

The aim of the targeted literature review was to answer the review question: what is the economic impact of interventions that aim to improve child mental and physical health, in pregnancy or up to age five?

The output of the targeted literature review has informed the Academy's policy work exploring the impact of improving mental and physical health and wellbeing in the early years on the individual, and the wider impacts of this on population health, national productivity, innovation and the prosperity of the nation [20].

2 Methods

To identify relevant evidence to answer the review question, a clear definition of the eligible study population, interventions, comparators, outcomes and study types of interest was required.

The potential scope based on the review question was very large. To meet the project resources, it was determined that the review would take a targeted review approach. The search was highly focused and pragmatic and was not designed to be exhaustive. The specific outcomes of interest were selected to answer the question around economic impact.

The eligibility criteria are described in Table 2.1.

2.1 Eligibility Criteria

Table 2.1: Summary of the review eligibility criteria

Eligibility criterion	Inclusion Criteria	Exclusion Criteria
Population	Pre-school children (age<5) whose mental or physical health has been targeted to improve through any intervention, including indirectly through parents, carers or in other settings. The eligible population included unborn babies, whose parents received the intervention.	▪ Studies including children at school/of school age. ▪ Mixed population studies (and where the study did not stratify outcome data by the eligible population).
Interventions and comparators	All interventions that impact mental or physical health, including those delivered outside of a healthcare setting but which aim to improve mental or physical health.	N/A
Outcomes	Economic impact expressed as either monetary or non-monetary outcomes, including those indicative of potential return on investment, specifically: ▪ Total costs. ▪ Quality-adjusted life years (QALYs). ▪ Incremental analyses outcomes, e.g. incremental cost-effectiveness ratios (ICERs) including utilities data (e.g. EQ-5D). ▪ Absenteeism/presenteeism data. ▪ Adult employment. ▪ Income. ▪ Educational attainment.	N/A
Study design	Any study design was eligible aside from case reports.	▪ Case reports.
Limits	▪ Studies published in the last ten years (2013 to present). ▪ Studies conducted in the UK, US, Canada and Australia. ▪ Studies published in English language.	We excluded the following publication types: ▪ Opinion pieces. ▪ News. ▪ Editorials. ▪ Preprints. ▪ Conference abstracts. Studies published before 2013. Studies not conducted in the UK, US, Canada or Australia. Studies not published in English Language.

Key: EQ-5D - European Quality of Life Five Dimension, GPD – gross domestic product, ICERs – incremental cost-effectiveness ratios, NA – not applicable, QALYs – quality-adjusted life years, SR – systematic reviews.

2.2 Identifying Relevant Studies

2.2.1 Search strategy

A highly targeted MEDLINE (OvidSP) search strategy was designed to identify studies on the economic impact of interventions in pre-school children in the UK, the USA, Canada and Australia. The final MEDLINE strategy is presented in Appendix A.

The strategy comprises eight concepts:

- Pre-school children (search lines 1 to 9).
- Economic impact (search lines 10 to 26).
- Health state utility values (HSUVs) (search lines 27 to 39).
- UK (search lines 42 to 50).
- USA (search lines 51 to 55).
- Canada (search lines 56 to 58).
- Australia (search lines 59 to 62).
- Lower- and middle-income countries (LMIC) (search lines 65 to 67).

The concepts are combined as follows: (pre-school children AND (economic impact OR HSUVs) AND (UK OR USA OR Canada OR Australia)) NOT LMIC.

The strategy was devised using a combination of subject indexing terms and free text search terms in the Title, Abstract and Keyword Heading Word fields. The search terms for population concept were identified through discussion within the research team, scanning background literature and browsing database thesauri.

The strategy excludes animal studies from MEDLINE using a standard algorithm (search line 69). The strategy also excludes some ineligible publication types which are unlikely to yield relevant study reports (editorials, news items and case reports) and records with the phrase 'case report' in the title (search line 70).

The strategy is restricted to studies published from 2013 to date (search line 72) in the English language (search line 73).

Strategy Limitations

The search strategy reflected the highly pragmatic nature of the project and timeline constraints. The search limitations and potential risks were discussed within the research team and with the Academy of Medical Sciences, and the final search approach was agreed. The strategy was not designed to be exhaustive but aimed to target studies likely to be relevant to the research question, whilst retrieving a volume of records manageable within the timescales and resources of the project. A number of pragmatic search approaches were used to achieve this. These included:

- Reflecting the highly focused search approach, the search terms for the population concept (search lines 1 to 9) were designed to only retrieve studies where the record made the pre-school child context explicit. The subject headings were focused to retrieve just those records where the subject heading was judged by the database producer to be a major focus of the study (rather than retrieving every record that is indexed with the subject heading). The range of textword search terms were deliberately restricted. The terms were designed to retrieve records that explicitly referred to the pre-school context (e.g. pre-school, infant, child age described in a limited number of ways), rather than retrieving all records that refer to children in a non-specific context.

- The search terms for the economic impact concept (search lines 10 to 26) are a highly targeted, adapted version of the filter developed by the University of York Centre for Reviews and Dissemination (CRD) for identification of economic evaluations to include in National Health Service Economic Evaluation Database (NHS EED) [27]. To reflect the highly targeted search approach, the filter was adapted by restricting subject heading search terms to retrieve those records where the subject heading is judged by the database producer to be a major focus of the study, and text word searches were restricted to records where the term appears only in the title of the record.

- The search strategy was designed to target studies where the database record referred to an explicit economics, costs or HSUVs context using the terms in lines 10 to 39. The strategy was not designed to retrieve studies that reported on absenteeism, presenteeism, adult employment, income, or educational attainment if the record did not also refer to an explicit economics, costs or HSUVs context.

- The search terms for the HSUVs concept are a highly targeted, adapted version of the YHEC precision-maximising filter for identifying studies reporting HSUVs (search lines 27 to 39) [28]. Again, this filter was adapted by restricting the search to terms to retrieve those records where the subject heading is judged to be the major focus of the study, and text word searches were restricted to records where the terms to identify HSUVs appear only in the title of record.

- The terms for the UK concept are adapted from a filter developed by the National Institute of Health and Care Excellence (NICE) [29]. The terms for the USA concept are adapted from a published filter [30]. The filters have been deliberately restricted to suit project timelines and budget by searching for the text word terms only in the title and abstract fields, and not the institutional affiliation field. The terms for the Canada and Australia concepts are a combination of terms for the country and terms for selected major cities and districts in each country in a limited number of fields.

- The strategy excludes lower- and middle-income countries using a filter developed by the Cochrane Effective Practice and Organisation of Care Group (search lines 65 to 68) [31].

The final Ovid MEDLINE strategy was peer-reviewed before execution by a second Information Specialist. Peer review considered the appropriateness of the strategy for the review scope and eligibility criteria, inclusion of key search terms, errors in spelling, syntax and line combinations, and application of exclusions.

2.2.2 Resources searched

We conducted the literature search in the databases and information sources shown in Table 2.2. The selection of resources reflected the highly pragmatic project context. Searching these two resources retrieved studies published in the journal literature and selected grey literature. However, there may be instances of cost-effective interventions where no economic evaluation has been conducted, or where the publication of the results of the economic evaluation is not published in either resource.

Table 2.2: Databases and information sources searched

Resource	**Interface / URL**
Databases	
MEDLINE(R) ALL	OvidSP
Paediatric Economic Database Evaluation (PEDE)	http://pede.ccb.sickkids.ca/pede/index.jsp
Reference list checking	n/a

Grey literature was searched through the PEDE database, which includes citations from unpublished reports and working papers. Highly targeted, title-only searches of the pre-school child concept were conducted in the PEDE database.

We also checked the included studies list of any retrieved relevant systematic reviews published in the last three years for any eligible studies that may have been missed by the database searches.

For each paper that was selected for inclusion in the review, a check was made to establish if any of the following notices were associated with the included paper: retraction notice, erratum notice, corrected and republished paper notice, expression of concern notice. The check was conducted via the PubMed record for the paper or (if no PubMed record was found) via the journal webpage for the paper.

2.2.3 Running the search strategies and downloading results

We conducted searches using each database or resource listed above, translating the agreed Ovid MEDLINE strategy appropriately. Translation included consideration of differences in database interfaces and functionality, in addition to variation in indexing languages and thesauri. The final translated database strategies were peer-reviewed by a second Information Specialist. Peer review considered the appropriateness of the translation for the database being searched, errors in syntax and line combinations, and application of exclusions.

Appendix A contains the full strategies (including search dates) for all sources searched.

Where possible, we downloaded the results of searches in a tagged format and loaded them into bibliographic software (EndNote) [32]. The results were deduplicated using several algorithms and the duplicate references held in a separate EndNote database for checking if required.

2.2.4 Assessing the relevance of the downloaded records to the review

Record assessment was undertaken as follows:

- A single researcher assessed the search results according to their relevance and removed the obviously irrelevant records such as those in adults.
- The titles and abstracts of remaining records were assessed for relevance by single independent reviewer selection.
- We obtained the full text of potentially relevant studies and these were assessed for relevance by a single reviewer.
- We recorded the number of records included and removed at each selection stage in a flow diagram adapted from PRISMA [33]. We listed studies excluded after assessment of the full document in an excluded studies table, with the reasons for exclusion.

We recorded the number of records included and removed at each stage in a flow diagram. Studies excluded after assessment of the full document for each review were described in a table with the reasons for exclusion (Appendix B). Where results for one trial are reported in more than one paper, all related papers were identified and grouped together to ensure that participants in individual trials were only included once.

2.3 Data Extraction

20 studies were prioritised by the Academy of Medical Sciences and data extracted. The prioritisation criteria used were:

- How widely applicable the given intervention is at a whole population level; wider applicability was prioritised.
- Whether the intervention is already being implemented; those that were not already implemented were prioritised.
- The location of the study; UK based studies were prioritised.
- Whether the intervention studied had a negative impact on the target population; those with a negative impact were not prioritised.
- The purpose of the study; studies which compared an intervention against lack of or different intervention were prioritised, whilst those studies which compared two methods of delivering the same intervention were not prioritised.

The eligible studies not extracted are listed at Appendix B.

One researcher extracted key data from the eligible studies covering: study objectives, design, country, population, intervention, methodology, outcomes (economic impact), study conclusions.

2.4 Synthesis

We have provided a narrative review that critically appraises individual studies and presents the data in tables. The summary provides data on the study characteristics, methods and outcomes related to this review.

3 Results

3.1 Literature Search Results

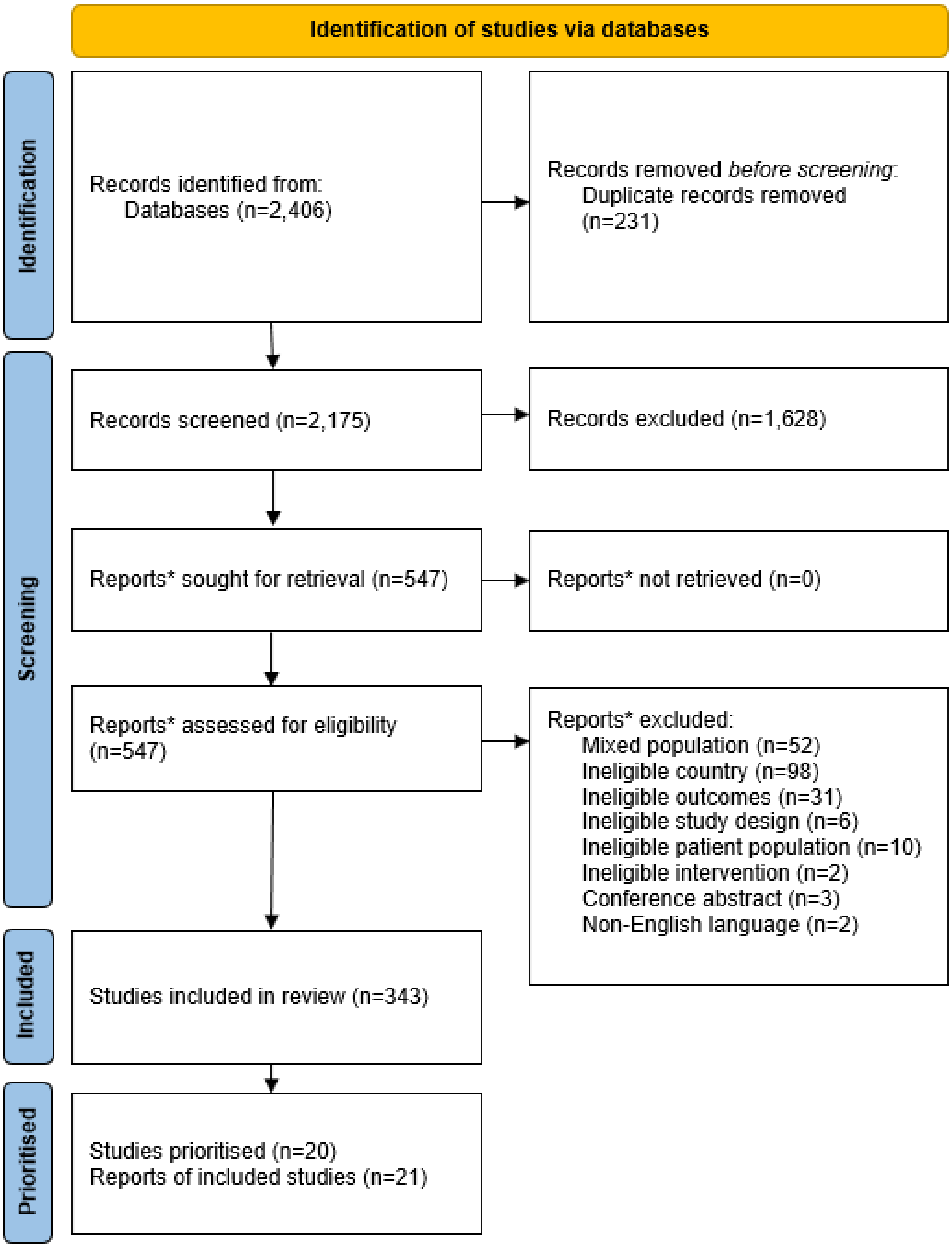
The searches were conducted between 08/06/2023 and 12/06/2023 and identified 2,406 records (Table 3.1).

Table 3.1: Literature search results

Resource	Number of records identified
Databases	
MEDLINE	2,090
Paediatric Economic Database Evaluation (PEDE)	316
Total records identified through database searching	**2,406**
Other sources	
Reference list checking	0
Total additional records identified through other sources	0
Total number of records retrieved	**2,406**
Total number of records after deduplication	**2,175**

Following deduplication, 2,175 records were assessed for relevance based on information in the title and abstract. Of the 2,175 records, 1,628 were excluded and 547 full text documents were assessed. Of the 547 full text documents screened, 204 documents were excluded, and 343 studies were eligible for the review (Figure 3.1). 20 studies in 21 papers were prioritised (Appendix D). The other 322 studies were not grouped and are listed in Appendix C.

Figure 3.1: Study flow diagram



3.2 Studies Identified and Selected

The twenty prioritised studies included in the review (Appendix D) relate to interventions that:

- Increase rates of breastfeeding (n=3) (Section 3.3) [1, 2, 34].
- Improve dental health (n=2) (Section 3.4) [3, 4].
- Reduce parental/carer smoking rates (n=3) (Section 3.5) [5-7].
- Improve antenatal and birth outcomes (n=2) (Section 3.6) [8, 9].
- Improve outcomes for children in families facing challenges (n=3) (Section 3.7) [10-12].
- Reduce the risk of obesity (n=2) (Section 3.8) [13, 14].
- Support children or parents with mental ill health (n=5) (Section 3.10) [15-19].

These studies are further described in sections 3.3 to 3.10. The study characteristics are presented in Table 3.2, methods in Table E.1 and results in Table 3.3.

Table 3.2: Study characteristics

Study	Intervention	Study country	Study objective(s)	Overall patient description	Key characteristics	Number of participants
Interventions to increase rates of breastfeeding						
Anokye, 2020 [11]	A financial incentive (up to £200) over the first six months of a child's life to encourage breastfeeding (Nourishing Start for Health (NOSH)). The study did not undertake explicit analysis of the benefits of breastfeeding.	England	To provide the first estimate of the cost- effectiveness of a financial incentive for breastfeeding compared with usual care.	Mothers of newborn children and newborn children.	Mothers in local authorities with low breastfeeding rates (<40% breastfeeding rates at 6 to 8 weeks).	5,393 mothers/infants
Camacho, 2020 [1]	Interventions were identified in a review: ▪ Group education and antenatal and postnatal home visits in South Africa (trial based economic evaluation). ▪ Staff promotion of breastfeeding in a neonatal unit with low birth weight (LBW) babies in the UK and Spain (model based on a meta-analysis). ▪ Community based breastfeeding promotion and peer counselling in Uganda (trial based economic evaluation).	UK based review	To bring together current knowledge to guide researchers and commissioners towards potentially cost-effective strategies to promote or support breastfeeding.	Mothers of newborn children and newborn children.	Four studies in South Africa, UK, Spain and Uganda (included due to UK results being presented separately)	Four studies - number of participants not reported
Pokhrel, 2015 [2]	No specific intervention. It considered benefits for women who are exclusively breastfeeding at one week to continue to four months and the benefits of doubling breastfeeding rates for 7 to 18 months.	UK	To calculate the potential cost savings attributable to increases in breastfeeding rates from the NHS perspective.	Newborn infants and their mothers.	Mothers who exclusively breastfeed at 1 week and mothers who are still breastfeeding (not necessarily exclusively) at 6 months.	788,486 infants
Dental interventions						
Anopa, 2015 [3]	Supervised nursery toothbrushing programme (became Childsmile in 2006).	Scotland	To compare the cost of providing the Scotland-wide nursery toothbrushing programme with associated NHS cost savings from improvements in the dental health of five-year-old children.	Three or four years olds attending nursery.	NR	Dental records inspected: 62,419

Study	Intervention	Study country	Study objective(s)	Overall patient description	Key characteristics	Number of participants
Anopa, 2022 [4]	Fluoride varnish applied at six monthly intervals in addition to the Childsmile programme to prevent dental caries.	Scotland	To explore the additional preventive value of fluoride varnish application at 6-monthly intervals in nursery schools compared to treatment as usual (TAU) (the Childsmile programme minus fluoride varnish) in nurseries.	Three-year-old children attending nursery schools.	Mean age of children was 3.52 years in the fluoride varnish group and 3.54 in the TAU group and children in both arms. Patients Scottish Index of Multiple Deprivation 2 and 3, accounting for 64% of all children.	Fluoride varnish: 265 TAU: 269
Smoking interventions						
Jones, 2019 [5]	MiQuit - self-help smoking cessation support as a 12-week programme of tailored text messages in addition to normal NHS smoking cessation support.	UK	To describe a smoking in pregnancy model with an illustration using trial data.	Smoking pregnant women and their children.	The model used UK smoking statistics to estimate ages of smoking mothers and length of time smoking.	NA - model
McMeekin, 2023 [6]	Financial incentives for pregnant women to stop smoking. £400 in shopping vouchers in total: £50 for engaging with stop smoking services and setting a quit date, £50 if carbon monoxide certified as quit at 4 weeks, £100 at 12 weeks and £200 in late pregnancy.	UK	To evaluate whether adding financial incentives to usual care is cost-effective in encouraging pregnant women to quit tobacco smoking, compared with usual care alone.	Smoking pregnant women and their children.	Mean age of mother was 28. No other information provided.	944 in the trial analysis
Renwick, 2018 [7]	An intervention to stop smoking in carers (the Smoke Free Home Trial). Participants were recruited from Sure Start Centres. The intervention was based around a smoke free homes advisor who undertook home visits to provide behavioural support and give feedback on air quality in the home. Participants were also provided with nicotine replacement patches.	UK	To estimate the cost-effectiveness of a complex intervention designed to reduce second hand smoke exposure of children whose primary caregiver feels unable or unwilling to quit smoking.	Children under 5 in homes where a main caregiver (aged over 18) smokes.	Details of carers only provided. The mean age was 28, 91% were female and 94% were white British. All participants were not willing to quit and lived in deprived areas of Nottingham.	102 parents in each arm of the trial
Immunisation intervention						
Giorgakoudi, 2018 [9]	Vaccination for group B streptococcus (GBS).	UK	To estimate the potential impact and cost-effectiveness of maternal immunisation against neonatal and maternal invasive GBS disease in the UK.	All babies born in the UK.	NR	Model used a population of 776,352 live births

Study	Intervention	Study country	Study objective(s)	Overall patient description	Key characteristics	Number of participants
Early childhood interventions to families facing challenges						
Barlow, 2019 [10]	Parents under Pressure, an intervention underpinned by the Integrated Theoretical Framework, developed for complex families with multiple adversities. The aim of the programme, delivered through 12 modules, was to enable parents to better regulate their emotions through mindfulness strategies. The intervention was delivered in family homes by fourteen practitioners. Outcomes were reduction in risk of child abuse and parental emotional regulation.	UK	To evaluate the Parents under Pressure program with parents currently engaged in community-based substance abuse treatment.	Parents engaged with community based substance misuse services with children under 2.5 years of age.	Across the intervention and control, the mean age of parents was 30.8 and 96% were female with 83% unemployed and 51% with a criminal record. The mean age of children was 9.2 months with 60% male and 82% were involved with child protective services.	Parents under pressure: 52 TAU: 48
Cannon, 2018 [11]	Interventions fell into four categories: ▪ Early care and education: support to children in group settings. ▪ Home visiting: individualised services delivered in homes to promote parent skills and knowledge. ▪ Parent education: individualised services delivered outside of homes to promote parent skills and knowledge. ▪ Transfers: cash or in-kind benefits direct to families.	USA	To examine a set of evaluations that meet criteria for scientific rigor and synthesizes their results to better understand the outcomes, costs, and benefits of early childhood programs.	Parents of children from before birth to age 5.	NR	25 studies were identified that provided economic evaluations of interventions in early childhood. No detail on specific studies was provided.
Hajizadeh, 2017 [12]	ParentCorps, a family-centred enhancement to pre- kindergarten programming promoting family engagement and safe, nurturing and predictable environments at home and at school. .	USA	To estimate the long-term cost-effectiveness of ParentCorps, a family-centred enhancement to pre-kindergarten programme in elementary schools and early education centres which has been found to yield benefits in childhood across domains of academic achievement, behaviour problems, and obesity.	Pre-kindergarten children with low levels of self-regulation.	Child inputs were chosen to match demographics of urban areas in the USA.	NA - model

Study	Intervention	Study country	Study objective(s)	Overall patient description	Key characteristics	Number of participants
Obesity interventions						
Brown, 2019 [13]	Childhood obesity interventions commencing before six months of age.	Australia	To estimate the long-term health benefits and health care cost-savings of reductions in BMI for the Australian population of children aged between 2 and 5 years.	Children aged between 2 and 5 years where obesity interventions were commenced before six months of age.	Children demographics matched those from Australian Bureau of Statistics but no detail was given.	NA - model
Tran, 2022 [14]	Romp and Chomp, a universal obesity prevention intervention that involved community capacity building, policy changes and the cultural and physical environments of early years settings. The intervention had four key messages: daily active play, daily water and fewer sweet drinks, daily fruit and vegetables, less screen time.	Australia	To assess the cost-effectiveness of the Romp & Chomp community-wide early childhood obesity prevention intervention if delivered across Australia in 2018 from a funder perspective, against a no-intervention comparator.	All Australian children aged 0 to 5 years.	Not applicable as all children as universal intervention.	1,906,075
Antenatal intervention to reduce adverse pregnancy outcomes (resulting from excess gestational weight gain)						
Bailey, 2022 [8]	Four broad categories of lifestyle interventions in pregnancy: diet, diet with physical activity, physical activity and "mixed" (lacking structured diet or physical activity components).	Australia	To compare the cost-effectiveness of 4 antenatal lifestyle intervention types with standard care.	Women with single pregnancies and births at more than 20 weeks gestation.	Of the pregnant women in the data set analysed and were eligible for inclusion in the analysis, 54% had a BMI less than 25, 27% between 25 and 30, and 20% greater than 30. Mean age was 29.7 years. 56% of pregnancies were multiparous. 83% of women did not smoke.	38,052 included in analysis
Child or parental mental health interventions						
Bee, 2014 [15]	The systematic review looked for any community based interventions that improved the QoL of children with parents with serious mental illness. Only one study was identified that was of a specialist psychiatric parent and baby day unit for treatment of postnatal depression.	UK	To conduct an evidence synthesis of the clinical effectiveness, cost-effectiveness and acceptability of community-based interventions for improving QoL in children of parents with serious mental illness.	Only one study was identified in the review, and this was of parents with post-natal depression.	Mothers of children aged 6 weeks to 12 months with a diagnosis of major or minor depressive disorder.	One study with 60 participants
Hodgson, 2022 [16]	Early intensive applied behaviour analysis (ABA) based interventions	UK	To evaluate the cost-effectiveness of early	Children with autism.	Pre-school children with autism with a start age in	NA - model

Study	Intervention	Study country	Study objective(s)	Overall patient description	Key characteristics	Number of participants
	that impact a child's development by shifting a child's developmental trajectory through early interventions. They are typically delivered to young autistic children for several years on a one-to-one basis, for between 20 to 50 hours per week.		intensive ABA-based interventions for autistic pre-school children in the UK.		the model of 3. In the model, 87.57% were male with 82.95% with a learning disability.	
Mihalopoulos, 2015 [17]	Children were screened for inhibition (a risk factor for anxiety disorders) in the preschool setting with questionnaires being sent home for parents to complete. The questionnaires were primarily assessed by psychologists. Parents of positively screened children were offered a six-session parenting course.	Australia	To assesses the cost-effectiveness of a parent-focussed psycho-educational programme intervention in children who exhibit inhibition to determine whether it could provide value-for-money across a population.	Children aged between 3 and 5 who exhibit inhibition in a screening questionnaire.	NR	16% of all children would exhibit some form of inhibition.
Sonuga-Barke, 2018 [18]	Two interventions were considered compared to treatment as usual (TAU): ▪ The New Forest Parenting Programme (NFPP) was a 12-week individual, home-delivered ADHD parent training programme. It included education about ADHD, communication strategies, play based activities and attention training. ▪ Incredible Years Toddler (IY) was a 12-week group-based programme comprising a series of developmentally based interventions for parents, children and teachers. It included problem-solving, videotape modelling and role playing.	UK	To compare the efficacy and cost of specialised individually delivered parent training for preschool children with ADHD against generic group-based parent training and TAU.	Children aged between 2 years 9 months and 4 years 6 months with a parent/caregiver 18 or over and a diagnosis of ADHD but not a full diagnosis of autism or severely delayed development.	Children had a mean aged of 42 to 43 months and were 24 to 29% female in the intervention groups and 40% female in the TAU group. Parents were almost 90% female with 62 to 66% unemployed.	264 in the two intervention groups and 42 in the TAU group
Varshney, 2022 [19]	Chicago Child-Parent Centres (CPC). The centres provide continuous education and family support to economically disadvantaged children	USA	To evaluate the long-term impacts of the CPC, a comprehensive early childhood program launched	Children aged 3 to 4, predominantly living in high poverty areas.	51.8% were female with 92.7% African American. 76.7% had single parents and 77.7% resided in a high poverty area.	989

Study	Intervention	Study country	Study objective(s)	Overall patient description	Key characteristics	Number of participants
	through to third grade (age 8 or 9). The programme had five key features: ▪ Early education no later than 4 years. ▪ Structured learning for language and basic skills. ▪ Increased parent involvement in home and school (at least half a day per week). ▪ Provision of health and social care services. ▪ Programme continuity between pre-school and elementary school. The programme was for 3 hours daily for 5 days a week with a child-to-staff ratio of 17:2. Promotion of health and good nutrition was also a component of the programme.		in the 1960s, on physical and mental health outcomes.			

Key: ABA - applied behaviour analysis; ADHD - attention deficit/hyperactivity disorder; BMI – body mass index; CO - carbon monoxide; CPC - child-parent centre; EE - economic evaluation; FV - fluoride varnish; GBS - group B streptococcus; IY - Incredible Years; NA - not applicable; NFPP - New Forest Parenting Programme; NHS - National Health Service; NOSH - Nourishing Start for Health; NR - not reported; QoL - quality of life; SMI - serious mental illness; TAU - treatment as usual; UK - United Kingdom; USA - United States of America.

3.3 Interventions to Increase Rates of Breastfeeding

Pokhrel 2015 [2] calculated the potential cost savings attributable to increases in breastfeeding rates from the National Health Service (NHS) perspective through an economic model, but did not consider a specific intervention to increase rates. The model considered the economic benefits for two distinct cohorts: women who are exclusively breastfeeding at one week who continue to four months and doubling the proportion of women who are breastfeeding for 7 to 18 months. The model considered short term (one year) benefits of breastfeeding to the child in terms of a reduction in infections (gastrointestinal, lower respiratory tract infection (LRTI) and acute otitis media) and the lifetime benefits to the mother from a reduced risk of breast cancer for mothers who breastfeed.

As a model of the potential benefits from increasing breastfeeding, no intervention costs were considered. Increasing the proportion of women exclusively breastfeeding for 4 months from 7% to 21% would reduce annual hospital infection costs by £4.08 million, with savings increasing to £16.95 million if rates were increased to 65%. Increasing the rate of breastfeeding at 7 to 18 months to 16% would save £21.17 million from reduced breast cancer. For first time mothers, 371 quality-adjusted life years (QALYs) could be generated if they were encouraged to breastfeed up to 6 months from avoided breast cancer.

The study does not show a return on investment as there is no actual intervention considered. However, the modelling does show the substantial potential returns that are realisable from a relatively narrow scope of benefits from breastfeeding to mother and child.

Anokye 2020 [34] assessed the cost-effectiveness of a financial incentive to encourage women to breastfeed compared with usual care in England. A financial incentive in the form of shopping vouchers of £40 was offered if women were breastfeeding at 2 days, 10 days, 6 weeks, 3 months and 6 months (so potentially £200 in vouchers in total). The economic assessment had an NHS perspective and was a within trial economic analysis of the Nourishing Start for Health (NOSH) randomised controlled trial (RCT) which included 10,000 mother/infant dyads in local authorities with low breastfeeding rates (<40% breastfeeding rates at 6 to 8 weeks). Limited information about the trial was provided in the publication.

Financial incentives for breastfeeding were estimated to cost £9,989 per ward or £91.45 per baby and increased breastfeeding rates by an average of 5.7 percentage points ($p<0.001$). The cost per additional baby breastfed at 6 to 8 weeks was £974 and the intervention would have to generate 0.05 QALYs to be cost-effective at a willingness to pay (WtP) threshold of £20,000 per QALY.

The return on investment on financial incentives for breastfeeding was not possible to estimate as the health benefits of breastfeeding and the consequent reduction in health care resource use was not captured in the trial or the analysis. The authors concluded that whilst the study provided information to help inform public health guidance on financial incentives for breastfeeding, evidence on financial incentives on long-term breastfeeding rates and modelling of outcomes linked to breastfeeding are both needed to understand whether such incentives should be funded.

Camacho 2020 [1] was a literature review of cost-effective strategies to promote or support breastfeeding. Four interventions were identified including: group education and antenatal and postnatal home visits in South Africa (a trial based economic evaluation); staff promotion of breastfeeding in a neonatal unit with low birth weight (LBW) babies in the UK and Spain (both models based on a meta-analysis); and community based breastfeeding promotion and peer counselling in Uganda (a trial based economic evaluation).

Net costs (in 2017/18 GBP) for group education and home visits (South Africa) were £11,513,022 at a population level. For breastfeeding support in neonatal units with LBW babies (UK), net costs were -£116 to -£1,030 per mother depending on weight (also cost saving in Spain). For peer support (Uganda) net costs were £116 per mother.

The benefit of group education and home visits (South Africa) was an increase of 281,927 months of exclusive breastfeeding (reviewer calculated). The benefit of breastfeeding support in neonatal units with LBW babies (UK) was 0.009 QALYs to 0.251 QALYs per mother depending on weight (also QALY gaining in Spain). The benefit of peer support (Uganda) was 0.01 disability adjusted life years (DALYs) per mother supported. Breastfeeding support in neonatal units with LBW babies was therefore a dominant strategy.

The neonatal interventions to support breastfeeding in mothers of LBW babies were likely to be dominant (cost less with better outcomes) and so have positive returns on investment. For the other interventions, the return on investment is dependent on the value placed on additional months breastfeeding and on the value of a DALY. The authors concluded that there was limited published evidence on the cost-effectiveness of strategies to promote breastfeeding and that studies should integrate evaluations of the effectiveness of interventions with economic analyses.

Table 3.3: Methods for studies of interventions to increase rates of breastfeeding

Study	Methodology description	Timeframe of the analysis	Analytic approach
Anokye, 2020 [11]	A within trial economic evaluation of an RCT. Limited information on the trial was provided but the costs of delivering the intervention were gathered as part of the trial.	Cost-effectiveness was determined over a 6-month period.	NA
Camacho, 2020 [1]	Systematic review.	Studies searched from 2000 to 2019.	NA
Pokhrel, 2015 [2]	Economic model linking breastfeeding with risks to baby of infections (gastrointestinal, LRTI and acute otitis media) and to mother of breast cancer.	Children: one year Mothers: lifetime	For children, a simple decision tree based upon risks for children who are and are not breastfed. For mothers, a simple markov model with cancer, no cancer and death.

Key: LRTI - lower respiratory tract infection; NA - not applicable; RCT - randomised controlled trial.

Table 3.4: Results for studies of interventions to increase rates of breastfeeding

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Anokye, 2020 [11]	Per ward: £9,989 Per baby: £91.45	The intervention increased breastfeeding rates by an average of 5.7 percentage points (p<0.001).	Cost per additional baby breastfed at 6 to 8 weeks: £974 The intervention would have to generate 0.05 QALYs to be cost-effective at a WtP threshold of £20,000 per QALY.	Not discussed.	The intervention increased breastfeeding rates at 6-8 weeks and has the potential to be cost effective if this increase in breastfeeding rates results in health gains for the infant and/or mother. However, the cost-effectiveness or return on investment was not estimated by the authors.	This study provided information to help inform public health guidance on breastfeeding. To make the economic case unequivocal, evidence on the varied and long-term health benefits of breastfeeding to both the baby and mother and the effectiveness of financial incentives for breastfeeding beyond 6 to 8 weeks is required.
Camacho, 2020 [1]	Net costs 2017/18 GBP Group education and home visits	Net benefit Group education and home visits vs no support	Group education and home visits vs no support (South Africa): £19 to £107 per additional month of	Not discussed.	The neonatal interventions with mothers of LBW babies in the UK and Spain were likely to cost less	There is limited published evidence on the cost-effectiveness of strategies to promote breastfeeding, although

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
	(South Africa): £11,513,022 Neonatal unit with LBW babies (UK): -£116 to -£1,030 depending on weight Neonatal unit with LBW babies (Spain): -£3,203 to -£23,859 depending on weight Peer support (Uganda): £116	(South Africa): Increase in months of exclusive breastfeeding of 281,927 (reviewer calculated) Neonatal unit with LBW babies (UK): 0.009 QALYs to 0.251 QALYs depending on weight Neonatal unit with LBW babies (Spain): 0.156 to 1.75 QALYs depending on weight Peer support (Uganda): 2 months of exclusive breastfeeding; 0.01 DALYs.	exclusive breastfeeding Neonatal unit with LBW babies (UK): Intervention dominant Neonatal unit with LBW babies (Spain): Intervention dominant Peer support (Uganda): £58 per month of exclusive breastfeeding; £9,617 per DALY		with better outcomes than no intervention and so have positive returns on investment. For the other interventions it is unclear whether they would generate a return on investment.	the quality of the current evidence is reasonably high. Future studies should integrate evaluations of the effectiveness of strategies with economic analyses.
Pokhrel, 2015 [2]	No intervention costs were considered. The annual total cost of the three childhood infections was £75.5 million and lifetime costs of breast cancer was £960 million.	For first time mothers, 371 QALYs could be generated from first time mothers being encouraged to breastfeed up to 6 months and avoided breast cancer.	For first time mothers, adding the value of 371 QALYs (at £20,000 per QALY) generated from first time mothers being encouraged to breastfeed up to 6 months and avoided breast cancer to the health costs averted would generate benefits	Not discussed.	No intervention costs were discussed. Instead, the modelling shows the potential economic benefits (from reduced infections in infants and risk of breast cancer in women) of increasing breastfeeding rates.	The economic impact of low breastfeeding rates is substantial. Investing in services that support women who want to breastfeed for longer is potentially cost saving.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
	Increasing women exclusively breastfeeding by 4 months from 7% to 21% would reduce annual hospital infection costs by £4.08 million, increasing to £16.95 million if increased to 65%. Increasing the rate of breastfeeding for <18 months to 32% and for 7 to 18 months to 16% would save £21.17 million from reduced breast cancer.		between £23 million and £41 million depending on the effectiveness of interventions in increasing breastfeeding rates.			

Key: DALY - disability adjusted life years; GBP – Great British Pounds; LBW – low birth weight; QALY - quality-adjusted life year; UK - United Kingdom; WTP - willingness-to-pay.

3.4 Dental Interventions

Anopa 2015 [3] compared the cost of the Childsmile programme in Scotland to cost savings from improved dental health in five-year old children from the programme from the perspective of the NHS. Childsmile is a nursery based toothbrushing and dental care programme delivered to three and four year olds. The study analysed a total of 62,419 dental records in five-year olds from 2000 to 2010 held by Scottish Health Boards. The records included dental extractions and fillings and were analysed before and after the introduction of Childsmile.

The total cost of Childsmile in Scotland in 2009/10 was £1,762,621 per year. In 1999/2000 (before Childsmile), in five year olds the total number of filled teeth was 19,030, decayed teeth was 107, 925 and children with two or more missing teeth was 6,479. In 2009/10 (after the introduction of Childsmile) these numbers had fallen substantially, as the number of filled teeth was 10,909, decayed teeth was 57,167 and children with two or more missing teeth being was 2,837.

In 2009/2010, supported toothbrushing in nurseries was estimated to have saved £4,371,097 in dental care costs compared to if Childsmile had not been introduced.

From a health inequalities perspective, the study found that absolute cost savings with the intervention increased as deprivation increased although the relative cost savings appeared to be broadly the same. This means that whilst the absolute differences may have reduced the relative level of inequality in health outcomes by income probably remained largely the same.

Supported toothbrushing as in the Childsmile programme would appear to generate a substantial return on investment (the authors concluded the savings could be 2.5 times the costs of the programme) although the before and after nature of the analysis could potentially not take into account other factors that may have improved dental health.

Anopa 2022 [4] explored the economic value of adding fluoride varnish at six months to the Childsmile programme in Scotland. The economic evaluation was a within trial assessment from an RCT from the perspective of the NHS. The trial and economic evaluation focussed on 534 children attending nursery schools with a mean age of 3.5 years with patients predominantly in lower socio-economic groups (64% were in Scottish Index of Multiple Deprivation 2 or 3). Costs were collected as part of the trial and utilities estimated using the Child Health Utility Index (CHU9D) with outcomes for children collected for two years.

The mean cost per child of 6-monthly fluoride varnish was £32.66 with the incremental costs per child compared to treatment as usual (TAU) of £63.87 (p=0.382). Over 24 months, there was a utility loss of 0.0044 (p=0.636) with fluoride varnish compared to TAU and as such TAU dominated six-monthly fluoride varnish.

As six-monthly fluoride varnish in addition to Childsmile was found to cost more with worse outcomes than Childsmile without fluoride varnish, it would not provide a positive return on investment.

Table 3.5: Methods for studies of dental interventions

Study	Methodology description	Timeframe of the analysis	Analytic approach
Anopa, 2015 [3]	Analysis of total number and spending on dental extractions, fillings and decay for children for five-year olds using data held by Scottish Health Boards and the Information Services Division (ISD). Treatments and costs were analysed before and after the introduction of supported toothbrushing in nurseries.	2000 to 2010.	NA
Anopa, 2022 [4]	A within trial economic evaluation of an RCT. Groups of children were randomised to receive Childsmile with fluoride varnish or Childsmile without fluoride varnish. Costs were collected as part of the trial and utilities estimated using the CHU9D tool.	Children in the trial were monitored for two years.	NA

Key: CHU9D - Child Health Utility Instrument; ISD - Information Services Division; NA – not applicable; RCT - randomised controlled trial.

Table 3.6: Results for studies of dental interventions

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Anopa, 2015 [3] Intervention: Supervised nursery toothbrushing programme (became Childsmile in 2006).	£1,762,621 per year (2009/10 pounds)	Dental health of five-year olds Number of filled teeth 1999/2000: 19,030 2009/2010: 10,909 Number of decayed teeth 1999/2000: 107,925 2009/2010: 57,167	In 2009/2010, supported toothbrushing in nurseries was estimated to have saved £4,371,097 in dental care costs compared to if the intervention had not taken place.	The study found that absolute cost savings with the intervention increased as deprivation increased; whilst the relative effect was broadly the same across deprivation levels the starting costs increased substantially as deprivation increased. This does mean however that whilst the absolute differences may have reduced the relative level of inequality in	Supported toothbrushing generated a substantial return on investment.	The NHS costs associated with the dental treatments for five-year-old children decreased over time. In the eighth year of the toothbrushing programme the expected savings were more than two and a half times the costs of the programme implementation.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
		Children with one tooth missing 1999/2000: 1,615 2009/2010: 776 Children with two or more teeth missing 1999/2000: 6,479 2009/2010: 2,837		health outcomes by income probably remained largely the same.		
Anopa, 2022 [4] Intervention: Fluoride varnish applied at six monthly intervals in addition to the Childsmile programme to prevent dental caries.	Mean incremental costs per child of 6 monthly fluoride varnish compared to treatment as usual (TAU): £63.87 (p=0.382) Intervention cost: £32.66 per child	Over 24 months, utility loss with fluoride varnish compared to TAU: 0.0044 (p=0.636).	TAU dominated six monthly fluoride varnish.	Not discussed	Six monthly fluoride varnish was found to cost more with worse outcomes than treatment as usual (TAU) (the Childsmile programme minus fluoride varnish) and so would not provide a positive return on investment.	Applying FV in nursery settings in addition to the Childsmile program is not likely to be cost-effective given current thresholds.

Key: ABA - applied behaviour analysis; ADHD - attention deficit/hyperactivity disorder; BMI - body mass index; CO - carbon monoxide; CPC - child-parent centre; DALY - disability adjusted life years; EE - economic evaluation; FV - fluoride varnish; GBP - gross domestic product; HALY - health adjusted life years; ICER - incremental cost-effectiveness ratio; IY - Incredible Years; LBW – low birth weight; NA - not applicable; NFPP - New Forest Parenting Programme; NHS - National Health Service; NICE - National Institute for Health and Care Excellence; NOSH - Nourishing Start for Health; NR – not reported; PT – parent training; QALY - quality-adjusted life year; QoL - quality of life; RCT - randomised controlled trial; SMI - serious mental illness; TAU - treatment as usual; UK - United Kingdom; WTP - willingness-to-pay.

3.5 Smoking Interventions

Jones 2019 [5] developed an economic model to understand the lifetime impact of smoking in pregnancy to mother and child from the perspective of the NHS and social services. The authors illustrated how the model could be used to estimate the cost-effectiveness of specific smoking cessation interventions by using the effectiveness of the MiQuit trial in the model. MiQuit was a trial of self-help smoking cessation support over 12 weeks using tailored text messages in addition to normal NHS smoking cessation support.

The model used UK smoking statistics to estimate ages of smoking mothers and length of time smoking and was built as a decision tree followed by Markov model. The decision tree component for mothers had two smoking outcomes (did or did not quit through pregnancy) followed by morbidity in pregnancy which was influenced by smoking status. The Markov model allowed mothers to be current or former smokers with associated risks of health-related events. The decision tree for the unborn child had the same smoking outcomes as in the mother's model, followed by adverse birth outcomes with a Markov model where the child is or is not exposed to passive smoking before the age of 15 with associated health outcomes and whether the child starts smoking past 16 with associated long-term health outcomes.

In the economic model, text message support was found, over a lifetime horizon, to save £38.37 and generate 0.04 QALYs per mother compared to usual NHS smoking cessation support alone and therefore was a dominant intervention (i.e., less costly, more effective). Text message support to stop smoking is likely to be highly cost-effective and generate a positive return on investment and as the model assumed that people cycle through smoking and not smoking, the short-term nature of the trial data is not necessarily limiting to findings. However, the study is primarily about the model itself which can be used for any smoking in pregnancy intervention.

McMeekin 2023 [6] used the same model as Jones 2019 [5] to evaluate the long-term (lifetime) cost-effectiveness of financial incentives to encourage pregnant women to quit smoking as assessed by the CPIT III trial. The authors also undertook a within trial economic analysis of the short term (less than one year) cost-effectiveness of the intervention. The financial incentives were up to £400 in shopping vouchers: £50 for engaging with stop smoking services and setting a quit date, £50 if carbon monoxide certified as having quit at 4 weeks, £100 at 12 weeks and £200 in late pregnancy. The mean age of mother was 28 with information on effectiveness (and costs and outcomes for the short-term model) taken from the 944 patients enrolled in the CPIT III trial.

Over the trial time horizon (less than 12 months), mean intervention costs, including smoking cessation services and nicotine patches, were £268 (compared to £91 with control). Adjusted analysis suggested total costs could be £637 in the intervention arm, although this was not statistically significant. The trial also showed an absolute difference in late pregnancy quitters of 14.4% with the intervention with a QALY gain of 0.004 resulting in an incremental cost-effectiveness ratio (ICER) of £150,000 per QALY gained with financial incentives. However, in the lifetime model, including mother and child outcomes, the mean cost saving was £37 (not statistically significant) with a QALY gain of 0.03 for mothers only and 0.171 if the lifetime for the infant and mother was taken into account with the majority of this QALY gain from the child after the age of 15. In the lifetime model, financial incentives are therefore a dominant intervention compared to no financial incentives.

Financial incentives to stop smoking is effective in the short term but will only have a substantial return on investment if the impact on mother and infant is projected over a lifetime. The authors concluded that offering up to £400 financial incentives to support pregnant women to stop smoking is cost-effective over a lifetime for mother and infants.

Renwick 2018 [7] estimated the cost-effectiveness of a complex intervention to reduce exposure to second hand smoke for children where the primary caregiver cannot quit smoking. The economic analysis was a within trial assessment of the Smoke Free Home randomised trial with participants recruited 204 cares from Sure Start Centres in deprived areas of Nottingham where a child under 5 lived in a home where a main caregiver was a smoker. The intervention included a smoke free homes advisor who undertook home visits to provide behavioural support and give feedback on air quality in the home. Participants were also provided with nicotine replacement patches. The mean age of carers was 28, 91% were female and 94% were white British.

The average cost of the intervention per household was £328 and of usual care was £45 giving an incremental cost of the intervention of £283. The intervention reduced particulate matter (PM) 2.5 (PM2.5) (ug/m3) by 21.6 compared to usual care and had 3.7% more quitters, a reduction of 7 in the number of cigarettes smoked per day and 20.7% more carers attempted to quit compared to usual care. The cost per additional quitter with the intervention was £71 and the cost per reduction in PM2.5 (ug/m3) was £131 compared to usual care.

The programme was aimed at disadvantaged areas and smoking was discussed as a cause of future health inequalities, but there was no assessment of the impact on health inequalities of the intervention. The return on investment is difficult to determine as although the intervention was found to reduce tobacco related harm to children, the economic benefits are dependent on the WtP for incremental improvements in air quality or per quitter and how these outcomes link to health consequences.

Table 3.7: Methods for studies of smoking interventions

Study	Methodology description	Timeframe of the analysis	Analytic approach
Jones, 2019 [5]	Decision tree followed by Markov model populated with published disease progression, cost and utility data.	Lifetime.	The decision tree for mothers had two smoking outcomes (did or did not quit through pregnancy) followed by pregnancy morbidity/no morbidity. The markov model cycled through current/former smoker with associated risks of health-related events. Decision tree for fetus and infants had the same maternal smoking outcomes as the mother's model followed by adverse birth outcomes before a markov model where the child is or is not exposed to passive smoking before the age of 15 and whether the child starts smoking past 16 with associated health outcomes.
McMeekin, 2023 [6]	Short-term analysis was a within trial analysis of the intervention (the CPIT III trial). The long-term analysis used the model by Jones 2019.	Short-term analysis: less than one year Long-term analysis: lifetime	For the long-term analysis, a decision tree for mothers had two smoking outcomes (did or did not quit through pregnancy) followed by pregnancy morbidity/no morbidity. The markov model cycled through current/former smoker with associated risks of health-related events. The decision tree for fetus and infants had the same maternal smoking outcomes as the mother's model followed by adverse birth outcomes before a markov model where the child is or is not exposed to passive smoking before the age of 15 and whether the child starts smoking past 16 with associated health outcomes.
Renwick, 2018 [7]	Within trial economic analysis from an open label RCT with micro costing for the costs of the intervention and usual care.	12 weeks.	NA

Key: NA – not applicable; RCT - randomised controlled trial.

Table 3.8: Results for studies of smoking interventions

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Jones, 2019 [5] Intervention: MiQuit - self-help smoking cessation support as a 12-week programme of tailored text messages in addition to normal NHS smoking cessation support.	Text message support saved £38.37 per mother compared to usual NHS smoking cessation support alone.	Text message support generated 0.04 QALYs per mother compared to usual NHS smoking cessation support alone.	Text message support dominated usual NHS smoking cessation support alone.	Not discussed.	Text message support to stop smoking was likely to be highly cost-effective and generate a positive return on investment. .	Using data from a trial which reported only short-term economic analysis showed that the intervention was very likely to be cost-effective in the longer term and to generate health-care savings.
McMeekin, 2023 [6] Intervention: Financial incentives for pregnant women to stop smoking. £400 in shopping vouchers in total: £50 for engaging with stop smoking services and setting a quit date, £50 if CO certified as quit at 4 weeks, £100 at 12 weeks and £200 in late pregnancy.	In the short-term model, mean intervention costs, including smoking cessation services and nicotine patches, were £268 (compared to £91 with control). Adjusted analysis suggested total costs could be £637 in the intervention arm, although this was not statistically significant. In the lifetime model, including mother and child outcomes, the mean cost saving was £37 (not statistically significant).	The short-term model showed an absolute difference in late pregnancy quitters of 14.4% with the intervention with a QALY gain of 0.004. The lifetime model showed a QALY gain of 0.03 for mothers only and 0.171 if the lifetime for the infant and mother was taken into account with the majority of this QALY gain (0.162 calculated by the reviewer) arising from the infant after the age of 15.	The short-term model suggested a cost per late pregnancy quitter of £4,400 and an ICER of £150,000 per QALY gained with the intervention. The long-term model including mother and infant lifetime outcomes suggested the intervention dominated usual care.	Not discussed.	The use of financial incentives to stop smoking was effective in the short term but was only likely to have a substantial return on investment if the impact on mother and infant was projected over a lifetime.	In the UK, offering up to £400 financial incentives, in addition to usual care, to support pregnant women to stop smoking appears to be highly cost-effective over a life-time for mother and infants.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Renwick, 2018 [7] Intervention: An intervention to stop smoking in carers (the Smoke Free Home Trial). A smoke free homes advisor undertook home visits to provide behavioural support and give feedback on air quality in the home. Participants were also provided with nicotine replacement patches.	The average cost of the intervention per household: £328 Usual care: £45 Incremental cost of the intervention: £283	The intervention reduced particulate matter of <2.5μm diameter (PM2.5 (ug/m3)) by 21.6 compared to usual care and had 3.7% more quitters, a reduction of 7 in the number of cigarettes smoked per day and 20.7% more carers attempted to quit compared to usual care.	The cost per additional quitter with the intervention was £71 and the cost per reduction in PM2.5 (ug/m3) was £131 compared to usual care.	Whilst the programme was aimed at disadvantaged areas and smoking was discussed as a cause of future health inequalities, there was no assessment of the impact on health inequalities of the intervention.	The intervention was found to reduce tobacco related harm to children, but the return on investment is dependent on the WtP for incremental improvements in air quality or per quitter. There is no consideration of the economic or health consequences of these improvements nor whether the improvements were maintained.	The complex intervention was more costly but more effective in reducing PM2.5 compared with the usual care. It offers huge potential to reduce children's tobacco-related harm by reducing exposure to second hand smoke in the home. The intervention is considered cost-effective if the decision maker is willing to pay £131 per additional 10μg/ m3 of PM2.5 reduction.

Key: ABA - applied behaviour analysis; ADHD - attention deficit/hyperactivity disorder; BMI - body mass index; CO - carbon monoxide; CPC - child-parent centre; DALY - disability adjusted life years; EE - economic evaluation; FV - fluoride varnish; GBP - gross domestic product; HALY - health adjusted life years; ICER - incremental cost-effectiveness ratio; IY - Incredible Years; LBW – low birth weight; NA - not applicable; NFPP - New Forest Parenting Programme; NHS - National Health Service; NICE - National Institute for Health and Care Excellence; NOSH - Nourishing Start for Health; NR – not reported; PT – parent training; QALY - quality-adjusted life year; QoL - quality of life; RCT - randomised controlled trial; SMI - serious mental illness; TAU - treatment as usual; UK - United Kingdom; WTP - willingness-to-pay.

3.6 Immunisation Intervention

Giorgakoudi 2018 [9] assessed the cost-effectiveness of maternal immunisation against neonatal and maternal invasive group B streptococcus (GBS) disease from the perspective of the NHS and social services. A decision tree was produced for the analysis, with three GBS outcomes (early onset, late onset and no infection) followed by sequalae of varying severity including death. The analysis was based on the total number of live births in the UK (776,352 in the analysis) and used published data on vaccine efficacy, uptake and risks to mother and baby for infection.

At a notional cost of £54 per vaccine, the total cost to vaccinate all pregnant women would be £30.7 million with a net cost of £17.4 million after taking into account savings from reduced infection which would also generate 870 QALYs. The ICER per QALY gained at a notional cost of £54 per vaccine would be £19,953 and so is the maximum price at which vaccination could be cost-effective at a WTP threshold of £20,000 per QALY (or £71 at £30,000 per QALY). Disease incidence and vaccine costs were the biggest determinants of cost-effectiveness.

The authors concluded that GBS immunisation is expected to be cost-effective at vaccine prices that could be considered reasonable to the NHS.

Table 3.9: Methods for study of immunisation intervention

Study	Methodology description	Timeframe of the analysis	Analytic approach
Giorgakoudi, 2018 [9]	Decision tree analysis using published data.	Lifetime.	Decision tree had three outcomes - early onset, late onset or no GBS disease followed by sequalae of varying severity including death. Vaccine uptake rate was assumed to be 0.6 with an efficacy of 0.85.

Key: GBS - group B streptococcus.

Table 3.10: Results for study of immunisation intervention

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Giorgakoudi, 2018 [9] Intervention: Vaccination for GBS.	At a price of £54 per vaccine, the total cost would be £30.7 million with a net cost of £17.4 million	Total QALY gain with vaccination: 870	The ICER per QALY gained at a notional cost of £54 per vaccine would be £19,953 and so is the maximum price at which vaccination could be cost-effective at a WTP threshold of £20,000 per QALY (or £71 at £30,000 per QALY). Disease incidence and vaccine costs were the biggest determinants of cost-effectiveness.	Universal programme and inequalities not discussed.	It is unlikely there are savings with vaccination but the QALYs generated from vaccination meant that the authors concluded that vaccination could be a cost-effective investment at £54 per dose which the authors considered to be a reasonable price for vaccination in the UK.	Maternal GBS immunisation is expected to be cost-effective, even at a relatively high vaccine price.

Key: ABA - applied behaviour analysis; ADHD - attention deficit/hyperactivity disorder; BMI - body mass index; CO - carbon monoxide; CPC - child-parent centre; DALY - disability adjusted life years; EE - economic evaluation; FV - fluoride varnish; GBP - gross domestic product; HALY - health adjusted life years; ICER - incremental cost-effectiveness ratio; IY - Incredible Years; LBW – low birth weight; NA - not applicable; NFPP - New Forest Parenting Programme; NHS - National Health Service; NICE - National Institute for Health and Care Excellence; NOSH - Nourishing Start for Health; NR – not reported; PT – parent training; QALY - quality-adjusted life year; QoL - quality of life; RCT - randomised controlled trial; SMI - serious mental illness; TAU - treatment as usual; UK - United Kingdom; WTP - willingness-to-pay.

3.7 Early Childhood Interventions to Families Facing Challenges

Cannon 2018 [11] was a systematic review of evaluations, including economic evaluations, of early childhood programs for children from birth to five that that were in one of four categories:

- Early care and education: support to children in group settings.
- Home visiting: individualised services delivered in homes to promote parent skills and knowledge.
- Parent education: individualised services delivered outside of homes to promote parent skills and knowledge.
- Transfers: cash or in-kind benefits direct to families.

In total 25 studies were identified that provided economic evaluations of interventions in early childhood although limited detail of specific studies and interventions was provided.

The review showed costs (in 2016 US dollars) ranged from $150 per family for a parent education programme to $48,800 per family for a comprehensive education and home visiting service. This variation in cost was driven by programme intensity, duration and local costs.

Benefit cost ratios were typically in region of $2 to $4 for every dollar invested. The review found that higher returns are associated with low cost programmes and resource intensive interventions with long term follow up and that both targeted and universal approaches can show positive returns. Further, monetary benefits arise from multiple domains but are often highest for income and reductions in crime. Benefits to the payer (usually the Government) rarely outweigh programme cost. Benefits to children from an intervention can take years or decades to be realised and not all outcomes can have an economic value assigned to them.

Barlow 2019 [10] evaluated the Parents under Pressure program, an intervention underpinned by the Integrated Theoretical Framework, developed for complex families with multiple adversities and delivered to parents currently engaged in community-based substance abuse treatment with children under 2.5 years. The programme was delivered in family homes through 12 modules and enabled parents to better regulate their emotions through mindfulness strategies. The study included a trial based economic evaluation from the perspective of the NHS and social services using data from an RCT with 100 parents where the key outcomes were reduction in risk of child abuse and parental emotional regulation.

The mean age of parents in the trial was 30.8, 96% were female with 83% unemployed and 51% with a criminal record. The mean age of children was 9.2 months with 60% of children male and 82% involved with child protective services. Utility data was captured through the EQ-5D utility tool for parents with micro costing during the trial was to capture health and social costs for the parent and child.

Over 12 months, the incremental costs of Parents under Pressure compared to TAU was £2,386.64 with incremental QALYs 0.07 giving Parents under Pressure an ICER of £34,094.86 per QALY gained.

The ICER per QALY gained is above the threshold normally considered cost-effective by NICE and so the intervention may have insufficient return on investment. However, the results only considered parental quality of life (QoL) and it is likely if the reduction in harm to children was taken into account the cost-effectiveness of the intervention would improve. Further, the short time horizon of the analysis will have limited the potential total benefits of the programme if any improvements were sustained beyond the trial time horizon. The authors concluded that whilst the trial had provided evidence that up to one-third of substance dependent parents of children under 3-years of age could be supported by Parents under Pressure, further research was needed.

Hajizadeh 2017 [12] estimated the long-term cost-effectiveness of ParentCorps, a programme promoting family engagement and safe, nurturing and predictable environments at home and at school for pre-kindergarten children with low-levels of self-regulation in the USA. Outcomes of the programme were increased achievement, reduced behaviour problems and lower levels of obesity. No further details of the intervention or how it is delivered were provided by the authors.

The cost-effectiveness analysis of ParentCorps was from the perspective of US public health, social care and judicial systems with child input chosen to match demographics of urban areas in the USA. A Markov model was used with effectiveness data from ParentCorps on short term evidence of the interventions' impact on academic achievement, self-regulation and obesity and then linking these to long-term outcomes into adulthood (graduation, drug use, diabetes, employment, crime and health outcomes) over a lifetime.

The costs of ParentCorps in a large school (72 pupils a year in four classrooms) would be $104,190 in year one falling to $39,755 in year three. Net lifetime savings of $4,387 per parent/child would result from a reduction in healthcare and criminal justice use and increases in productivity with a lifetime QALY gain of 0.27 QALYs. As it is cost saving with improved outcomes, ParentCorps dominated usual care.

Whilst inequalities are not explicitly mentioned, ParentCorps was targeted at high poverty areas and so could potentially improve health inequalities. Whilst the return on investment seems high, this is dependent on effectiveness seen at the end of the programme being maintained effectively for life and this assumption was not tested in the study. The authors concluded that interventions early in life such as ParentCorps can improve academic, behavioural and health outcomes among children attending high-poverty, urban schools generate substantial cost savings in the long-term.

Table 3.11: Methods for studies of early childhood interventions to families facing challenges

Study	Methodology description	Timeframe of the analysis	Analytic approach
Barlow, 2019 [10]	Pragmatic RCT with financial incentives for parents to engage with the study assessments. Utility was captured through the EQ-5D for parents. Micro costing during the trial was used to capture costs and included health and social care costs for the parent and child. Bootstrapping was used to model uncertainty.	Assessments were conducted at six and twelve months.	NA
Cannon, 2018 [11]	Systematic review.	Unclear but appears to be studies from 2005 to no later than 2018.	NA
Hajizadeh, 2017 [12]	A markov model based upon odds ratios for ParentCorps on academic achievement, self-regulation and obesity and then linking these to long-term outcomes into adulthood. Essentially this was a social return on investment analysis with assumed costs for long term outcomes.	Lifetime.	The model was based upon an 'influence model' whereby short-term outcomes on achievement, behaviour and obesity were linked to longer term outcomes in terms of graduation, drug use and diabetes which then linked to employment, crime and health outcomes.

Key: EQ-5D - EuroQoL-5 dimensions; RCT - randomised controlled trial.

Table 3.12: Results for studies of early childhood interventions to families facing challenges

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Barlow, 2019 [10] Intervention: Parents under Pressure, an intervention underpinned by the Integrated Theoretical Framework, developed for complex families with multiple adversities. The aim of the programme, delivered through 12	Incremental costs of Parents under Pressure compared to TAU: £2,386.64	Incremental QALYs of Parents under Pressure compared to TAU: 0.07	Cost per QALY for Parents under Pressure compared to TAU: £34,094.86	Not discussed explicitly but the target group for the intervention were unemployed and so would be on low incomes.	The incremental cost-effectiveness ratio I(CER) per quality-adjusted life-year (QALY) gained was above the threshold normally considered cost-effective by NICE. However, the results only considered parental quality of life (QoL) and it is likely if the reduction in harm to children was taken into account the cost-effectiveness (and	Up to one-third of substance dependent parents of children under 3-years of age can be supported to improve their parenting, using a modular, one-to-one parenting program. Further research is needed.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
modules, is to enable parents to better regulate their emotions through mindfulness strategies. The intervention was delivered in family homes by fourteen practitioners. Outcomes were reduction in risk of child abuse and parental emotional regulation.					therefore return on investment) of the intervention would improve.	
Cannon, 2018 [11] Intervention: Interventions fell into four categories: early care and education - support to children in group settings; home visiting - individualised services delivered in homes to promote parent skills and knowledge; parent education - individualised services delivered outside of homes to promote parent skills and knowledge; transfers - cash or in-kind benefits direct to families.	Cost analysis (2016 US dollars) showed that costs ranged from $150 per family for a parent education programme to $48,800 per family for a comprehensive education and home visiting service. Variation was due to programme intensity, duration and local costs applied in the analysis.	NR	Benefit cost ratios were typically in region of $2 to $4 for every dollar invested.	Not discussed.	The review highlighted the following key findings about economic return: Higher returns are associated with low cost programmes and resource intensive interventions with long term follow up Targeted and universal approaches can show positive returns Monetary benefits arise from multiple domains but are often highest for income and reductions in crime. Government benefits (i.e. to the payer of the intervention) rarely outweigh programme cost Benefits to children can take years or decades to unfold Not all outcomes can have an economic value assigned to them.	Most of the reviewed programs have favourable effects on at least one child outcome and those with an economic evaluation tend to show positive economic returns.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Hajizadeh, 2017 [12] Intervention: ParentCorps, a family-cantered enhancement to pre- kindergarten programming promoting family engagement and safe, nurturing and predictable environments at home and at school. No further details of the intervention were provided.	Costs of ParentCorps in a large school (72 pupils a year in four classrooms): ▪ Year one: $104,190 ▪ Year two: $89,755 ▪ Year three: $39,755. Net lifetime savings of $4,387 from reduction in healthcare, criminal justice and productivity.	Lifetime QALY gain: 0.27 QALYs	ParentCorps dominated usual care.	Not explicitly mentioned but the intervention was targeted at high poverty areas.	Potential for high return on investment but this is dependent on effectiveness seen being maintained effectively for life.	Effective family-centred interventions early in life such as ParentCorps that impact academic, behavioural and health outcomes among children attending high-poverty, urban schools have the potential to result in longer-term health benefits and substantial cost savings.

Key: ABA - applied behaviour analysis; ADHD - attention deficit/hyperactivity disorder; BMI - body mass index; CO - carbon monoxide; CPC - child-parent centre; DALY - disability adjusted life years; EE - economic evaluation; FV - fluoride varnish; GBP - gross domestic product; HALY - health adjusted life years; ICER - incremental cost-effectiveness ratio; IY - Incredible Years; LBW – low birth weight; NA - not applicable; NFPP - New Forest Parenting Programme; NHS - National Health Service; NICE - National Institute for Health and Care Excellence; NOSH - Nourishing Start for Health; NR – not reported; PT – parent training; QALY - quality-adjusted life year; QoL - quality of life; RCT - randomised controlled trial; SMI - serious mental illness; TAU - treatment as usual; UK - United Kingdom; WTP - willingness-to-pay.

3.8 Obesity Interventions

Brown 2019 [13] estimated the cost effectiveness of obesity interventions in children aged 2 to 5 years from the perspective of the Australian Healthcare System. No specific intervention was considered, but rather the effectiveness of a generic intervention that reduced body mass index (BMI) by 0.13 was taken from a review of reviews. The economic analysis used a pre-existing lifetime model (Centre of Research Excellence in Obesity Policy Model (CRE-Obesity Policy model)) that linked BMI to health outcomes, although details of the model were not provided. Scenarios were undertaken on maintenance of intervention effect.

The costs of interventions are not considered, but total cost savings were estimated at between $0 (if intervention effect was not maintained to adulthood) to $301 million (if the treatment effect was maintained for life). Total health adjusted life years (HALYs) were estimated at between 7,425 (if treatment effect was not maintained to adulthood) to 36,946 (if the treatment effect was maintained for life). At a WtP of $50,000 per HALY, the intervention cost per child aged 0 to 5 years that would still be cost-effective was between $215 (if intervention effect was not maintained to adulthood) to $1,228 (if effect lasted a lifetime).

The study results suggest there is potential for substantial return on investment from obesity interventions, but the level of return is dependent on the length of time of the effect on BMI from the intervention being maintained.

Tran 2022 [14] assessed the cost-effectiveness of a community-wide universal early childhood (0 to 5 years) obesity prevention intervention from an Australian funder perspective if delivered nationwide. The intervention was Romp and Chomp and involved community capacity building, policy changes and the cultural and physical environments of early years settings. Romp and Chomp had four key messages: daily active play, daily water and fewer sweet drinks, daily fruit and vegetables and less screen time.

An existing obesity model (Early Prevention of Obesity in Childhood (EPOCH) was populated with published effectiveness data from Romp and Chomp Ten years (from 5 to 15). Whilst little detail of the model was provided, EPOCH is a microsimulation model that extrapolates BMI trajectories with utility values and costs based on BMI.

Annual intervention costs at a population level were estimated to be $177,536,705 or $93 per participant but this could be as high as $475 per participant if pessimistic cost and outcome values are chosen. The net cost after healthcare savings was estimated to be $78 per participant ($472 in worst case scenario). The mean QALY gain per participant with the intervention was 0.003 in the base case and 0.0005 in the worst case with a base case ICER of $26,399 per QALY gained with Romp and Chomp ($956,146 in the worst case scenario).

In the base case analysis, Romp and Chomp has a positive return on investment and the authors considered that Romp and Chomp has a fair probability of being cost-effective if delivered nationally in Australia. However, under a plausible worst case scenario the intervention is unlikely to be cost-effective.

Table 3.13: Methods for studies of obesity interventions

Study	Methodology description	Timeframe of the analysis	Analytic approach
Brown, 2019 [13]	Lifetime cohort modelling using a pre-existing model (CRE-Obesity Policy model) with details not provided. Effectiveness was taken from a meta-analysis and estimated as a reduction in BMI of 0.13. Scenarios were undertaken on maintenance of intervention effect. Health-related quality of life (HRQoL) was derived from published literature. Cost-savings resulted from diseases averted.	Lifetime.	Details of model not provided.
Tran, 2022 [14]	An obesity model (Early Prevention of Obesity in Childhood) populated with published effectiveness data from Romp and Chomp.	Ten years (from 5 to 15).	The obesity model is a microsimulation model that extrapolates BMI trajectories with utility values and costs based on BMI.

Key: BMI - body mass index; CRE-Obesity - Centre of Research Excellence in Obesity; HRQoL – health related quality of life.

Table 3.14: Results for studies of obesity interventions

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Brown, 2019 [13] Intervention: Childhood obesity interventions commencing before six months of age.	Costs of interventions were not considered. Total cost savings were estimated at between $0 (if treatment effect was not maintained to adulthood) to $301 million (if the treatment effect was maintained for life).	Total HALYs were estimated at between 7,425 (if treatment effect was not maintained to adulthood) to 36,946 (if the treatment effect was maintained for life).	At a WTP of $50,000 per HALY, the intervention cost per child aged 0 to 5 years that would still be cost-effective was between $215 (if effect not maintained to adulthood) to $1,228 (if effect lasted a lifetime). At a WTP of $50,000 per HALY, the intervention cost per child aged 2 to 5 years that would still be cost effective was between $326 (if effect was not maintained to adulthood) to $1,866 (if effect lasted a lifetime).	Not discussed.	The study highlighted there is potential for substantial return on investment but the level of return is dependent on the length of time the effect on BMI from intervention is maintained.	Results suggest significant potential for cost-effectiveness of obesity prevention interventions in preschool-aged children if intervention effect can be maintained.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Tran, 2022 [14] Intervention: Romp and Chomp, a universal obesity prevention intervention and involved community capacity building, policy changes and the cultural and physical environments of early years settings. The intervention had four key messages: daily active play, daily water and fewer sweet drinks, daily fruit and vegetables, less screen time.	Total annual intervention costs were $177,536,705 or $93 per participant. If only 4 to 5 year olds bore the costs the intervention would be $276 per participant and in a worst case scenario could be $475 (highest costs and lowest efficacy from 95% confidence intervals). The net cost after healthcare savings was $78 ($472 in worst case scenario).	The intervention had a mean decrease in BMI per participant of 0.06 in the base case and 0.01 in the worst case. Mean QALY gain per participant with intervention was 0.003 (not statistically significant) in base case and 0.0005 in the worst case.	The base case ICER was $26,399 in the base case with a 64% chance of being cost effective at a WTP of $50,000 per QALY. In the worst case scenario the ICER was $956,146 with a 1.6% chance of being cost effective.	Not discussed.	The authors considered that the intervention has a fair probability of being cost-effective, although the QALY gains are small (based on a small average BMI increase) and the total costs of the intervention very high.	Romp & Chomp has a fair probability of being cost-effective if delivered at scale.

Key: ABA - applied behaviour analysis; ADHD - attention deficit/hyperactivity disorder; BMI - body mass index; CO - carbon monoxide; CPC - child-parent centre; DALY - disability adjusted life years; EE - economic evaluation; FV - fluoride varnish; GBP - gross domestic product; HALY - health adjusted life years; ICER - incremental cost-effectiveness ratio; IY - Incredible Years; LBW – low birth weight; NA - not applicable; NFPP - New Forest Parenting Programme; NHS - National Health Service; NICE - National Institute for Health and Care Excellence; NOSH - Nourishing Start for Health; NR – not reported; PT – parent training; QALY - quality-adjusted life year; QoL - quality of life; RCT - randomised controlled trial; SMI - serious mental illness; TAU - treatment as usual; UK - United Kingdom; WTP - willingness-to-pay.

3.9 Antenatal Intervention to Reduce Adverse Pregnancy Outcomes (Resulting from Excess Gestational Weight Gain)

Bailey 2022 [8] assessed the cost-effectiveness of four types of antenatal lifestyle intervention: diet, diet with physical activity, physical activity and "mixed" (lacking structured diet or physical activity components). Details on the actual interventions were not provided. The analysis was from an Australian healthcare perspective and used a decision tree with effectiveness data from a meta-analysis of each type of intervention on reducing complications (gestational diabetes, hypertensive disorders, caesarean delivery and neonatal intensive care unit (NICU) stay for the infant).

Average incremental costs (taking into account healthcare costs averted/incurred) per mother were $169 for diet interventions, $59 for diet and physical activity interventions, -$95 for physical activity interventions and $182 for mixed intervention. The average incremental cost per mother over all interventions was $75. The percentage of complications avoided was 3.46% with diet interventions, 2.90% with diet and physical interventions, 4.23% with physical activity interventions and an increase in complications of 0.68% with mixed interventions. For all interventions combined, 1.94% of complications were avoided.

Diet and physical activity interventions in pregnancy, provided they are structured, are likely to have minimal incremental costs or save money and reduce complications and so therefore are likely to provide a positive return on investment or this would depend on the value of the complications averted. For other interventions, the return on investments is unclear and would depend on the value of complications avoided.

Table 3.15: Methods for study of antenatal intervention to reduce adverse pregnancy outcomes (resulting from excess gestational weight gain)

Study	Methodology description	Timeframe of the analysis	Analytic approach
Bailey, 2022 [8]	Decision tree analysis of four categories of interventions incorporating their costs and their effectiveness at stopping gestational diabetes, hypertensive disorders and caesarean delivery. Data on costs and effectiveness were drawn from a previously published meta-analysis and applied to a retrospective population of pregnant mothers with data from a health service network.	During pregnancy up to and including delivery.	NA

Key: NA – not applicable.

Table 3.16: Results for study of antenatal intervention to reduce adverse pregnancy outcomes (resulting from excess gestational weight gain)

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Bailey, 2022 [8] Intervention: Four broad categories of lifestyle interventions in pregnancy: diet, diet with physical activity, physical activity and "mixed" (lacking structured diet or physical activity components).	Average intervention costs per mother Diet: $168 Diet and physical activity: $187 Physical activity: $217 Mixed: $184 All interventions combined: $198 Incremental costs with intervention compared to standard care (none were statistically significantly different) Diet: $169 Diet and physical activity: $59 Physical activity: -$95 Mixed: $182 All interventions combined: $75	Percentage of complications avoided with intervention compared to standard care (all were statistically significantly different) Diet: 3.46% Diet and physical activity: 2.90% Physical activity: 4.23% Mixed: -0.68% All interventions combined: 1.94%	Cost per averted complication (none statistically significantly different from zero) Diet: $4,882 Diet and physical activity: $2,020 Physical activity: Dominant (costs less and reduces complications) Mixed: Dominated (costs more and increases complications) All interventions combined: $3,855	The study did not consider health inequalities.	Diet and physical activity interventions in pregnancy, provided they are structured, are likely to have minimal incremental costs or to save money and reduce complications and so therefore are likely to provide a positive return on investment.	Governments can expect a good return on investment and cost savings when implementing effective lifestyle interventions population-wide.

Key: ABA - applied behaviour analysis; ADHD - attention deficit/hyperactivity disorder; BMI - body mass index; CO - carbon monoxide; CPC - child-parent centre; DALY - disability adjusted life years; EE - economic evaluation; FV - fluoride varnish; GBP - gross domestic product; HALY - health adjusted life years; ICER - incremental cost-effectiveness ratio; IY - Incredible Years; LBW – low birth weight; NA - not applicable; NFPP - New Forest Parenting Programme; NHS - National Health Service; NICE - National Institute for Health and Care Excellence; NOSH - Nourishing Start for Health; NR – not reported; PT – parent training; QALY - quality-adjusted life year; QoL - quality of life; RCT - randomised controlled trial; SMI - serious mental illness; TAU - treatment as usual; UK - United Kingdom; WTP - willingness-to-pay.

3.10 Child or Parental Mental Health Interventions

Bee 2014 [15] conducted a systematic review that in part looked for cost-effectiveness evidence of community-based interventions for improving quality of life (QoL) in children of parents with serious mental illness. Only one study was identified that looked at the cost-effectiveness of specialist psychiatric parent and baby day unit for treatment of postnatal depression. The intervention included 60 mothers of children aged 6 weeks to 12 months with a diagnosis of major or minor depressive disorder.

From the one economic study identified by the authors, median costs of the intervention per patient were £1,351 compared to £231 with usual care. At 6 months follow up, 21/30 women in the intervention group and 7/30 in control group had recovered from depression.

The evidence on the return on investment from community-based interventions to enhance QoL in children of parents with serious mental illness is lacking. The authors concluded (noting that the study is from 2012 and so potentially now out of date) that capacity to recommend evidence-based approaches is limited.

Hodgson 2022 [16] updated an economic evaluation by Rodgers 2020 [35] assessing the cost-effectiveness of early intensive Applied Behaviour Analysis (ABA)-based interventions for pre-school children with autism from the perspective of UK NHS and social services and from a wider public sector perspective. ABA interventions are typically delivered to young children with autism for several years on a one-to-one basis, for between 20 to 50 hours per week, and "promote a range of techniques (such as the breaking down of skills into their basic components) that emphasise discrimination, learning and positive reinforcement" [35].

The authors used a Markov model to estimate cost-effectiveness of ABA interventions using published data from a systematic review. The model linked the impact of ABA interventions with children from the age of 3 on outcomes to the age of 18.5 through improvements in the Vineland Adaptive Behaviour Scales and their projected influence on education (and related adult outcomes), QoL and social care medical costs. In the model, 87.57% of children were male with 82.95% had a learning disability.

The cost of ABA was £36,682.78 compared to the cost of TAU of £8,634.33. Depending on assumptions chosen, notably on long term efficacy of ABA, from an NHS perspective, incremental costs were £57,233 to £57,879 and from a public sector perspective £36,242 to £43,940. Incremental QALYs ranged from 0.24 to 0.84 giving ICERs from the NHS perspective of £68,362 to £236,837 per QALY gained with ABA and from a public sector perspective £43,289 to £179,799 per QALY gained.

With current evidence, ABAs with young children with autism are unlikely to provide a sufficient return on investment to justify investment. The authors conclude however, that gaps in the available evidence particularly on the outcome trajectory of autistic children, limit the strength of the conclusions that can be drawn and further research is required.

Mihalopoulos 2015 [17] assessed the cost-effectiveness of a parent-focussed psycho-educational programme for children aged 3 to 5 who exhibited an inhibited or ‘shy’ temperament from the perspective of the Australian healthcare system. As part of the intervention, children were screened for inhibition in the preschool setting through questionnaires completed by parents which were then assessed primarily by psychologists. Parents of positively screened children were then offered a six-session parenting course.

The model used effectiveness evidence of a parenting intervention from a previous trial and assumed that 16% of screened children would exhibit some form of inhibition. The model itself was poorly described but appears to be a decision tree with a three-year time horizon that links the proportions of parents engaging with the intervention with a reduction in anxiety disorders in children.

The population level costs of the intervention were estimated to be AU$5.2m to the government and AU$0.44 million in private costs. The net cost after offsets for reduced costs of treating anxiety were AU$3.8m with 460 DALYs averted producing an ICER of 8,000 per DALY averted.

Whilst the authors conclude that screening young children in a preschool setting for inhibition followed by a brief intervention offers very good value-for-money, the return on investment is dependent on the value placed on the DALYs averted and with no WtP threshold for DALYs in the UK it is not possible to generalise the return on investment to the UK.

Sonuga-Barke 2018 [18] undertook a within trial economic analysis of specialised individually delivered parent training for preschool children with attention-deficit/ hyperactivity disorder (ADHD) in the UK compared with generic group-based parent training and TAU. The individually delivered intervention in the trial was the New Forest Parenting Programme (NFPP), a 12-week home-delivered programme including education about ADHD, communication strategies, play based activities and attention training. The group-based intervention was in the trial Incredible Years Toddler (IY), a 12-week programme comprising a series of developmentally based interventions for parents, children and teachers including problem-solving, videotape modelling and role playing.

The within trial economic analysis (based on 306 trial participants) was from an NHS and societal perspective with a six-month time horizon. The trial included children aged between 2 years 9 months and 4 years 6 months with a parent/caregiver 18 years or over and a diagnosis of ADHD but not a full diagnosis of autism or severely delayed development. The mean age of children in the trial was 42 to 43 months with 24 to 29% female in the intervention groups and 40% female in the TAU group. Parents were 90% female with 62 to 66% unemployed.

The average cost per family for NFPP delivery was £1,081 and for IY delivery was £1,569. Net costs including health services and family borne costs were £1,591 per family with NFPP and £2,103 with IY. There were no differences in measured parental and child outcomes with NFPP compared to IY and only NFPP only showed a statistically significant difference over TAU in any outcome and only for parent related conduct problems. Whilst NFPP and IY did not appear different in effectiveness, NFPP was less expensive.

The return on investment is unclear as both NFPP and IY cost several thousand pounds per family but the improvement in outcomes over usual care is unclear. However, IY, recommended by NICE, seems to be more costly than NFPP and so NFPP would deliver a higher return on investment than IY. It is however unclear that either intervention actually generates a positive return on investment. The authors’ conclusion was similar, stating that whilst there were no outcomes differences between NFPP and IY, NFPP cost less although this difference may be lower in practice than a trial setting.

Varshney 2022 [19] assessed the cost-effectiveness of the Chicago Child-Parent Centres (CPC) in the USA from a societal perspective. CPCs were launched in the 1960s with the longitudinal study on which the effectiveness was based starting in the early 1980s. The centres provide continuous education and family support to economically disadvantaged children in Chicago through to third grade (age 8 or 9). The programme delivered in the centres has five key features: early education no later than 4 years, structured learning for language and basic skills, increased parent involvement in home and school (at least half a day per week), provision of health and social care services, continuity between pre-school and elementary school. The programme is delivered for 3 hours daily for 5 days a week with a child-to-staff ratio of 17:2 with promotion of health and good nutrition a key component.

The economic evaluation used data from 989 children engaged with the programme followed up to the age of 37. The children were 51.8% female with 92.7% African American with 76.7% having a single parent and 77.7% residing in a high poverty area. Outcomes were compared with a matched cohort and the analysis focussed on the costs and QALY gains associated with reduced smoking status and diabetes with the programme over a lifetime.

The average cost of the preschool CPC programme was $11,000 (2021 dollars) per participant. The cost and productivity savings were $14,896 (using the foregone earnings approach). Actual QALYs were not provided, but the value of the QALY gain from the reduction in diabetes was $24,134 (with an additional 'utility' gain of $5,076) and from a reduction in smoking of $7,855. The mean benefit-cost ratio was 1.36.

The programme was targeted in low-income areas and the majority of participants lived in high poverty areas. However, the impact of CPC on health inequalities was not discussed. The return on investment was estimated to be between $1.35 and $3.66 per dollar spent and could be higher if crime reduction, welfare and earnings were taken into account. As a longitudinal study, with almost 40 years follow up, concerns of persistence of effect of CPC are not present in the same way as interventions with limited follow up. The authors concluded that the health impacts of early educational intervention are significant and may by themselves offset the costs of the intervention before incorporating other benefits.

Table 3.17: Methods for studies for child and parental mental health interventions

Study	Methodology description	Timeframe of the analysis	Analytic approach
Bee, 2014 [15]	Systematic review.	Literature was searched up to May 2012. The one identified study was from 2003.	NA
Hodgson, 2022 [16]	A markov model linking impact of ABAs on cognitive ability and onto cost and QALY outcomes. Data was drawn from published studies on ABAs rather than a specific intervention.	To age 18.5.	A markov model based upon impact of ABAs on Vineland Adaptive Behaviour Scales which are then linked to education (and adult outcomes), QoL and social care medical costs.
Mihalopoulos, 2015 [17]	Cost-utility model using data from a single trial of a parenting intervention to prevent anxiety.	Three years in the base case and eleven years in a sensitivity analysis.	The model was poorly described but would appear to be a simple decision tree that links the proportions of parents engaging with the intervention with a reduction in anxiety disorders in children.
Sonuga-Barke, 2018 [18]	Within trial economic analysis.	Six months.	NR
Varshney, 2022 [19]	Longitudinal study (children were followed to age 37) with outcomes compared with a matched cohort. The analysis focussed on the costs and QALY gains associated with reduced smoking status and diabetes with the programme.	Lifetime.	NA

Key: ABA - applied behaviour analysis; NA – not applicable; NR – not reported; QALY - quality-adjusted life years; QoL – quality of life.

Table 3.18: Results for studies for child and parental mental health interventions

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Bee, 2014 [15] Intervention: The systematic review looked for any community based interventions that improved the QoL of children with parents with serious	From the one identified study, median costs per patient were £1,351 compared to £231 with usual care.	At 6 months follow up, 21/30 women in the intervention group and 7/30 in control group had recovered from depression. It was unclear if	NA	Not discussed.	The return on investment is unclear from the one study identified.	Evidence for community-based interventions to enhance QoL in children of parents with serious mental illness is lacking. The capacity to recommend evidence-based approaches is limited. Rigorous

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
mental illness. Only one study was identified that was of a specialist psychiatric parent and baby day unit for treatment of postnatal depression.		this was maintained.				development work is needed to establish feasible and acceptable child- and family-based interventions, prior to evaluating clinical effectiveness and cost-effectiveness via a RCT.
Hodgson, 2022 [16] Intervention: Early intensive ABA based interventions that impact a child's developmental by shifting a child's developmental trajectory through early interventions. They are typically delivered to young autistic children for several years on a one-to-one basis, for between 20 to 50 hours per week.	Cost of ABA was assumed to be £36,682.78 compared to TAU of £8,634.33. From an NHS perspective, under pessimistic assumptions on long term efficacy of ABA, incremental costs were £57,879 and under optimistic assumptions on long term efficacy of ABA, incremental costs were £57,233. From a public sector perspective, under pessimistic assumptions on long term efficacy of ABA, incremental costs were £43,940 and under optimistic assumptions on long term efficacy of ABA, incremental costs were £36,242.	Under pessimistic assumptions on long term efficacy of ABA, incremental QALYs were 0.24 and under optimistic assumptions on long term efficacy of ABA, incremental QALYs were 0.84.	From an NHS perspective, under pessimistic assumptions on long term efficacy of ABA, the ICER per QALY gained with ABA was £236,837 and under optimistic assumptions on long term efficacy of ABA, the ICER was £68,362. From a public sector perspective, under pessimistic assumptions on long term efficacy of ABA, the ICER per QALY gained with ABA was £179,799 and under optimistic assumptions on long term efficacy of ABA, the ICER was £43,289.	Not discussed.	With current evidence, ABAs are unlikely to provide a sufficient return on investment to justify investment.	The results of this economic analysis suggest that early intensive ABA-based interventions are unlikely to represent value for money, based on a £20,000 to £30,000 per QALY threshold typically adopted to inform UK healthcare funding decisions. However, important gaps in the available evidence limit the strength of the conclusions that can be drawn from the presented analysis. Further research, focusing on the trajectory of autistic children following intervention is likely to be highly beneficial to resolving some of these uncertainties.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Mihalopoulos, 2015 [17] Intervention: Children were screened for inhibition in the preschool setting with questionnaires being sent home for parents to complete. The questionnaires were primarily assessed by psychologists. Parents of positively screened children were offered a six session parenting course.	The population level costs of the intervention were estimated to be AU$5.2m to the government and AU$0.44 million in private costs. The cost of the intervention itself was not provided. The net cost after cost-offsets for treating anxiety were AU$3.8m.	Total DALYs averted with the intervention were 460.	ICER with cost offsets: AU$8,000 per DALY averted ICER without cost offsets: AU$12,000 per DALY averted	Not discussed.	The return on investment was dependent on the value placed on the DALYs averted.	Screening young children in a preschool setting for an inhibited temperament and providing a brief intervention to the parents of children with high levels of inhibition appears to provide very good value-for-money and worth considering in any package of preventive care. Further evaluation of this intervention under routine health service conditions would strengthen conclusions.
Sonuga-Barke, 2018 [18] Intervention: Two interventions were considered compared to TAU: ▪ The New Forest Parenting Programme (NFPP) was a 12-week individual, home-delivered ADHD PT programme. It included education about ADHD, communication strategies, play	The average cost per family for NFPP delivery was £1,081 and for IY delivery was £1,569. Net costs including health services and family borne costs were £1,591 per family with NFPP and £2,103 with IY.	There were no differences in measured parental and child outcomes with NFPP compared to IY. NFPP only showed a statistically significant difference over TAU for parent related conduct problems. IY showed no statistical difference for any outcome compared to TAU.	Whilst NFPP and IY did not appear different in effectiveness, NFPP was less expensive.	Not discussed.	The return on investment is unclear as both NFPP and IY cost several thousand pounds per family and the improvement in outcomes over usual care is unclear. However, IY, recommended by NICE, seems to be more costly than NFPP.	Although, there were no differences between NFPP and IY with regards clinical effectiveness, individually delivered NFPP cost less. However, this difference may be reduced when implemented in routine clinical practice. Clinical decisions should take into account parental preferences between delivery approaches.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
based activities and attention training. Incredible Years Toddler (IY) was a 12-week group-based programme comprising a serious of developmentally based interventions for parents, children and teachers. It included problem-solving, videotape modelling and role playing.						
Varshney, 2022 [19] Intervention: Chicago Child-Parent Centres (CPCs). The centres provided continuous education and family support to economically disadvantaged children through to third grade (age 8 or 9). The programme had five key features: ▪ Early education no later than 4 years. ▪ Structured learning for language and basic skills.	The average cost of the preschool CPC programme was $11,000 (2021 dollars) per participant. The cost and productivity savings were $14,896 (using the foregone earnings approach).	Actual QALYs were not reported, but the value of the QALY gain from reduction in diabetes was $24,134 (with an additional 'utility' gain of $5,076) and from a reduction in smoking of $7,855.	The benefit-cost ratio was 0.30 to 2.72 with a mean of 1.36.	The programme was targeted in low income areas but the impact on health inequalities was not discussed.	The return on investment was estimated to be between $1.35 and $3.66 per dollar spent and could be higher if crime reduction, welfare and earnings were taken into account.	The results suggest that the health impacts of early educational intervention were significant and may by themselves offset the costs of the intervention, even if no other benefits were observed. However, a future study may look at incorporating benefits across a domain of outcomes such as gain in income and reduction in crime, in addition to health. This would help in calculating a comprehensive benefit-cost ratio of the program.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
▪ Increased parent involvement in home and school (at least half a day per week). ▪ Provision of health and social care services. ▪ Programme continuity between pre-school and elementary school. Promotion of health and good nutrition was also a component of the programme.						

Key: ABA - applied behaviour analysis; ADHD - attention deficit/hyperactivity disorder; BMI - body mass index; CO - carbon monoxide; CPC - child-parent centre; DALY - disability adjusted life years; EE - economic evaluation; FV - fluoride varnish; GBP - gross domestic product; HALY - health adjusted life years; ICER - incremental cost-effectiveness ratio; IY - Incredible Years; LBW – low birth weight; NA - not applicable; NFPP - New Forest Parenting Programme; NHS - National Health Service; NICE - National Institute for Health and Care Excellence; NOSH - Nourishing Start for Health; NR – not reported; PT – parent training; QALY - quality-adjusted life year; QoL - quality of life; RCT - randomised controlled trial; SMI - serious mental illness; TAU - treatment as usual; UK - United Kingdom; WTP - willingness-to-pay.

4 Discussion

The extracted studies highlight that there are a range of interventions that can be, or are being, implemented often at a national level that potentially generate significant returns on investment. These include interventions to improve dental health, reduce smoking rates in parents, increase breast feeding rates and prevent obesity. Positive returns on investment are easiest to show where interventions can prevent poor short-term outcomes. However, this review also identified interventions that were shown to be cost effective even when positive outcomes from an intervention may not be fully realised for many years after the intervention.

Looking specifically at health inequalities, whilst there were studies of interventions in low income areas because of high levels of need in those areas [7, 19], no studies extracted (or identified) explicitly looked at interventions designed to reduce specific inequalities and only one of the extracted studies showed results by deprivation levels [3]. The searches in total only identified fewer than 10 studies that were explicitly in low income or disadvantaged groups. This is not to say that any of the interventions identified in the review could not be used to address health inequalities if they were targeted at disadvantaged groups, but that studies in the literature that were identified in the searches have, on the whole, had not looked at interventions in children under five as an explicit means of addressing health inequalities. It should be noted that the targeted searches included one grey literature resource and it is possible that a number of evaluations of interventions funded by central and local government as well as by charities have been undertaken and are available but have not been published in peer-review journals or PEDE and so would not have been picked up in the searches.

The findings of the review should be considered within the context of a number of limitations that came about due to the highly pragmatic nature of the project. The limitations of the searches are outlined in detail in section 2.2.1. Notably, the search strategy was highly targeted. It was not designed to be exhaustive but aimed to target studies likely to be relevant to the research question, whilst retrieving a volume of records manageable within the timescales and resources of the project. Therefore, not all interventions are captured, nor are studies in the EU or lower income countries.

In summary, this targeted review has highlighted interventions targeted towards children under five that could generate positive returns on investment and be considered alongside other evidence to improve health in the early years, and as a result, have the potential to improve health across the life course.

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34. Anokye N, Coyle K, Relton C, Walters S, Strong M, Fox-Rushby J. Cost-effectiveness of offering an area-level financial incentive on breast feeding: a within-cluster randomised controlled trial analysis. Arch Dis Child. 2020.105(2):155-59. doi: https://dx.doi.org/10.1136/archdischild-2018-316741

35. Rodgers M, Marshall D, Simmonds M, Le Couteur A, Biswas M, Wright K*, et al.* Interventions based on early intensive applied behaviour analysis for autistic children: a systematic review and cost-effectiveness analysis. Health Technology Assessment 2020.24(35):1-306. doi: https://dx.doi.org/10.3310/hta24350

Appendix A: Search Strategies

A.1: Source: MEDLINE ALL

Interface / URL: Ovid SP

Database coverage dates: 1946 to 8 June 2023

Search date: 08/06/2023

Retrieved records: 2,090

Search strategy:

1	*child, preschool/ (624)
2	exp *infant/ (66267)
3	exp *fetus/ (86552)
4	(preemie* or baby or babies or infant* or toddler* or neo-nat* or neonat* or newborn* or new-born* or newly born* or preschool* or pre-school* or prekindergarten* or kindergarten* or nurser* or LBW or VLBW or ELBW or "low birth weight" or PICU or creche* or NICU).ti,ab. (878617)
5	((child* or p?ediatric*) adj5 (month* old* or 1 year old* or one year old* or 2 year* old* or two year* old* or 3 year* old* or three year* old* or 4 year* old* or four year* old* or 5 year* old* or five year* old* or under five* or under 5* or birth to five or birth to 5)).ti,ab. (42593)
6	(age* adj3 (month* or 1 year* or one year* or two year* or 2 year* or three year* or 3 year* or four year* or 4 year* or five year* or 5 year*)).ti,ab. (217777)
7	(fetus* or foetus* or fetal* or foetal*).ti,ab. (345767)
8	(early adj (childhood or years or life)).ti,ab. (64659)
9	or/1-8 (1378317)
10	*economics/ (10806)
11	exp *"costs and cost analysis"/ (79650)
12	*economics, dental/ (1051)
13	exp *economics, hospital/ (13775)
14	*economics, medical/ (5690)
15	*economics, nursing/ (2330)
16	*economics, pharmaceutical/ (1604)
17	(economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic*).ti. (198760)
18	(expenditure* not energy).ti. (6521)
19	value for money.ti. (314)
20	budget*.ti. (7799)
21	or/10-20 (263824)
22	((energy or oxygen) adj cost).ti,ab. (4754)
23	(metabolic adj cost).ti,ab. (1707)
24	((energy or oxygen) adj expenditure).ti,ab. (28953)
25	or/22-24 (34354)
26	21 not 25 (261746)
27	*quality-adjusted life years/ (2551)
28	(quality adjusted or adjusted life year*).ti. (888)
29	(qaly* or qald* or qale* or qtime*).ti. (469)
30	(illness state*1 or health state*1).ti. (1325)

31 (hui or hui1 or hui2 or hui3).ti. (363)
32 (multiattribute* or multi attribute*).ti. (386)
33 (utility adj3 (score*1 or valu* or health* or cost* or measur* or disease* or mean or gain or gains or index*)).ti. (4259)
34 utilities.ti. (1069)
35 (eq-5d or eq5d or eq-5 or eq5 or euro qual or euroqual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or eurqol or eur qol5d or eur qol5d or eur?qul or eur?qul5d or euro* quality of life or european qol).ti. (1817)
36 (euro* adj3 (5 d or 5d or 5 dimension* or 5dimension* or 5 domain* or 5domain*)).ti. (161)
37 (sf36* or sf 36* or sf thirtysix or sf thirty six).ti. (1063)
38 (time trade off*1 or time tradeoff*1 or tto or timetradeoff*1).ti. (328)
39 or/27-38 (12237)
40 26 or 39 (270147)
41 9 and 40 (9053)
42 exp Great Britain/ (389716)
43 (national health service* or nhs*).ti,ab. (51353)
44 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab. (49178)
45 (gb or "g.b." or britain* or british or uk or "u.k." or united kingdom* or england* or northern ireland* or northern irish* or scotland* or scottish* or wales* or welsh*).ti,ab. (335778)
46 (bath or "bath's" or birmingham or "birmingham's" or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or cambridge* or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or durham or "durham's" or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or lincoln or "lincoln's" or liverpool or "liverpool's" or london or "london's" or manchester or "manchester's" or newcastle or "newcastle's" or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or worcester or "worcester's" or york or "york's").ti,ab. (277370)
47 (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab. (3403)
48 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or perth or "perth's" or stirling or "stirling's").ti,ab. (43185)
49 (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab. (1554)
50 or/42-49 (908339)
51 exp United States/ (1459870)
52 exp Medicare/ or exp Medicaid/ (74455)

53 (america* or united states* or usa* or "u.s.*" or veteran* or alabama* or montgomery* or alaska* or juneau* or anchorage* or arizona* or phoenix* or arkansas* or little rock* or california* or sacramento* or los angeles* or san francisco* or colorado* or denver* or connecticut* or hartford* or bridgeport* or delaware* or dover* or wilmington* or florida* or tallahassee* or jacksonville* or miami* or atlanta* or hawai?i* or honolulu* or idaho* or boise* or illinois* or springfield* or chicago* or indiana* or indianapolis* or iowa* or des moines* or kansas* or topeka* or wichita* or kentucky* or frankfort* or louisville* or louisiana* or baton rouge* or new orleans* or maine* or augusta* or portland* or maryland* or annapolis* or baltimore* or massachusetts* or boston* or michigan* or lansing* or detroit* or minnesota* or st paul* or minneapolis* or mississippi* or jackson* or missouri* or jefferson city* or montana* or billings* or nebraska* or omaha* or nevada* or carson city* or las vegas* or new hampshire* or concord* or new jersey* or trenton* or newark* or new mexico* or santa fe* or albuquerque* or new york* or albany* or north carolina* or raleigh* or north dakota* or bismarck* or fargo* or ohio* or columbus* or oklahoma* or oregon* or salem* or pennsylvania* or harrisburg* or philadelphia* or rhode island* or providence* or south carolina* or columbia* or charleston* or south dakota* or sioux falls* or tennessee* or nashville* or texas* or austin* or houston* or utah* or salt lake city* or vermont* or montpelier* or burlington* or virginia* or richmond* or washington* or olympia* or seattle* or wisconsin* or madison* or milwaukee* or wyoming* or cheyenne*).ti,ab. (13691054)
54 (appalachia* or great lake* or medicare* or medicaid* or mid?atlantic* or mid?west* or pacific state*).ti,ab. (92843)
55 or/51-54 (14397540)
56 exp Canada/ (181300)
57 (Canada* or Canadi* or Alberta* or Calgary* or Edmonton* or British Columbia* or Vancouver* or Victoria* or Manitoba* or Winnipeg* or New Brunswick* or Fredericton* or Moncton* or Newfoundland* or New Foundland* or Labrador* or St John* or Saint John* or Northwest Territor* or Yellowknife* or Nova Scotia* or Halifax* or Dalhousie* or Nunavut* or Igaluit* or Ontario* or Ontarian* or Toronto* or Ottawa* or Hamilton or "Queen's" or McMaster* or Kingston* or Sudbury* or Prince Edward Island* or Charlottetown* or Quebec* or Montreal* or McGill* or Laval* or Sherbrooke* or Nunavik* or Kuujjuaq* or Inukjuak* or Puvirnituq* or Saskatchewan* or Saskatoon* or Yukon* or Whitehorse*).ti,ab. (283363)
58 56 or 57 (349424)
59 exp australia/ (169648)
60 (australia* or tasmania*).ti,ab. (173800)
61 (Sydney* or Melbourne* or Brisbane* or Perth* or Adelaide* or Canberra* or Hobart* or Darwin* or New South Wales* or Northern Territor* or Queensland* or Victoria*).ti,ab. (77453)
62 or/59-61 (262549)
63 50 or 55 or 58 or 62 (15074153)
64 41 and 63 (6992)
65 exp africa/ or exp asia/ or exp caribbean region/ or exp south america/ or exp central america/ or exp latin america/ or antartic regions/ or arctic regions/ (1578815)
66 (afghan* or africa* or albania* or algeria* or angola* or antigua* or barbuda* or argentin* or armenia* or aruba* or azerbaijan* or bahrain* or bangladesh* or bengal* or bangal* or barbados* or barbadian* or bajan or bajans or belarus* or belorus* or byelarus* or byelorus* or belize* or benin* or dahomey or bhutan* or bolivia* or bosnia* or herzegovin*

or botswan* or batswan* or bechuanaland* or brazil* or brasil* or bulgaria* or burkina* or burkinese* or upper volta* or burundi* or urundi* or cabo verde* or cape verde* or cambodia* or kampuchea* or khmer* or cameroon* or cameroun* or ubangi shari* or chad* or chile* or china* or chinese or colombia* or comoro* or comore* or comorian* or mayotte* or congo* or zaire* or costa rica* or "cote d'ivoir*" or "cote d' ivoir*" or cote divoir* or cote d ivoir* or ivory coast* or ivorian* or croatia* or cuba or cuban or cubans or "cuba's" or cyprus* or cypriot* or czech* or djibouti* or french somaliland* or dominica* or ecuador* or egypt* or united arab republic* or el salvador* or salvadoran* or guinea* or equatoguinea* or eritrea* or estonia* or eswatini* or swaziland* or swazi* or swati* or ethiopia* or fiji* or gabon* or gabonese* or gabonaise* or gambia* or ((georgia or georgian or georgians) not (atlanta or california or florida)) or ghana* or gibraltar* or greece* or greek* or grecian* or grenada* or grenadian* or guam* or guatemala* or guyana* or guiana* or guyanese* or haiti* or hispaniola* or hondura* or hungary* or hungarian* or india* or indonesia* or iran* or iraq* or isle of man* or jamaica* or jordan* or kazakh* or kenya* or karabati* or korea* or kosovo* or kosova* or kyrgyz* or kirgiz* or kirghiz* or laos or lao or laotian* or latvia* or lebanon* or lebanese* or lesotho* or lesothan* or lesothonian* or basutoland* or mosotho* or basotho* or liberia* or libya* or jamahiriya* or lithuania* or macedonia* or madagasca* or malagasy* or malawi* or nyasaland* or malaysia* or malay* federation or maldives* or maldivian* or indian ocean or mali or malian* or "mali's" or malta or maltese* or "malta's" or micronesia* or marshallese* or kiribati* or marshall island* or nauru or nauran or nauruans or "naurian's" or mariana or marianas or palau or paluan* or tuvalu* or mauritania* or mauritan* or mauritius* or mexico* or mexican* or moldova* or moldovia* or mongol* or montenegr* or morocco* or moroccan* or ifni or mozambique* or mozambican* or myanmar* or burma* or burmese or namibia* or nepal* or new caledonia* or netherlands antill* or nicaragua* or niger* or oman or omani or omanis or "oman's" or pakistan* or palestin* or gaza* or west bank* or panama* or paraguay* or peru or peruvian* or "peru's" or philippine* or philipine* or phillipine* or phillippine* or filipino* or filipina* or poland* or polish or pole or poles or portugal* or portuguese or puerto ric* or romania* or russia* or ussr* or soviet* or rwanda* or rwandese or ruanda* or ruandese or samoa* or navigator island* or pacific island* or polynesia* or "sao tome and principe*" or sao tomean* or santomean* or saudi arabia* or saudi or saudis or senegal* or serbia* or seychell* or sierra leone* or slovak* or sloven* or melanesia* or solomon island* or norfolk island* or somali* or sri lanka* or ceylon* or "saint kitts and nevis*" or "st kitts and nevis*" or kittian* or nevisian* or saint lucia* or st lucia* or saint vincent* or st vincent* or vincentian* or grenadine* or sudan* or surinam* or syria* or tajik* or tadjik* or tadzhik* or tanzania* or tanganyika* or thai* or timor leste* or east timor* or timorese* or togo or togoles* or "togo's" or tonga* or trinidad* or tobago* or tunisia* or turkiy* or turkey* or turk or turks or turkish or turkmen* or uganda* or ukrain* or uruguay* or uzbek* or vanuatu* or new hebrides* or venezuela* or vietnam* or viet nam* or yemen* or yugoslav* or zambia* or zimbabwe* or rhodesia* or arab* countr* or middle east* or global south or sahara* or subsahara* or magreb* or maghrib* or west indies* or caribbean* or central america* or latin america* or south america* or central asia* or north asia* or northern asia* or southeastern asia* or south eastern asia* or southeast asia* or south east asia* or west asia* or western asia* or east europe* or eastern europe* or developing countr* or developing nation* or developing population* or developing world or less developed countr* or less developed nation* or less developed world or lesser developed countr* or lesser developed nation* or lesser developed world or under developed countr* or under developed nation* or under developed world or underdeveloped countr* or underdeveloped nation* or underdeveloped world or middle income countr* or middle income nation* or middle income population* or low income countr* or low income nation* or low income population* or lower income countr* or lower income nation* or lower income population* or underserved countr* or underserved nation* or underserved population* or under served population* or under served nation* or under served population* or deprived countr* or deprived population* or high burden countr* or high burden nation* or countdown countr* or countdown nation* or poor countr* or poor nation* or poor population* or poor world or poorer countr* or poorer nation* or poorer population* or poorer world or developing econom* or less developed econom* or underdeveloped econom* or under developed econom* or middle income econom* or low income econom* or lower income econom* or low gdp or low gnp or low gross domestic or low gross national or lower gdp or lower gnp or lower gross domestic or lower gross national or lmic or lmics or third world or lami countr* or transitional countr* or emerging econom* or emerging nation*).ti,ab,hw,kf. (3167954)

67 65 or 66 (3427973)
68 64 not 67 (4324)
69 exp animals/ not humans/ (5127681)
70 (news or editorial or case reports).pt. or case report.ti. (3254277)
71 68 not (69 or 70) (4198)
72 limit 71 to yr="2013 -Current" (2116)
73 limit 72 to english language (2090)

A.2: Source: Paediatric Economic Database Evaluation

Interface / URL: http://pede.ccb.sickkids.ca/pede/
Database coverage dates: The information at the following URL states that the database contains records for studies published from January 1, 1980 to December 31, 2022 http://pede.ccb.sickkids.ca/pede/database.jsp
Search date: 12/06/2023
Retrieved records: 316
Search strategy:

The basic search interface at the following URL was used: http://pede.ccb.sickkids.ca/pede/search.jsp.
Searches were limited to 2013 to 2021.

Separate, highly targeted searches of the title field only were conducted on each of the following terms:

premie: 0 records retrieved
premies: 0 records retrieved
baby: 3 records retrieved
babies: 5 records retrieved
toddler: 2 records retrieved
toddlers: 2 records retrieved
neonate: 12 records retrieved
neonates: 12 records retrieved
neo nate: 0 records retrieved

neo nates: 0 records retrieved
neonatal: 25 records retrieved
neo natal: 0 records retrieved
neonatally: 0 records retrieved
neo natally: 0 records retrieved
new born: 1 record retrieved
new borns: 1 record retrieved
newborn: 27 records retrieved
newborns: 15 records retrieved
newly born: 0 records retrieved
newly borns: 0 records retrieved
kindergarten: 1 record retrieved
kindergartens: 0 records retrieved
prekindergarten: 0 records retrieved
prekindergartens: 0 records retrieved
nursery: 1 record retrieved
nurseries: 0 records retrieved
LBW: 0 records retrieved
VLBW: 0 records retrieved
ELBW: 0 records retrieved
low birth weight: 7 records
low birth weights: 0 records retrieved
PICU: 0 records retrieved
PICUs: 0 records retrieved
pediatric intensive care: 5 records retrieved
paediatric intensive care: 3 records retrieved
NICU: 0 records retrieved
NICUs: 0 records retrieved
creche: 1 record retrieved
creches: 0 records retrieved
preschool: 11 records retrieved
preschools: 0 records retrieved
preschooler: 1 records retrieved
preschoolers: 1 records retrieved
pre school: 0 records retrieved
pre schools: 0 records retrieved
pre schooler: 0 records retrieved
pre schoolers: 0 records retrieved
infant: 66 records retrieved
infants: 47 records retrieved
infancy: 4 records retrieved
infancies: 0 records retrieved
fetus: 1 record retrieved
fetuses: 1 record retrieved
foetus: 0 records retrieved
foetuses: 0 records retrieved
fetal: 28 records retrieved
fetally: 0 records retrieved

foetal: 2 records retrieved
foetally: 0 records retrieved
under five: 7 records retrieved
under fives: 0 records retrieved
under 5: 6 records retrieved
under 5s: 0 records retrieved
birth to five: 0 records retrieved
birth to 5: 0 records retrieved
early childhood: 8 records retrieved
early life: 0 records retrieved
early years: 1 record retrieved
month old: 1 records retrieved
months old: 0 records retrieved
month olds: 0 records retrieved
one year old: 0 records retrieved
1 year old: 0 records retrieved
one year olds: 0 records retrieved
1 year olds: 0 records retrieved
two year old: 0 records retrieved
2 year old: 2 records retrieved
two years old: 0 records retrieved
2 years old: 1 record retrieved
two year olds: 0 records retrieved
2 year olds: 0 records retrieved
three year old: 0 records retrieved
3 year old: 0 records retrieved
three years old: 0 records retrieved
3 years old: 1 record retrieved
three year olds: 0 records retrieved
3 year olds: 0 records retrieved
four year old: 0 records retrieved
4 year old: 1 record retrieved
four years old: 0 records retrieved
4 years old: 0 records retrieved
four year olds: 0 records retrieved
4 year olds: 0 records retrieved
five year old: 0 records retrieved
5 year old: 2 records retrieved
five years old: 0 records retrieved
5 years old: 0 records retrieved
five year olds: 0 records retrieved
5 year olds: 1 record retrieved

Appendix B: Excluded Studies and Reasons for Exclusion (n=204)

Reference	Exclusion reason
Aaltio J, Hyttinen V, Kortelainen M, Frederix GWJ, Lonnqvist T, Suomalainen A, et al. Cost-effectiveness of whole-exome sequencing in progressive neurological disorders of children. Eur J Paediatr Neurol. 2022.36:30-36. doi: https://dx.doi.org/10.1016/j.ejpn.2021.11.006	Ineligible country
Abushanab D, Abounahia FF, Alsoukhni O, Abdelaal M, Al-Badriyeh D. Clinical and economic evaluation of the impact of midazolam on morphine therapy for pain relief in critically Ill ventilated infants with respiratory distress syndrome. Paediatr Drugs. 2021.23(2):143-57. doi: https://dx.doi.org/10.1007/s40272-020-00432-0	Ineligible country
Abushanab D, Rouf PA, Al Hail M, Kamal R, Viswanathan B, Parappil H, et al. Cost-effectiveness of oral versus intravenous ibuprofen therapy in preterm infants with patent ductus artieriosus in the neonatal intensive care setting: a cohort-based study. Clin Ther. 2021.43(2):336-48.e7. doi: https://dx.doi.org/10.1016/j.clinthera.2020.12.004	Ineligible country
Alfonso YN, Hyder AA, Alonge O, Salam SS, Baset K, Rahman A, et al. Cost-effectiveness analysis of a large-scale creche intervention to prevent child drowning in rural Bangladesh. Injury Epidemiology. 2021.8(1):61. doi: https://doi.org/10.1186/s40621-021-00351-9	Ineligible country
Ali A, Nudel J, Heberle CR, Santorino D, Olson KR, Hur. Cost effectiveness of a novel device for improving resuscitation of apneic newborns. BMC Pediatr. 2020.20(1):46. doi: https://doi.org/10.1186/s12887-020-1925-5	Ineligible country
Alkmark M, Wennerholm U-B, Saltvedt S, Bergh C, Carlsson Y, Elden H, et al. Induction of labour at 41 weeks of gestation versus expectant management and induction of labour at 42 weeks of gestation: a cost-effectiveness analysis. BJOG. 2022.129(13):2157-65. doi: https://dx.doi.org/10.1111/1471-0528.16929	Ineligible country
Al-Shaibi S, Abushanab D, Abounahia F, Awaisu A, Al-Badriyeh D. Cost-effectiveness analysis of ibuprofen versus indomethacin or paracetamol for the treatment of patent ductus arteriosus in preterm neonates. Curr Probl Cardiol. 2023.48(9):101751. doi: https://dx.doi.org/10.1016/j.cpcardiol.2023.101751	Ineligible country
Appelberg K, Sorensen L, Zetterstrom RH, Henriksson M, Wedell A, Levin L-A. Cost-effectiveness of newborn screening for phenylketonuria and congenital hypothyroidism. J Pediatr. 2023.256:38-43.e3. doi: https://dx.doi.org/10.1016/j.jpeds.2022.10.046	Ineligible country
Azor-Martinez E, Garcia-Mochon L, Lopez-Lacort M, Strizzi JM, Munoz-Vico FJ, Jimenez-Lorente CP, et al. Child care center hand hygiene programs' cost-effectiveness in preventing respiratory infections. Pediatrics. 2021.148(6):46-55. doi: https://dx.doi.org/10.1542/peds.2021-052496	Ineligible country
Bar-Zeev N, Tate JE, Pecenka C, Chikafa J, Mvula H, Wachepa R, et al. Cost-effectiveness of monovalent rotavirus vaccination of infants in Malawi: a postintroduction analysis using individual patient-level costing data. Clin Infect Dis. 2016.Suppl 2:S220-28. doi: https://doi.org/10.1093/cid/civ1015	Ineligible country
Bayon JC, Orruno E, Portillo MI, Asua J. The consequences of implementing non-invasive prenatal testing with cell-free foetal DNA for the detection of down syndrome in the Spanish National Health Service: a cost-effectiveness analysis. Cost Eff Resour Alloc. 2019.17:6. doi: https://dx.doi.org/10.1186/s12962-019-0173-8	Ineligible country
Bell JM, Shields MD, Agus A, Dunlop K, Bourke T, Kee F, et al. Clinical and cost-effectiveness of procalcitonin test for prodromal meningococcal disease-a meta-analysis. PLoS ONE 2015.10(6):e0128993. doi: https://dx.doi.org/10.1371/journal.pone.0128993	Mixed population
Blair JC, McKay A, Ridyard C, Thornborough K, Bedson E, Peak M, et al. Continuous subcutaneous insulin infusion versus multiple daily injection regimens in children and young people at diagnosis of type 1 diabetes: pragmatic randomised controlled trial and economic evaluation. BMJ. 2019.365:l1226. doi: https://dx.doi.org/10.1136/bmj.l1226	Mixed population
Blanken MO, Frederix GW, Nibbelke EE, Koffijberg H, Sanders EAM, Rovers MM, et al. Cost-effectiveness of rule-based immunoprophylaxis against respiratory syncytial virus infections in preterm infants. Eur J Pediatr. 2018.177(1):133-44. doi: https://dx.doi.org/10.1007/s00431-017-3046-1	Ineligible country
Bobic B, Villena I, Stillwaggon E. Prevention and mitigation of congenital toxoplasmosis. Economic costs and benefits in diverse settings. Food Waterborne Parasitol. 2019.16:e00058. doi: https://dx.doi.org/10.1016/j.fawpar.2019.e00058	Ineligible country
Bruijning-Verhagen P, van Dongen JAP, Verberk JDM, Pijnacker R, van Gaalen RD, Klinkenberg D, et al. Updated cost-effectiveness and risk-benefit analysis of two infant rotavirus vaccination strategies in a high-income, low-endemic setting. BMC Med. 2018.16(1):168. doi: https://dx.doi.org/10.1186/s12916-018-1134-3	Ineligible country

Reference	Exclusion reason
Burstein D, Kimmel S, Putt M, Rossano J, VanderPluym C, Ankola A, et al. Cost-effectiveness of bivalirudin in pediatric ventricular assist devices. J Heart Lung Transplant. 2023.42(3):390-97. doi: https://dx.doi.org/10.1016/j.healun.2022.10.006	Mixed population
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Higgins ST, Slade EP, Shepard DS. Decreasing smoking during pregnancy: potential economic benefit of reducing sudden unexpected infant death. Prev Med. 2020.140:106238. doi: https://dx.doi.org/10.1016/j.ypmed.2020.106238	Ineligible intervention
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Kanters TA, Hoogenboom-Plug I, Rutten-Van Molken MPMH, Redekop WK, van der Ploeg AT, Hakkaart L. Cost-effectiveness of enzyme replacement therapy with alglucosidase alfa in classic-infantile patients with Pompe disease. Orphanet J Rare Dis. 2014.9:75. doi: https://dx.doi.org/10.1186/1750-1172-9-75	Ineligible country
Kerris EJ, Patregnani JT, Sharron M, Sochet AA. Use of the pediatric intensive care unit for post-procedural monitoring in young children following microlaryngobronchoscopy: Impact on resource utilization and hospital cost. Int J Pediatr Otorhinolaryngol. 2018.115:1-5. doi: https://dx.doi.org/10.1016/j.ijporl.2018.09.004	Ineligible outcomes
Key S, Chia C, Nixon G, Paddle P. Cost-minimisation analysis of polysomnography and pulse oximetry in a risk stratification protocol for paediatric adenotonsillectomy. ANZ J Surg. 2022.92(9):2292-98. doi: https://dx.doi.org/10.1111/ans.17858	Mixed population
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Kiencke P, Viehmann K, Rychlik R. Cost-effectiveness analysis, prevention of atopic dermatitis by oral application of bacterial lysate in newborns/small children. Eur J Health Econ. 2013.14(6):995-1002. doi: https://dx.doi.org/10.1007/s10198-012-0448-x	Ineligible country
Kienhorst S, van Aarle MHD, Jobsis Q, Bannier MAGE, Kersten ETG, Damoiseaux J, et al. The ADEM2 project: early pathogenic mechanisms of preschool wheeze and a randomised controlled trial assessing the gain in health and cost-effectiveness by application of the breath test for the diagnosis of asthma in wheezing preschool children. BMC Public Health. 2023.23(1):629. doi: https://dx.doi.org/10.1186/s12889-023-15465-6	Ineligible country
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Kodabuckus SS, Quinlan-Jones E, McMullan DJ, Maher ER, Hurles ME, Barton PM, et al. Exome dequencing for prenatal detection of genetic abnormalities in fetal ultrasound anomalies: an economic evaluation. Fetal Diagn Ther. 2020.47(7):554-64. doi: https://dx.doi.org/10.1159/000504976	Ineligible outcomes
Koh R, Pukallus M, Kularatna S, Gordon LG, Barnett AG, Walsh LJ, et al. Relative cost-effectiveness of home visits and telephone contacts in preventing early childhood caries. Community Dent Oral Epidemiol. 2015.43(6):560-68. doi: https://dx.doi.org/10.1111/cdoe.12181	Mixed population
Kostenko E, Chantraine F, Vandeweyer K, Schmid M, Lefevre A, Hertz D, et al. Clinical and economic impact of adopting noninvasive prenatal testing as a primary screening method for fetal aneuploidies in the general pregnancy population. Fetal Diagn Ther. 2019.45(6):413-23. doi: https://dx.doi.org/10.1159/000491750	Ineligible country
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Lee KKC, Chia Wu DB, Topachevskyi O, Delgleize E, DeAntonio R. The health economic impact of universal infant vaccination with the 10-valent pneumococcal nontypeable	Ineligible country

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Liu S, Cipriano LE, Holodniy M, Goldhaber-Fiebert JD. Cost-effectiveness analysis of risk-factor guided and birth-cohort screening for chronic hepatitis C infection in the United States. PLoS ONE. 2013.8(3):e58975. doi: https://dx.doi.org/10.1371/journal.pone.0058975	Ineligible patient population
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Lu C-Y, Chung C-H, Huang L-M, Kruger E, Tan S-C, Zhang X-H, et al. Cost-effectiveness evaluation of the 10-valent pneumococcal non-typeable haemophilus influenzae protein D conjugate vaccine for children in Taiwan. Cost Eff Resour Alloc. 2020.18:30. doi: https://dx.doi.org/10.1186/s12962-020-00225-9	Ineligible country
Lubogo P, Lukyamuzi JE, Kyambadde D, Komakech AA, Kitutu FE, Mulogo, et al. Cost-effectiveness analysis of integrated community case management delivery models utilizing drug sellers and community health workers for treatment of under-five febrile cases of malaria, pneumonia, diarrhoea in rural Uganda. Malar J. 2021.20(1):407. doi: https://doi.org/10.1186/s12936-021-03944-3	Ineligible country
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Norrie O, Pharand L. Cost effectiveness of a fluoride varnish daycare program versus usual care in central Winnipeg, Canada. Can. 2020.54(2):68-74. doi: https://files.cdha.ca/profession/journal/2727.pdf	Mixed population
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Peters RD, Petrunka K, Khan S, Howell-Moneta A, Nelson G, Pancer SM, et al. Cost-savings analysis of the better beginnings, better futures community-based project for young children and their families: a 10-year follow-up. Prev Sci. 2016.17(2):237-47. doi: https://dx.doi.org/10.1007/s11121-015-0595-2	Mixed population
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Shakerian S, Lakeh MM, Esteghamati A, Zahraei M, Yaghoubi. Cost-effectiveness of rotavirus vaccination for under-five children in Iran. Iran J Pediatr. 2015.25(4):e2766. doi: https://doi.org/10.5812%2Fijp.2766	Ineligible country
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Tanaka M, Wang Q, Morikawa Y, Tsukamoto J, Sammori H, Takehira K, et al. Efficacy, safety, and economic impact of diazepam suppositories with as-needed acetaminophen for prevention of seizure recurrence during the same fever episode in children with suspected simple febrile seizures. Epilepsia. 2022.63(7):1704-13. doi: https://dx.doi.org/10.1111/epi.17271	Ineligible country
Tawiah T, Hansen KS, Baiden F, Bruce J, Tivura M, Delimini R, et al. Cost-effectiveness analysis of test-based versus presumptive treatment of uncomplicated malaria in children under five years in an area of high transmission in central Ghana. PLoS ONE. 2016.11(10):e0164055. doi: https://doi.org/10.1371/journal.pone.0164055	Ineligible country
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Vallejo-Torres L, Castilla I, Couce ML, Perez-Cerda C, Martin-Hernandez E, Pineda M, et al. Cost-effectiveness analysis of a national newborn screening program for biotinidase deficiency. Pediatrics. 2015.136(2):e424-e32. doi: https://dx.doi.org/10.1542/peds.2014-3399	Conference abstract
van Baaren G-J, Vis JY, Grobman WA, Bossuyt PM, Opmeer BC, Mol BW. Cost-effectiveness analysis of cervical length measurement and fibronectin testing in women with threatened preterm labor. Am J Obstet Gynecol. 2013.209(5):436.e1-36.e8. doi: https://dx.doi.org/10.1016/j.ajog.2013.06.029	Ineligible country
van de Vooren K, Duranti S, Curto A, Garattini L. Cost effectiveness of the new pneumococcal vaccines: a systematic review of European studies. Pharmacoeconomics. 2014.32(1):29-45. doi: https://dx.doi.org/10.1007/s40273-013-0113-y	Ineligible country
van der Ploeg CPB, van den Akker-van Marle ME, Vernooij-van Langen AMM, Elvers LH, Gille JJP, Verkerk PH, et al. Cost-effectiveness of newborn screening for cystic fibrosis determined with real-life data. J Cyst Fibros. 2015.14(2):194-202. doi: https://dx.doi.org/10.1016/j.jcf.2014.08.007	Ineligible country
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van't Hooft J, Vink M, Opmeer BC, Ensing S, Kwee A, Mol, et al. ST-analysis in electronic foetal monitoring is cost-effective from both the maternal and neonatal perspective. J Matern Fetal Neonatal Med. 2016.29(20):3260-65. doi: https://doi.org/10.3109/14767058.2015.1126820	Ineligible country
Varghese L, Talbot L, Govender A, Zhang X-H, Mungall BA. A cost-effectiveness analysis of the 10-valent pneumococcal non-typeable haemophilus influenzae protein D conjugate vaccine (PHiD-CV) compared to the 13-valent pneumococcal conjugate vaccine (PCV13) for universal mass vaccination implementation in New Zealand. Appl Health Econ Health Policy. 2018.16(3):331-45. doi: https://dx.doi.org/10.1007/s40258-018-0387-5	Ineligible country
Verkleij ML, Heijnsdijk EAM, Busse AML, Carr G, Goedegebure A, Mackey AR, et al. Cost-effectiveness of neonatal hearing screening programs: a micro-simulation modeling analysis. Ear Hear. 2021.42(4):909-16. doi: https://doi.org/10.1097/aud.0000000000000981	Ineligible country
Vijgen SMC, Boers KE, Opmeer BC, Bijlenga D, Bekedam DJ, Bloemenkamp KWM, et al. Economic analysis comparing induction of labour and expectant management for intrauterine growth restriction at term (DIGITAT trial). Eur J Obstet Gynecol Reprod Biol. 2013.170(2):358-63. doi: https://dx.doi.org/10.1016/j.ejogrb.2013.07.017	Ineligible country
Viriato D, Bennett N, Sidhu R, Hancock E, Lomax H, Trueman D, et al. An economic evaluation of voretigene neparvovec for the treatment of biallelic RPE65-mediated inherited retinal dystrophies in the UK. Adv Ther. 2020.37(3):1233-47. doi: https://dx.doi.org/10.1007/s12325-020-01243-y	Mixed population
Vossius C, Lotto E, Lyanga S, Mduma E, Msemo G, Perlman J, et al. Cost-effectiveness of the "helping babies breathe" program in a missionary hospital in rural Tanzania. PLoS ONE. 2014.9(7):e102080. doi: https://doi.org/10.1371/journal.pone.0102080	Ineligible country
Walker KF, Dritsaki M, Bugg G, Macpherson M, McCormick C, Grace N, et al. Labour induction near term for women aged 35 or over: an economic evaluation. BJOG. 2017.124(6):929-34. doi: https://dx.doi.org/10.1111/1471-0528.14557	Ineligible outcomes
Wang C, Su L, Mu Q, Gu X, Guo X, Wang. Cost-effectiveness analysis of domestic 13-valent pneumococcal conjugate vaccine for children under 5 years of age in mainland China. Hum Vaccin Immunother. 2021.17(7):2241-48. doi: https://doi.org/10.1080/21645515.2020.1870396	Ineligible country
Wastlund D, Moraitis AA, Dacey A, Sovio U, Wilson ECF, Smith GCS. Screening for breech presentation using universal late-pregnancy ultrasonography: a prospective cohort study and cost effectiveness analysis. PLos Med. 2019.16(4):e1002778. doi: https://doi.org/10.1371%2Fjournal.pmed.1002778	Ineligible patient population
Webb NJA, Woolley RL, Lambe T, Frew E, Brettell EA, Barsoum EN, et al. Long term tapering versus standard prednisolone treatment for first episode of childhood nephrotic	Mixed population

Reference	Exclusion reason
syndrome: phase III randomised controlled trial and economic evaluation. BMJ. 2019.365:l1800. doi: https://dx.doi.org/10.1136/bmj.l1800	
Weber Z, Sutter D, Baltensperger A, Carr N. Economic evaluation: onsite HSV PCR capabilities for pediatric care. Pediatric Quality and Safety. 2020.5(2):e266. doi: https://dx.doi.org/10.1097/pq9.0000000000000266	Mixed population
Weghorst AA, Holtman GA, Bonvanie IJ, Wolters PI, Kollen BJ, Vermeulen KM, et al. Cost-effectiveness of oral ondansetron for children with acute gastroenteritis in primary care: a randomised controlled trial. Br J Gen Pract. 2021.71(711):e736-e43. doi: https://dx.doi.org/10.3399/BJGP.2020.1093	Ineligible country
Wenzel NS, Atkins KE, van Leeuwen E, Halloran ME, Baguelin M. Cost-effectiveness of live-attenuated influenza vaccination among school-age children. Vaccine. 2021.39(2):447-56. doi: https://dx.doi.org/10.1016/j.vaccine.2020.10.007	Mixed population
Wilson ECF, Wastlund D, Moraitis AA, Smith GCS. Late pregnancy iltrasound to screen for and manage potential birth complications in nulliparous women: a cost-effectiveness and value of information analysis. Value Health. 2021.24(4):513-21. doi: https://dx.doi.org/10.1016/j.jval.2020.11.005	Ineligible study design
Wolf A, McKay A, Spowart C, Granville H, Boland A, Petrou S, et al. Prospective multicentre randomised, double-blind, equivalence study comparing clonidine and midazolam as intravenous sedative agents in critically ill children: the SLEEPS (safety profile, efficacy and equivalence in paediatric intensive care sedation) study. 2014. 1-242. doi: http://dx.doi.org/10.3310/hta18710	Mixed population
Xie X, Wang M, Goh ES-Y, Ungar WJ, Little J, Carroll JC, et al. Noninvasive prenatal testing for trisomies 21, 18, and 13, sex chromosome aneuploidies, and microdeletions in average-risk pregnancies: a cost-effectiveness analysis. Journal of Obstetrics and Gynaecology Canada: JOGC. 2020.42(6):740-49.e12. doi: https://dx.doi.org/10.1016/j.jogc.2019.12.007	Ineligible outcomes
Xie YY, Cheng ML, Xu MR, Si Y, Xu. Cost-effectiveness analysis of comprehensive oral health care for severe early childhood caries in urban Beijing, China. The Chinese Journal of Dental Research. 2019.22(1):45-50. doi: https://doi.org/10.3290/j.cjdr.a41774	Ineligible country
Xiong X, Huang L, Herd D, Borland M, Davidson A, Hearps S, et al. Cost-effectiveness of prednisolone to treat Bell palsy in Children: an economic evaluation alongside a randomized controlled trial. Neurol. 2023.100(24):18. doi: https://dx.doi.org/10.1212/WNL.0000000000207284	Mixed population
Zahedi Z, Karimi M, Keshavarz K, Haghpanah S, Ravangard. A cost-effectiveness analysis of the prophylaxis versus on-demand regimens in severe hemophilia A patients under 12 years old in southern Iran. Hematol. 2021.26(1):240-48. doi: https://doi.org/10.1080/16078454.2021.1885123	Ineligible country
Zaror C, Munoz-Millan P, Espinoza-Espinoza G, Vergara-Gonzalez C, Martinez Z, Mj. Cost-effectiveness of adding fluoride varnish to a preventive protocol for early childhood caries in rural children with no access to fluoridated drinking water. J Dent. 2020.98:103374. doi: https://doi.org/10.1016/j.jdent.2020.103374	Ineligible country

Appendix C: Included Studies (n=343)

Included Study (n=343) (Prioritised studies n=20 in 21 papers are in bold)
Abu-Raya B, Coyle D, Bettinger JA, Vaudry W, Halperin SA, Sadarangani M. Pertussis vaccination in pregnancy in Canada: a cost-utility analysis. CMAJ Open. 2020.8(4):E651-E58. doi: https://dx.doi.org/10.9778/cmajo.20200060
Ademi Z, Marquina C, Perucca P, Hitchcock A, Graham J, Eadie MJ, et al. Economic evaluation of the community benefit of the Australian pregnancy register of antiseizure medications. Neurol. 2023.100(10):e1028-e37. doi: https://doi.org/10.1212/WNL.0000000000201655
Ahmed RJ, Gafni A, Hutton EK, Hu ZJ, Pullenayegum E, von Dadelszen P, et al. The cost implications of less tight versus tight control of hypertension in pregnancy (CHIPS Trial). Hypertension. 2016.68(4):1049-55. doi: https://dx.doi.org/10.1161/HYPERTENSIONAHA.116.07466
Albright CM, Emerson JB, Werner EF, Hughes BL. Third-trimester prenatal syphilis screening: a cost-effectiveness analysis. Obstet Gynecol. 2015.126(3):479-85. doi: https://dx.doi.org/10.1097/AOG.0000000000000997
Albright CM, MacGregor C, Sutton D, Theva M, Hughes BL, Werner EF. Group B streptococci screening before repeat cesarean delivery: a cost-effectiveness analysis. Obstet Gynecol. 2017.129(1):111-19. doi: https://dx.doi.org/10.1097/AOG.0000000000001800
Andrejko K, Whittles LK, Lewnard JA. Health-economic value of vaccination against group A streptococcus in the United States. Clin Infect Dis. 2022.74(6):983-92. doi: https://dx.doi.org/10.1093/cid/ciab597
Anokye N, Coyle K, Relton C, Walters S, Strong M, Fox-Rushby J. Cost-effectiveness of offering an area-level financial incentive on breast feeding: a within-cluster randomised controlled trial analysis. Arch Dis Child. 2020.105(2):155-59. doi: https://dx.doi.org/10.1136/archdischild-2018-316741
Anopa Y, Macpherson L, McIntosh E. Systematic review of economic evaluations of primary caries prevention in 2- to 5-year-old preschool children. Value Health. 2020.23(8):1109-18. doi: https://dx.doi.org/10.1016/j.jval.2020.04.1823
Anopa Y, Macpherson LMD, McMahon AD, Wright W, Conway DI, McIntosh E. Economic evaluation of the protecting teeth @ 3 randomized controlled trial. JDR clin. 2022.8(3):207-14. doi: https://dx.doi.org/10.1177/23800844221090444
Anopa Y, McMahon AD, Conway DI, Ball GE, McIntosh E, Macpherson LMD. Improving child oral health: cost analysis of a national nursery toothbrushing programme. PLoS ONE. 2015.10(8):e0136211. doi: https://dx.doi.org/10.1371/journal.pone.0136211
Asare AO, Maurer D, Wong AMF, Saunders N, Ungar WJ. Cost-effectiveness of universal School- and community-based vision testing strategies to detect amblyopia in children in Ontario, Canada. JAMA netw. 2023.6(1):e2249384. doi: https://dx.doi.org/10.1001/jamanetworkopen.2022.49384
Asciutto R, Di Napoli A, Vecchi S, Sicuro J, Mirisola C, Petrelli A. A systematic review of economic evaluations of neonatal and maternal healthcare in immigrant and ethnic minority women. Epidemiol Prev. 2020.44(5-6 Suppl 1):142-52. doi: https://dx.doi.org/10.19191/EP20.5-6.S1.P142.084
Atkins CY, Thomas TK, Lenaker D, Day GM, Hennessy TW, Meltzer MI. Cost-effectiveness of preventing dental caries and full mouth dental reconstructions among Alaska Native children in the Yukon-Kuskokwim delta region of Alaska. J Public Health Dent. 2016.76(3):228-40. doi: https://dx.doi.org/10.1111/jphd.12141
Atkins KE, Fitzpatrick MC, Galvani AP, Townsend JP. Cost-effectiveness of pertussis vaccination during pregnancy in the United States. Am J Epidemiol. 2016.183(12):1159-70. doi: https://dx.doi.org/10.1093/aje/kwv347
Avram CM, Caughey AB, Norton ME, Sparks TN. Cost-effectiveness of exome sequencing versus targeted gene panels for prenatal diagnosis of fetal effusions and non-immune hydrops fetalis. Am J Obstet Gynecol MFM. 2022.4(6):100724. doi: https://dx.doi.org/10.1016/j.ajogmf.2022.100724
Avram CM, Dyer AL, Shaffer BL, Caughey AB. The cost-effectiveness of genotyping versus sequencing for prenatal cystic fibrosis carrier screening. Prenat Diagn. 2021.41(11):1449-59. doi: https://dx.doi.org/10.1002/pd.6027
Avram CM, Greiner KS, Tilden E, Caughey AB. Point-of-care HIV viral load in pregnant women without prenatal care: a cost-effectiveness analysis. Am J Obstet Gynecol. 2019.221(3):265.e1-65.e9. doi: https://dx.doi.org/10.1016/j.ajog.2019.06.021
Avram CM, Shaffer BL, Sparks TN, Allen AJ, Caughey AB. Cell-free fetal DNA screening for detection of microdeletion syndromes: a cost-effectiveness analysis. J Matern Fetal Neonatal Med. 2021.34(11):1732-40. doi: https://dx.doi.org/10.1080/14767058.2019.1647161
Avram CM, Yieh L, Dukhovny D, Caughey AB. A cost-effectiveness analysis of rooming-in and breastfeeding in neonatal opioid withdrawal. Am J Perinatol. 2020.37(1):1-7. doi: https://dx.doi.org/10.1055/s-0039-1693716
Avsar TS, Jackson L, Barton P, Jones M, McLeod H. Supporting pregnant women not ready to quit smoking: an economic evaluation. BMC Pregnancy Childbirth. 2022.22(1):865. doi: https://dx.doi.org/10.1186/s12884-022-05150-8
Bacheller HL, Hersh AR, Caughey AB. Behavioral smoking cessation counseling during pregnancy: a cost-effectiveness analysis. Obstet Gynecol. 2021.137(4):703-12. doi: https://dx.doi.org/10.1097/AOG.0000000000004327
Baguelin M, Camacho A, Flasche S, Edmunds WJ. Extending the elderly- and risk-group programme of vaccination against seasonal influenza in England and Wales: a cost-effectiveness study. BMC Med. 2015.13:236. doi: https://dx.doi.org/10.1186/s12916-015-0452-y

Included Study (n=343) (Prioritised studies n=20 in 21 papers are in bold)
Bailey C, Skouteris H, Harrison CL, Hill B, Thangaratinam S, Teede H, et al. A comparison of the cost-effectiveness of lifestyle interventions in pregnancy. Value Health. 2022.25(2):194-202. doi: https://dx.doi.org/10.1016/j.jval.2021.07.013
Bak GS, Shaffer BL, Madriago E, Allen A, Kelly B, Caughey AB, et al. Detection of fetal cardiac anomalies: cost-effectiveness of increased number of cardiac views. Ultrasound Obst Gynecol. 2020.55(6):758-67. doi: https://dx.doi.org/10.1002/uog.21977
Bak GS, Shaffer BL, Madriago E, Allen A, Kelly B, Caughey AB, et al. Impact of maternal obesity on fetal cardiac screening: which follow-up strategy is cost-effective? Ultrasound Obst Gynecol. 2020.56(5):705-16. doi: https://dx.doi.org/10.1002/uog.21895
Balegar V KK, Azeem MI, Spence K, Badawi N. Extending total parenteral nutrition hang time in the neonatal intensive care unit: is it safe and cost effective? J Paediatr Child Health. 2013.49(1):E57-61. doi: https://dx.doi.org/10.1111/jpc.12023
Banerji A, Ng K, Moraes TJ, Panzov V, Robinson J, Lee BE. Cost-effectiveness of palivizumab compared to no prophylaxis in term infants residing in the Canadian Arctic. CMAJ Open. 2016.4(4):E623-E33. doi: https://dx.doi.org/10.9778/cmajo.20150052
Bangs AC, Gastanaduy P, Neilan AM, Fiebelkorn AP, Walker AT, Rao SR, et al. The clinical and economic impact of measles-mumps-rubella vaccinations to prevent measlesimportations from US pediatric travelers returning from abroad. J Pediatric Infect Dis Soc. 2022.11(6):257-66. doi: https://dx.doi.org/10.1093/jpids/piac011
Barbosa C, Smith EA, Hoerger TJ, Fenlon N, Schillie SF, Bradley C, et al. Cost-effectiveness analysis of the national perinatal hepatitis B prevention program. Pediatrics. 2014.133(2):243-53. doi: https://dx.doi.org/10.1542/peds.2013-0718
Barlow J, Sembi S, Parsons H, Kim S, Petrou S, Harnett P, et al. A randomized controlled trial and economic evaluation of the parents under pressure program for parents in substance abuse treatment. Drug Alcohol Depend. 2019.194:184-94. doi: https://dx.doi.org/10.1016/j.drugalcdep.2018.08.044
Barnes J, Stuart J, Allen E, Petrou S, Sturgess J, Barlow J, et al. Randomized controlled trial and economic evaluation of nurse-led group support for young mothers during pregnancy and the first year postpartum versus usual care. Trials. 2017.18(1):508. doi: https://dx.doi.org/10.1186/s13063-017-2259-y
Bartsch SM, O'Shea KJ, Wedlock PT, Ferguson MC, Siegmund SS, Lee BY. Potential clinical and economic value of norovirus vaccination in the community setting. Am J Prev Med. 2021.60(3):360-68. doi: https://dx.doi.org/10.1016/j.amepre.2020.10.022
Battarbee AN, Vora NL, Hardisty EE, Stamilio DM. Cost-effectiveness of ultrasound before non-invasive prenatal screening for fetal aneuploidy. Ultrasound Obst Gynecol. 2023.61(3):325-32. doi: https://dx.doi.org/10.1002/uog.26100
Beaulieu E, Rajabali F, Zheng A, Pike I. The lifetime costs of pediatric abusive head trauma and a cost-effectiveness analysis of the period of purple crying program in British Columbia, Canada. Child Abuse Negl. 2019.97:104133. doi: https://dx.doi.org/10.1016/j.chiabu.2019.104133
Beck E, Klint J, Neine M, Garcia S, Meszaros K. Cost-effectiveness of 4CMenB infant vaccination in England: a comprehensive valuation considering the broad impact of serogroup B invasive meningococcal disease. Value Health. 2021.24(1):91-104. doi: https://dx.doi.org/10.1016/j.jval.2020.09.004
Bee P, Bower P, Byford S, Churchill R, Calam R, Stallard P, et al. The clinical effectiveness, cost-effectiveness and acceptability of community-based interventions aimed at improving or maintaining quality of life in children of parents with serious mental illness: a systematic review. Health Technol Assess. 2014.18(8):1-250. doi: https://dx.doi.org/10.3310/hta18080
Benn P, Curnow KJ, Chapman S, Michalopoulos SN, Hornberger J, Rabinowitz M. An economic analysis of cell-free DNA non-invasive prenatal testing in the US general pregnancy population. PLoS ONE 2015.10(7):e0132313. doi: https://dx.doi.org/10.1371/journal.pone.0132313
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Bergevin A, Zick CD, McVicar SB, Park AH. Cost-benefit analysis of targeted hearing directed early testing for congenital cytomegalovirus infection. Int J Pediatr Otorhinolaryngol. 2015.79(12):2090-93. doi: https://dx.doi.org/10.1016/j.ijporl.2015.09.019
Berrigan P, Andrew G, Reynolds JN, Zwicker JD. The cost-effectiveness of screening tools used in the diagnosis of fetal alcohol spectrum disorder: a modelled analysis. BMC Public Health. 2019.19(1):1746. doi: https://dx.doi.org/10.1186/s12889-019-8110-5
Bessey A, Chilcott J, Leaviss J, de la Cruz C, Wong R. A cost-effectiveness analysis of newborn screening for severe combined immunodeficiency in the UK. International Journal of Neonatal Screening. 2019.5(3):28. doi: https://dx.doi.org/10.3390/ijns5030028
Bessey A, Chilcott J, Pandor A, Paisley S. The cost-effectiveness of expanding the NHS newborn bloodspot screening programme to include homocystinuria (Hcu), maple syrup urine disease (Msud), glutaric aciduria type 1 (Ga1), isovaleric acidaemia (Iva), and long-chain hydroxyacyl-coa dehydrogenase deficiency (Lchadd). Value Health. 2014.17(7):A531. doi: https://dx.doi.org/10.1016/j.jval.2014.08.1685
Bessey A, Chilcott J, Pandor A, Paisley S. The cost-effectiveness of expanding the UK newborn bloodspot screening programme to include five additional inborn errors of metabolism. International Journal of Neonatal Screening. 2020.6(4):93. doi: https://dx.doi.org/10.3390/ijns6040093

Included Study (n=343) (Prioritised studies n=20 in 21 papers are in bold)
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Bick D, Briley A, Brocklehurst P, Hardy P, Juszczak E, Lynch L, et al. A multicentre, randomised controlled trial of position during the late stages of labour in nulliparous women with an epidural: clinical effectiveness and an economic evaluation (BUMPES). Health Technol Assess. 2017.21(65):1-176. doi: https://dx.doi.org/10.3310/hta21650
Bickford CD, Magee LA, Mitton C, Kruse M, Synnes AR, Sawchuck D, et al. Magnesium sulphate for fetal neuroprotection: a cost-effectiveness analysis. BMC Health Serv Res. 2013.13:527. doi: https://dx.doi.org/10.1186/1472-6963-13-527
Biondi MJ, Estes C, Razavi-Shearer D, Sahdra K, Lipton N, Shah H, et al. Cost-effectiveness modelling of birth and infant dose vaccination against hepatitis B virus in Ontario from 2020 to 2050. CMAJ Open. 2023.11(1):E24-E32. doi: https://dx.doi.org/10.9778/cmajo.20210284
Bohingamu Mudiyanselage S, Price AMH, Mensah FK, Bryson HE, Perlen S, Orsini F, et al. Economic evaluation of an Australian nurse home visiting programme: a randomised trial at 3 years. BMJ Open. 2021.11(12):e052156. doi: https://dx.doi.org/10.1136/bmjopen-2021-052156
Boyd K, McIntosh E, Lewis S, Rodriguez A, Cunningham. Cost-effective management of bronchiolitis in infants: 90% versus 94% oxygen saturation. Eur Respir J. 2015.46(Suppl 59):OA1988. doi: https://doi.org/10.1183/13993003.congress-2015.OA1988
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Brown V, Tan EJ, Hayes A, Baur L, Campbell K, Taylor R, et al. Cost comparison of five Australasian obesity prevention interventions for children aged from birth to two years. Pediatr Obes. 2020.15(12):e12684. doi: https://dx.doi.org/10.1111/ijpo.12684
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Burchard J, Markenson GR, Saade GR, Laurent LC, Heyborne KD, Coonrod DV, et al. Clinical and economic evaluation of a proteomic biomarker preterm birth risk predictor: cost-effectiveness modeling of prenatal interventions applied to predicted higher-risk pregnancies within a large and diverse cohort. J Med Econ. 2022.25(1):1255-66. doi: https://dx.doi.org/10.1080/13696998.2022.2147771
Burgette JM, Quinonez RB. Cost-effectiveness of treating severe childhood caries under general anesthesia versus conscious sedation. JDR clin. 2018.3(4):336-45. doi: https://dx.doi.org/10.1177/2380084418780712
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Callander EJ, Slavin V, Gamble J, Creedy DK, Brittain H. Cost-effectiveness of public caseload midwifery compared to standard care in an Australian setting: a pragmatic analysis to inform service delivery. Int J Qual Health Care. 2021.33(2):28. doi: https://dx.doi.org/10.1093/intqhc/mzab084
Camacho EM, Hussain H. Cost-effectiveness evidence for strategies to promote or support breastfeeding: a systematic search and narrative literature review. BMC Pregnancy Childbirth. 2020.20(1):757. doi: https://dx.doi.org/10.1186/s12884-020-03460-3
Camacho EM, Whyte S, Stock SJ, Weir CJ, Norman JE, Heazell AEP. Awareness of fetal movements and care package to reduce fetal mortality (AFFIRM): a trial-based and model-based cost-effectiveness analysis from a stepped wedge, cluster-randomised trial. BMC Pregnancy Childbirth. 2022.22(1):235. doi: https://dx.doi.org/10.1186/s12884-022-04563-9
Cannon JS, Kilburn MR, Karoly LA, Mattox T, Muchow AN, Buenaventura M. Investing early: taking stock of outcomes and economic returns from early childhood programs. 2018.Available from: https://www.rand.org/pubs/research_reports/RR1993.html
Carsley S, Fu R, Borkhoff CM, Reid N, Baginska E, Birken CS, et al. Iron deficiency screening for children at 18 months: a cost-utility analysis. CMAJ Open. 2019.7(4):E689-E98. doi: https://dx.doi.org/10.9778/cmajo.20190084
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Christensen KD, McMahon PM, Galbraith LN, Yeh JM, Stout NK, Lu CY, et al. Benefits, harms, and costs of newborn genetic screening for hypertrophic cardiomyopathy: estimates from the PreEMPT model. Genet Med. 2023.25(4):100797. doi: https://dx.doi.org/10.1016/j.gim.2023.100797
Chung EH, Lim SL, Havrilesky LJ, Steiner AZ, Dotters-Katz SK. Cost-effectiveness of prenatal screening methods for congenital heart defects in pregnancies conceived by in-vitro fertilization. Ultrasound Obst Gynecol. 2021.57(6):979-86. doi: https://dx.doi.org/10.1002/uog.22048
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Appendix D: Prioritised Studies (n=20)

Prioritised Study (n=20)
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Prioritised Study (n=20)
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Appendix E: Tabulated Methods and Results of All the Included Studies

Table E.1: Methods of included studies

Study	Methodology description	Timeframe of the analysis	Analytic approach
Interventions to increase rates of breastfeeding			
Anokye, 2020 [11]	A within trial economic evaluation of an RCT. Limited information on the trial was provided but the costs of delivering the intervention were gathered as part of the trial.	Cost-effectiveness was determined over a 6-month period.	NA
Camacho, 2020 [1]	Systematic review.	Studies searched from 2000 to 2019.	NA
Pokhrel, 2015 [2]	Economic model linking breastfeeding with risks to baby of infections (gastrointestinal, LRTI and acute otitis media) and to mother of breast cancer.	Children: one year Mothers: lifetime	For children, a simple decision tree based upon risks for children who are and are not breastfed. For mothers, a simple markov model with cancer, no cancer and death.
Dental interventions			
Anopa, 2015 [3]	Analysis of total number and spending on dental extractions, fillings and decay for children for five-year olds using data held by Scottish Health Boards and the Information Services Division (ISD). Treatments and costs were analysed before and after the introduction of supported toothbrushing in nurseries.	2000 to 2010.	NA
Anopa, 2022 [4]	A within trial economic evaluation of an RCT. Groups of children were randomised to receive Childsmile with fluoride varnish or Childsmile without fluoride varnish. Costs were collected as part of the trial and utilities estimated using the CHU9D tool.	Children in the trial were monitored for two years.	NA
Smoking interventions			
Jones, 2019 [5]	Decision tree followed by Markov model populated with published disease progression, cost and utility data.	Lifetime.	The decision tree for mothers had two smoking outcomes (did or did not quit through pregnancy) followed by pregnancy morbidity/no morbidity. The markov model cycled through current/former smoker with associated risks of health-related events.

Study	Methodology description	Timeframe of the analysis	Analytic approach
			Decision tree for fetus and infants had the same maternal smoking outcomes as the mother's model followed by adverse birth outcomes before a markov model where the child is or is not exposed to passive smoking before the age of 15 and whether the child starts smoking past 16 with associated health outcomes.
McMeekin, 2023 [6]	Short-term analysis was a within trial analysis of the intervention (the CPIT III trial). The long-term analysis used the model by Jones 2019.	Short-term analysis: less than one year Long-term analysis: lifetime	For the long-term analysis, a decision tree for mothers had two smoking outcomes (did or did not quit through pregnancy) followed by pregnancy morbidity/no morbidity. The markov model cycled through current/former smoker with associated risks of health-related events. The decision tree for fetus and infants had the same maternal smoking outcomes as the mother's model followed by adverse birth outcomes before a markov model where the child is or is not exposed to passive smoking before the age of 15 and whether the child starts smoking past 16 with associated health outcomes.
Renwick, 2018 [7]	Within trial economic analysis from an open label RCT with micro costing for the costs of the intervention and usual care.	12 weeks.	NA
Immunisation interventions			
Giorgakoudi, 2018 [9]	Decision tree analysis using published data.	Lifetime.	Decision tree had three outcomes - early onset, late onset or no GBS disease followed by sequalae of varying severity including death. Vaccine uptake rate was assumed to be 0.6 with an efficacy of 0.85.
Early childhood interventions to families facing challenges			
Barlow, 2019 [10]	Pragmatic RCT with financial incentives for parents to engage with the study assessments. Utility was captured through the EQ-5D for parents. Micro costing during the trial was used to capture costs and included health and social care costs for the parent and child. Bootstrapping was used to model uncertainty.	Assessments were conducted at six and twelve months.	NA
Cannon, 2018 [11]	Systematic review.	Unclear but appears to be studies from 2005 to no later than 2018.	NA
Hajizadeh, 2017 [12]	A markov model based upon odds ratios for ParentCorps on academic achievement, self-regulation and obesity and then linking these to long-term outcomes into adulthood. Essentially this was a social return on investment analysis with assumed costs for long term outcomes.	Lifetime.	The model was based upon an 'influence model' whereby short-term outcomes on achievement, behaviour and obesity were linked to longer term outcomes in terms of graduation, drug use and diabetes which then linked to employment, crime and health outcomes.
Obesity interventions			

Study	Methodology description	Timeframe of the analysis	Analytic approach
Brown, 2019 [13]	Lifetime cohort modelling using a pre-existing model (CRE-Obesity Policy model) with details not provided. Effectiveness was taken from a meta-analysis and estimated as a reduction in BMI of 0.13. Scenarios were undertaken on maintenance of intervention effect. Health-related quality of life (HRQoL) was derived from published literature. Cost-savings resulted from diseases averted.	Lifetime.	Details of model not provided.
Tran, 2022 [14]	An obesity model (Early Prevention of Obesity in Childhood) populated with published effectiveness data from Romp and Chomp.	Ten years (from 5 to 15).	The obesity model is a microsimulation model that extrapolates BMI trajectories with utility values and costs based on BMI.
Antenatal intervention to reduce adverse pregnancy outcomes			
Bailey, 2022 [8]	Decision tree analysis of four categories of interventions incorporating their costs and their effectiveness at stopping gestational diabetes, hypertensive disorders and caesarean delivery. Data on costs and effectiveness were drawn from a previously published meta-analysis and applied to a retrospective population of pregnant mothers with data from a health service network.	During pregnancy up to and including delivery.	NA
Child or parental mental health interventions			
Bee, 2014 [15]	Systematic review.	Literature was searched up to May 2012. The one identified study was from 2003.	NA
Hodgson, 2022 [16]	A markov model linking impact of ABAs on cognitive ability and onto cost and QALY outcomes. Data was drawn from published studies on ABAs rather than a specific intervention.	To age 18.5.	A markov model based upon impact of ABAs on Vineland Adaptive Behaviour Scales which are then linked to education (and adult outcomes), QoL and social care medical costs.
Mihalopoulos, 2015 [17]	Cost-utility model using data from a single trial of a parenting intervention to prevent anxiety.	Three years in the base case and eleven years in a sensitivity analysis.	The model was poorly described but would appear to be a simple decision tree that links the proportions of parents engaging with the intervention with a reduction in anxiety disorders in children.
Sonuga-Barke, 2018 [18]	Within trial economic analysis.	Six months.	NR
Varshney, 2022 [19]	Longitudinal study (children were followed to age 37) with outcomes compared with a matched cohort. The analysis focussed on the costs and QALY gains associated with reduced smoking status and diabetes with the programme.	Lifetime.	NA

Key: ABA - applied behaviour analysis; BMI - body mass index; CHU9D - Child Health Utility Instrument; CRE-Obesity - Centre of Research Excellence in Obesity; EQ-5D - EuroQoL-5 dimensions; GBS - group B streptococcus; HRQoL – health related quality of life; ISD - Information Services Division; LRTI - lower respiratory tract infection; NA - not applicable; QALY - quality-adjusted life years; QoL – quality of life; RCT - randomised controlled trial.

Table E.2: Results of included studies

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Interventions to increase rates of breastfeeding						
Anokye, 2020 [34] Intervention: A financial incentive to encourage breastfeeding (NOSH). The study itself did not undertake explicit analysis of the benefits of breastfeeding.	Per ward: £9,989 Per baby: £91.45	The intervention increased breastfeeding rates by an average of 5.7 percentage points (p<0.001).	Cost per additional baby breastfed at 6 to 8 weeks: £974 The intervention would have to generate 0.05 QALYs to be cost-effective at a WtP threshold of £20,000 per QALY.	Not discussed.	The intervention increased breastfeeding rates at 6-8 weeks and has the potential to be cost effective if this increase in breastfeeding rates results in health gains for the infant and/or mother. However, the cost-effectiveness or return on investment was not estimated by the authors.	This study provided information to help inform public health guidance on breastfeeding. To make the economic case unequivocal, evidence on the varied and long-term health benefits of breastfeeding to both the baby and mother and the effectiveness of financial incentives for breastfeeding beyond 6 to 8 weeks is required.
Camacho, 2020 [1] Interventions: Group education and antenatal and postnatal home visits; staff promotion of breastfeeding in a neonatal unit with LBW babies; community based breastfeeding promotion and peer counselling.	Net costs 2017/18 GBP Group education and home visits (South Africa): £11,513,022 Neonatal unit with LBW babies (UK): -£116 to -£1,030 depending on weight Neonatal unit with LBW babies (Spain): -£3,203 to -£23,859 depending on weight Peer support (Uganda): £116	Net benefit Group education and home visits vs no support (South Africa): Increase in months of exclusive breastfeeding of 281,927 (reviewer calculated) Neonatal unit with LBW babies (UK): 0.009 QALYs to 0.251 QALYs depending on	Group education and home visits vs no support (South Africa): £19 to £107 per additional month of exclusive breastfeeding Neonatal unit with LBW babies (UK): Intervention dominant Neonatal unit with LBW babies (Spain): Intervention dominant Peer support (Uganda): £58 per month of exclusive breastfeeding; £9,617 per DALY	Not discussed.	The neonatal interventions with mothers of LBW babies in the UK and Spain were likely to cost less with better outcomes than no intervention and so have positive returns on investment. For the other interventions it is unclear whether they would generate a return on investment.	There is limited published evidence on the cost-effectiveness of strategies to promote breastfeeding, although the quality of the current evidence is reasonably high. Future studies should integrate evaluations of the effectiveness of strategies with economic analyses.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
		weight Neonatal unit with LBW babies (Spain): 0.156 to 1.75 QALYs depending on weight Peer support (Uganda): 2 months of exclusive breastfeeding; 0.01 DALYs.				
Pokhrel, 2015 [2] Intervention: No specific intervention. It considered the benefits for women who are exclusively breastfeeding at one week to continue to four months and the benefits of doubling breastfeeding rates for 7 to 18 months.	No intervention costs were considered. The annual total cost of the three childhood infections was £75.5 million and lifetime costs of breast cancer was £960 million. Increasing women exclusively breastfeeding by 4 months from 7% to 21% would reduce annual hospital infection costs by £4.08 million, increasing to £16.95 million if increased to 65%.	For first time mothers, 371 QALYs could be generated from first time mothers being encouraged to breastfeed up to 6 months and avoided breast cancer.	For first time mothers, adding the value of 371 QALYs (at £20,000 per QALY) generated from first time mothers being encouraged to breastfeed up to 6 months and avoided breast cancer to the health costs averted would generate benefits between £23 million and £41 million depending on the effectiveness of interventions in increasing breastfeeding rates.	Not discussed.	No intervention costs were discussed. Instead, the modelling shows the potential economic benefits (from reduced infections in infants and risk of breast cancer in women) of increasing breastfeeding rates.	The economic impact of low breastfeeding rates is substantial. Investing in services that support women who want to breastfeed for longer is potentially cost saving.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
	Increasing the rate of breastfeeding for <18 months to 32% and for 7 to 18 months to 16% would save £21.17 million from reduced breast cancer.					
Dental interventions						
Anopa, 2015 [3] Intervention: Supervised nursery toothbrushing programme (became Childsmile in 2006).	£1,762,621 per year (2009/10 pounds)	Dental health of five-year olds Number of filled teeth 1999/2000: 19,030 2009/2010: 10,909 Number of decayed teeth 1999/2000: 107,925 2009/2010: 57,167 Children with one tooth missing 1999/2000: 1,615 2009/2010: 776 Children with two or more teeth missing 1999/2000: 6,479 2009/2010: 2,837	In 2009/2010, supported toothbrushing in nurseries was estimated to have saved £4,371,097 in dental care costs compared to if the intervention had not taken place.	The study found that absolute cost savings with the intervention increased as deprivation increased; whilst the relative effect was broadly the same across deprivation levels the starting costs increased substantially as deprivation increased. This does mean however that whilst the absolute differences may have reduced the relative level of inequality in health outcomes by income probably remained largely the same.	Supported toothbrushing generated a substantial return on investment.	The NHS costs associated with the dental treatments for five-year-old children decreased over time. In the eighth year of the toothbrushing programme the expected savings were more than two and a half times the costs of the programme implementation.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Anopa, 2022 [4] Intervention: Fluoride varnish applied at six monthly intervals in addition to the Childsmile programme to prevent dental caries.	Mean incremental costs per child of 6 monthly fluoride varnish compared to treatment as usual (TAU): £63.87 (p=0.382) Intervention cost: £32.66 per child	Over 24 months, utility loss with fluoride varnish compared to TAU: 0.0044 (p=0.636).	TAU dominated six monthly fluoride varnish.	Not discussed	Six monthly fluoride varnish was found to cost more with worse outcomes than treatment as usual (TAU) (the Childsmile programme minus fluoride varnish) and so would not provide a positive return on investment.	Applying FV in nursery settings in addition to the Childsmile program is not likely to be cost-effective given current thresholds.
Smoking interventions						
Jones, 2019 [5] Intervention: MiQuit - self-help smoking cessation support as a 12-week programme of tailored text messages in addition to normal NHS smoking cessation support.	Text message support saved £38.37 per mother compared to usual NHS smoking cessation support alone.	Text message support generated 0.04 QALYs per mother compared to usual NHS smoking cessation support alone.	Text message support dominated usual NHS smoking cessation support alone.	Not discussed.	Text message support to stop smoking was likely to be highly cost-effective and generate a positive return on investment. .	Using data from a trial which reported only short-term economic analysis showed that the intervention was very likely to be cost-effective in the longer term and to generate health-care savings.
McMeekin, 2023 [6] Intervention: Financial incentives for pregnant women to stop smoking. £400 in shopping vouchers in total: £50 for engaging with stop smoking services and setting a quit date, £50 if CO certified as quit at 4 weeks, £100 at 12 weeks and £200 in late pregnancy.	In the short-term model, mean intervention costs, including smoking cessation services and nicotine patches, were £268 (compared to £91 with control). Adjusted analysis suggested total costs could be £637 in the intervention arm, although this was not statistically significant.	The short-term model showed an absolute difference in late pregnancy quitters of 14.4% with the intervention with a QALY gain of 0.004. The lifetime model showed a QALY gain of 0.03 for mothers only and 0.171 if the lifetime for the	The short-term model suggested a cost per late pregnancy quitter of £4,400 and an ICER of £150,000 per QALY gained with the intervention. The long-term model including mother and infant lifetime outcomes suggested the intervention dominated usual care.	Not discussed.	The use of financial incentives to stop smoking was effective in the short term but was only likely to have a substantial return on investment if the impact on mother and infant was projected over a lifetime.	In the UK, offering up to £400 financial incentives, in addition to usual care, to support pregnant women to stop smoking appears to be highly cost-effective over a life-time for mother and infants.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
	In the lifetime model, including mother and child outcomes, the mean cost saving was £37 (not statistically significant).	infant and mother was taken into account with the majority of this QALY gain (0.162 calculated by the reviewer) arising from the infant after the age of 15.				
Renwick, 2018 [7] Intervention: An intervention to stop smoking in carers (the Smoke Free Home Trial). A smoke free homes advisor undertook home visits to provide behavioural support and give feedback on air quality in the home. Participants were also provided with nicotine replacement patches.	The average cost of the intervention per household: £328 Usual care: £45 Incremental cost of the intervention: £283	The intervention reduced particulate matter of <2.5μm diameter (PM2.5 (ug/m3)) by 21.6 compared to usual care and had 3.7% more quitters, a reduction of 7 in the number of cigarettes smoked per day and 20.7% more carers attempted to quit compared to usual care.	The cost per additional quitter with the intervention was £71 and the cost per reduction in PM2.5 (ug/m3) was £131 compared to usual care.	Whilst the programme was aimed at disadvantaged areas and smoking was discussed as a cause of future health inequalities, there was no assessment of the impact on health inequalities of the intervention.	The intervention was found to reduce tobacco related harm to children, but the return on investment is dependent on the WtP for incremental improvements in air quality or per quitter. There is no consideration of the economic or health consequences of these improvements nor whether the improvements were maintained.	The complex intervention was more costly but more effective in reducing PM2.5 compared with the usual care. It offers huge potential to reduce children's tobacco-related harm by reducing exposure to second hand smoke in the home. The intervention is considered cost-effective if the decision maker is willing to pay £131 per additional 10μg/ m3 of PM2.5 reduction.
Immunisation interventions						
Giorgakoudi, 2018 [9] Intervention: Vaccination for GBS.	At a price of £54 per vaccine, the total cost would be £30.7 million with a net cost of £17.4 million	Total QALY gain with vaccination: 870	The ICER per QALY gained at a notional cost of £54 per vaccine would be £19,953 and so is the maximum price at which vaccination could be	Universal programme and inequalities not discussed.	It is unlikely there are savings with vaccination but the QALYs generated from vaccination meant that the authors concluded that vaccination could	Maternal GBS immunisation is expected to be cost-effective, even at a relatively high vaccine price.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
			cost-effective at a WTP threshold of £20,000 per QALY (or £71 at £30,000 per QALY). Disease incidence and vaccine costs were the biggest determinants of cost-effectiveness.		be a cost-effective investment at £54 per dose which the authors considered to be a reasonable price for vaccination in the UK.	
Early childhood interventions to families facing challenges						
Barlow, 2019 [10] Intervention: Parents under Pressure, an intervention underpinned by the Integrated Theoretical Framework, developed for complex families with multiple adversities. The aim of the programme, delivered through 12 modules, is to enable parents to better regulate their emotions through mindfulness strategies. The intervention was delivered in family homes by fourteen practitioners. Outcomes were reduction in risk of child abuse and parental emotional regulation.	Incremental costs of Parents under Pressure compared to TAU: £2,386.64	Incremental QALYs of Parents under Pressure compared to TAU: 0.07	Cost per QALY for Parents under Pressure compared to TAU: £34,094.86	Not discussed explicitly but the target group for the intervention were unemployed and so would be on low incomes.	The incremental cost-effectiveness ratio I(CER) per quality-adjusted life-year (QALY) gained was above the threshold normally considered cost-effective by NICE. However, the results only considered parental quality of life (QoL) and it is likely if the reduction in harm to children was taken into account the cost-effectiveness (and therefore return on investment) of the intervention would improve.	Up to one-third of substance dependent parents of children under 3-years of age can be supported to improve their parenting, using a modular, one-to-one parenting program. Further research is needed.
Cannon, 2018 [11] Intervention: Interventions fell into four categories: early	Cost analysis (2016 US dollars) showed that costs ranged from $150 per family for a parent	NR	Benefit cost ratios were typically in region of $2 to $4 for every dollar invested.	Not discussed.	The review highlighted the following key findings about economic return:	Most of the reviewed programs have favourable effects on at least one child outcome and those with an

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
care and education - support to children in group settings; home visiting - individualised services delivered in homes to promote parent skills and knowledge; parent education - individualised services delivered outside of homes to promote parent skills and knowledge; transfers - cash or in-kind benefits direct to families.	education programme to $48,800 per family for a comprehensive education and home visiting service. Variation was due to programme intensity, duration and local costs applied in the analysis.				Higher returns are associated with low cost programmes and resource intensive interventions with long term follow up Targeted and universal approaches can show positive returns Monetary benefits arise from multiple domains but are often highest for income and reductions in crime. Government benefits (i.e. to the payer of the intervention) rarely outweigh programme cost Benefits to children can take years or decades to unfold Not all outcomes can have an economic value assigned to them.	economic evaluation tend to show positive economic returns.
Hajizadeh, 2017 [12] Intervention: ParentCorps, a family-cantered enhancement to pre- kindergarten programming promoting family engagement and safe, nurturing and predictable environments at home and at school. No further details of the	Costs of ParentCorps in a large school (72 pupils a year in four classrooms): ▪ Year one: $104,190 ▪ Year two: $89,755 ▪ Year three: $39,755. Net lifetime savings of $4,387 from reduction in healthcare, criminal	Lifetime QALY gain: 0.27 QALYs	ParentCorps dominated usual care.	Not explicitly mentioned but the intervention was targeted at high poverty areas.	Potential for high return on investment but this is dependent on effectiveness seen being maintained effectively for life.	Effective family-centred interventions early in life such as ParentCorps that impact academic, behavioural and health outcomes among children attending high-poverty, urban schools have the potential to result in longer-term health benefits and substantial cost savings.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
intervention were provided.	justice and productivity.					
Obesity interventions						
Brown, 2019 [13] Intervention: Childhood obesity interventions commencing before six months of age.	Costs of interventions were not considered. Total cost savings were estimated at between $0 (if treatment effect was not maintained to adulthood) to $301 million (if the treatment effect was maintained for life).	Total HALYs were estimated at between 7,425 (if treatment effect was not maintained to adulthood) to 36,946 (if the treatment effect was maintained for life).	At a WTP of $50,000 per HALY, the intervention cost per child aged 0 to 5 years that would still be cost-effective was between $215 (if effect not maintained to adulthood) to $1,228 (if effect lasted a lifetime). At a WTP of $50,000 per HALY, the intervention cost per child aged 2 to 5 years that would still be cost effective was between $326 (if effect was not maintained to adulthood) to $1,866 (if effect lasted a lifetime).	Not discussed.	The study highlighted there is potential for substantial return on investment but the level of return is dependent on the length of time the effect on BMI from intervention is maintained.	Results suggest significant potential for cost-effectiveness of obesity prevention interventions in preschool-aged children if intervention effect can be maintained.
Tran, 2022 [14] Intervention: Romp and Chomp, a universal obesity prevention intervention and involved community capacity building, policy changes and the cultural and physical environments of early years settings. The intervention had four key messages: daily active play, daily water and fewer sweet drinks, daily fruit and	Total annual intervention costs were $177,536,705 or $93 per participant. If only 4 to 5 year olds bore the costs the intervention would be $276 per participant and in a worst case scenario could be $475 (highest costs and lowest efficacy from 95% confidence intervals). The net cost after healthcare savings was $78	The intervention had a mean decrease in BMI per participant of 0.06 in the base case and 0.01 in the worst case. Mean QALY gain per participant with intervention was 0.003 (not statistically significant) in base case and 0.0005 in the worst case.	The base case ICER was $26,399 in the base case with a 64% chance of being cost effective at a WTP of $50,000 per QALY. In the worst case scenario the ICER was $956,146 with a 1.6% chance of being cost effective.	Not discussed.	The authors considered that the intervention has a fair probability of being cost-effective, although the QALY gains are small (based on a small average BMI increase) and the total costs of the intervention very high.	Romp & Chomp has a fair probability of being cost-effective if delivered at scale.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
vegetables, less screen time.	($472 in worst case scenario).					
Antenatal intervention to reduce adverse pregnancy outcomes						
Bailey, 2022 [8] Intervention: Four broad categories of lifestyle interventions in pregnancy: diet, diet with physical activity, physical activity and "mixed" (lacking structured diet or physical activity components).	Average intervention costs per mother Diet: $168 Diet and physical activity: $187 Physical activity: $217 Mixed: $184 All interventions combined: $198 Incremental costs with intervention compared to standard care (none were statistically significantly different) Diet: $169 Diet and physical activity: $59 Physical activity: -$95 Mixed: $182 All interventions combined: $75	Percentage of complications avoided with intervention compared to standard care (all were statistically significantly different) Diet: 3.46% Diet and physical activity: 2.90% Physical activity: 4.23% Mixed: -0.68% All interventions combined: 1.94%	Cost per averted complication (none statistically significantly different from zero) Diet: $4,882 Diet and physical activity: $2,020 Physical activity: Dominant (costs less and reduces complications) Mixed: Dominated (costs more and increases complications) All interventions combined: $3,855	The study did not consider health inequalities.	Diet and physical activity interventions in pregnancy, provided they are structured, are likely to have minimal incremental costs or to save money and reduce complications and so therefore are likely to provide a positive return on investment.	Governments can expect a good return on investment and cost savings when implementing effective lifestyle interventions population-wide.
Child or parental mental health interventions						
Bee, 2014 [15] Intervention: The systematic review looked for any community based interventions that improved the QoL of children with parents with serious mental illness. Only one study	From the one identified study, median costs per patient were £1,351 compared to £231 with usual care.	At 6 months follow up, 21/30 women in the intervention group and 7/30 in control group had recovered from depression. It was unclear if	NA	Not discussed.	The return on investment is unclear from the one study identified.	Evidence for community-based interventions to enhance QoL in children of parents with serious mental illness is lacking. The capacity to recommend evidence-based approaches is limited. Rigorous development work is

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
was identified that was of a specialist psychiatric parent and baby day unit for treatment of postnatal depression.		this was maintained.				needed to establish feasible and acceptable child- and family-based interventions, prior to evaluating clinical effectiveness and cost-effectiveness via a RCT.
Hodgson, 2022 [16] Intervention: Early intensive ABA based interventions that impact a child's developmental by shifting a child's developmental trajectory through early interventions. They are typically delivered to young autistic children for several years on a one-to-one basis, for between 20 to 50 hours per week.	Cost of ABA was assumed to be £36,682.78 compared to TAU of £8,634.33. From an NHS perspective, under pessimistic assumptions on long term efficacy of ABA, incremental costs were £57,879 and under optimistic assumptions on long term efficacy of ABA, incremental costs were £57,233. From a public sector perspective, under pessimistic assumptions on long term efficacy of ABA, incremental costs were £43,940 and under optimistic assumptions on long term efficacy of ABA, incremental costs were £36,242.	Under pessimistic assumptions on long term efficacy of ABA, incremental QALYs were 0.24 and under optimistic assumptions on long term efficacy of ABA, incremental QALYs were 0.84.	From an NHS perspective, under pessimistic assumptions on long term efficacy of ABA, the ICER per QALY gained with ABA was £236,837 and under optimistic assumptions on long term efficacy of ABA, the ICER was £68,362. From a public sector perspective, under pessimistic assumptions on long term efficacy of ABA, the ICER per QALY gained with ABA was £179,799 and under optimistic assumptions on long term efficacy of ABA, the ICER was £43,289.	Not discussed.	With current evidence, ABAs are unlikely to provide a sufficient return on investment to justify investment.	The results of this economic analysis suggest that early intensive ABA-based interventions are unlikely to represent value for money, based on a £20,000 to £30,000 per QALY threshold typically adopted to inform UK healthcare funding decisions. However, important gaps in the available evidence limit the strength of the conclusions that can be drawn from the presented analysis. Further research, focusing on the trajectory of autistic children following intervention is likely to be highly beneficial to resolving some of these uncertainties.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
Mihalopoulos, 2015 [17] Intervention: Children were screened for inhibition in the preschool setting with questionnaires being sent home for parents to complete. The questionnaires were primarily assessed by psychologists. Parents of positively screened children were offered a six session parenting course.	The population level costs of the intervention were estimated to be AU$5.2m to the government and AU$0.44 million in private costs. The cost of the intervention itself was not provided. The net cost after cost-offsets for treating anxiety were AU$3.8m.	Total DALYs averted with the intervention were 460.	ICER with cost offsets: AU$8,000 per DALY averted ICER without cost offsets: AU$12,000 per DALY averted	Not discussed.	The return on investment was dependent on the value placed on the DALYs averted.	Screening young children in a preschool setting for an inhibited temperament and providing a brief intervention to the parents of children with high levels of inhibition appears to provide very good value-for-money and worth considering in any package of preventive care. Further evaluation of this intervention under routine health service conditions would strengthen conclusions.
Sonuga-Barke, 2018 [18] Intervention: Two interventions were considered compared to TAU: ▪ The New Forest Parenting Programme (NFPP) was a 12-week individual, home-delivered ADHD PT programme. It included education about ADHD, communication strategies, play based activities and attention training. ▪ Incredible Years Toddler (IY) was a	The average cost per family for NFPP delivery was £1,081 and for IY delivery was £1,569. Net costs including health services and family borne costs were £1,591 per family with NFPP and £2,103 with IY.	There were no differences in measured parental and child outcomes with NFPP compared to IY. NFPP only showed a statistically significant difference over TAU for parent related conduct problems. IY showed no statistical difference for any outcome compared to TAU.	Whilst NFPP and IY did not appear different in effectiveness, NFPP was less expensive.	Not discussed.	The return on investment is unclear as both NFPP and IY cost several thousand pounds per family and the improvement in outcomes over usual care is unclear. However, IY, recommended by NICE, seems to be more costly than NFPP.	Although, there were no differences between NFPP and IY with regards clinical effectiveness, individually delivered NFPP cost less. However, this difference may be reduced when implemented in routine clinical practice. Clinical decisions should take into account parental preferences between delivery approaches.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
12-week group-based programme comprising a serious of developmentally based interventions for parents, children and teachers. It included problem-solving, videotape modelling and role playing.						
Varshney, 2022 [19] Intervention: Chicago Child-Parent Centres (CPCs). The centres provided continuous education and family support to economically disadvantaged children through to third grade (age 8 or 9). The programme had five key features: ▪ Early education no later than 4 years. ▪ Structured learning for language and basic skills. ▪ Increased parent involvement in home and school (at least half a day per week). ▪ Provision of health and social care services.	The average cost of the preschool CPC programme was $11,000 (2021 dollars) per participant. The cost and productivity savings were $14,896 (using the foregone earnings approach).	Actual QALYs were not reported, but the value of the QALY gain from reduction in diabetes was $24,134 (with an additional 'utility' gain of $5,076) and from a reduction in smoking of $7,855.	The benefit-cost ratio was 0.30 to 2.72 with a mean of 1.36.	The programme was targeted in low income areas but the impact on health inequalities was not discussed.	The return on investment was estimated to be between $1.35 and $3.66 per dollar spent and could be higher if crime reduction, welfare and earnings were taken into account.	The results suggest that the health impacts of early educational intervention were significant and may by themselves offset the costs of the intervention, even if no other benefits were observed. However, a future study may look at incorporating benefits across a domain of outcomes such as gain in income and reduction in crime, in addition to health. This would help in calculating a comprehensive benefit-cost ratio of the program.

Study and intervention description	Total costs	Effectiveness	Economic evaluation outcomes	Reducing health inequalities	Return on investment	Overall study conclusions
- Programme continuity between pre-school and elementary school. Promotion of health and good nutrition was also a component of the programme.						

Key: ABA - applied behaviour analysis; ADHD - attention deficit/hyperactivity disorder; BMI - body mass index; CO - carbon monoxide; CPC - child-parent centre; DALY - disability adjusted life years; EE - economic evaluation; FV - fluoride varnish; GBP - gross domestic product; HALY - health adjusted life years; ICER - incremental cost-effectiveness ratio; IY - Incredible Years; LBW – low birth weight; NA - not applicable; NFPP - New Forest Parenting Programme; NHS - National Health Service; NICE - National Institute for Health and Care Excellence; NOSH - Nourishing Start for Health; NR – not reported; PT – parent training; QALY - quality-adjusted life year; QoL - quality of life; RCT - randomised controlled trial; SMI - serious mental illness; TAU - treatment as usual; UK - United Kingdom; WTP - willingness-to-pay.