Evaluating childhood public health interventions: An exploration of the evidence and methods

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Abstract

Background: Decisions to fund public health interventions in early childhood may include reducing health inequalities, improving life chances and setting health trajectories throughout the child's life. However, it is unclear whether these aspects of potential value are captured in the health economics evidence base and whether their inclusion would impact the value for money of the intervention.

Aims: To identify the evidence available of how childhood public health interventions have been evaluated in the past. Then, to explore methods available to introduce additional aspects of value.

Methods: The evidence was identified through a systematic review. The E-SEE Steps trial was then introduced as a case study to explore methods. This was done first by introducing health equity though the means of a distributional cost-effectiveness analysis (DCEA); longer term time horizons through the use of the LifeSim microsimulation model; and non-health costs and outcomes which were estimated using LifeSim and incorporated using an adapted framework proposed in the literature.

Findings: The systematic literature review identified inconsistencies across methodological approaches used. The DCEA revealed that although E-SEE Steps was not cost-effective for the children in the trial, it could be considered equity-improving but is sensitive to the measure of socioeconomic position. The results of the LifeSim extrapolation revealed little difference in cost-effectiveness compared to the within-trial results. Finally, incorporation of the non-health costs and outcomes has an impact on the results and the incorporation of equity alongside the non-health costs and outcomes has a considerable impact on the determination of value for money for some groups.

Conclusions: The reason for implementing public health interventions for children go beyond simply maximising health for the population and may consider reducing health inequalities and improving non-health outcomes. This research demonstrates the impact of including wider aspects of value.

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Declaration

I declare that this thesis is a presentation of original work and I am the sole author. This work has not previously been presented for a degree or other qualification at this University or elsewhere. All sources are acknowledged as references.

Chapter 1: Background

1.1 Evaluating early years interventions

Early life experiences are important determinants of development and health throughout the life course (Halfon and Hochstein, 2002, Hertzman and Power, 2004, Cunha and Heckman, 2007, Marmot, 2017). The impact of the early life environment on health itself has long been known (Barker, 1990, Waaler, 1984, Notkola et al., 1985, Marmot et al., 1984, Barker and Osmond, 1986, Buck and Simpson, 1982), with Barker and colleagues first describing the environmental origins of later-life disease beginning as early as *in utero* (Barker, 1990). More recently, causal pathways of disease (and pre-disease) have been expanded to consider the role of social systems and socioeconomic disparities (Ben-Shlomo and Kuh, 2002, Marmot, 2013). This approach to incorporating biological and social determinants of health experienced throughout the life course includes the impact of childhood and adulthood development on health itself (Halfon and Hochstein, 2002).

Important developmental changes occur in early life, including crucial periods of sensitivity and plasticity of neurons which are vital in the development of the brain and behaviour (Knudsen, 2004). It is within this stage of life that fundamental skills are developed and provide the foundations for the formation of future skills (Cunha and Heckman, 2007).

There is a large body of literature linking development and long-term health. The events in the first few years of life play a critical role in the future mental, physical and emotional health of the child (Center on the Developing Child, 2010), lay the foundations for development (Marmot, 2013), and prove essential in the formation of skills for early life and beyond (Nelson et al., 2020, Almond et al., 2018a, Black et al., 2017, Goodman et al., 2015, O'Donnell et al., 2015, Layard et al., 2014, Adler and

Stewart, 2010, Cunha and Heckman, 2007). A number of frameworks describing the role development plays on health throughout the life course exist through genetic, biological, behavioural, social and economic determinants of health (Halfon and Hochstein, 2002, Hanson and Gluckman, 2008, Shonkoff, 2010); and empirical studies supporting these links (Heindel and Vandenberg, 2015, Ben-Shlomo and Kuh, 2002, Lereya et al., 2015). In addition to health, cognitive skills developed in early life are believed to play a role in educational development and promote economic wellbeing (Hanushek and Woessmann, 2008).

A number of seminal contributions to the economics literature identify the vast economic and social returns available from investments in the early life period (Cunha and Heckman, 2007) through means of increased productivity (Grossman, 1972).

The impacts of the environment on health both directly and indirectly via development have therefore established early life as an important period for the targeting of health interventions. These programmes are important policy tools which have been demonstrated to be key to improving life-chances, health and wellbeing and reducing health inequalities (Strelitz et al., 2012, Tickell, 2011, Allen, 2011). Their potential has been recognised in the UK and elsewhere and as a result, a number of universal and targeted early years interventions have been implemented. A recent House of Commons Briefing Paper on Early Intervention (Powell et al., 2021) describes a number of such interventions introduced in the UK.

It is important that decisions to fund and reimburse these health interventions are supported by systematic and robust assessments of clinical and economic evidence

(i.e., how well the programme or policy works and its value for money). Methods of health economic evaluation are well established (Drummond et al., 2015) but there remains concern regarding the applicability of these methods when moving beyond the pharmaceutical paradigm with a narrow health service perspective, to evaluating more complex PHIs such as those implemented in early life (Deidda et al., 2019, Weatherly et al., 2009, Edwards et al., 2013, Greco et al., 2016, Petrou and Gray, 2005, Payne et al., 2013).

One fundamental difference between pharmaceutical interventions, medical technologies and devices (referred to hereafter as 'health technologies'), and PHIs such as early childhood interventions, is the latter's preventive nature. That is, the main purpose is to prevent ill health rather than to treat it. This brings with it challenges in terms of improving health (Donaldson and Donaldson, 2003), such as population heterogeneity and difficulties in intervention targeting, as well as unique challenges in assessing value for money (Wagstaff, 1986).

The remainder of the chapter is structured as follows. First, the nature of early childhood interventions as preventive goods is presented to help define some of the unique challenges in evaluating these complex interventions. Second, the motivation for requiring health economic evidence and economic evaluation is described through the resource allocation problem. Third, the dominant approaches to health economic evaluation are presented. Fourth, the challenges in applying the identified approaches to health economic evaluation of early years interventions are described. Finally, the landscape regarding the evaluation of early childhood PHIs will be discussed.

1.2 Early years interventions as preventive goods

Many early childhood interventions are concerned with preventing ill health and promoting health behaviour. This simple but fundamental goal of such interventions impacts the way in which they are provided as 'prevention goods and services' may be considered distinct from normal goods and services when it comes to the allocation of resources (Wagstaff, 1986).

In microeconomic theory, the concept of demand relates to how much of the good or service consumers (or public health services uses) wish to purchase at different prices. Demand is rooted in consumer preference where it is assumed economic actors are rational and maximise their utility, along with other axiomatic assumptions.[1] *Utility* is a concept in economic theory and is often used synonymously to represent 'welfare', 'happiness', or 'wellbeing', albeit there remains ambiguity in its exact definition (Brouwer et al., 2008).

Supply on the other hand is rooted in decisions made by the providers of the goods and service. When supply equals demand (graphically this is depicted as the downward sloping demand curve crossing the upward sloping supply curve when price and quantity are plotted) there is said to be a market equilibrium.[2] At this point market forces result in the efficient provision of the goods and services. However, there are a number of reasons to consider that when left to market forces alone, the

[1] The four axioms of preference are completeness, transitivity, continuity and rationality.
[2] The relationship between preferences and demand results in a demand curve.

provision of prevention goods and services will not be socially efficient, referred to as 'market failure' [3] (Donaldson et al., 2017).

Such market failure occurs due to: *time inconsistent preferences* (i.e. individuals do not consider the costs and benefits of engaging in health improving behaviour equally at different points in time meaning individuals may not honour commitments made now about behaviour tomorrow); *the violation of the rationality assumption* (i.e., individuals may not make decisions to maximise their utility over the long term and engage in health harming behaviour); *the nature of prevention goods being 'merit goods'* (i.e., the benefit of the good to society is greater than the benefit to the individual); and *the goods being considered 'public goods'* (i.e., consumption of the good does not diminish the amount of the good and any individual is free to use it meaning there is no incentive to produce it).

The result is the under provision of the good in the market. In his seminal contribution, Arrow (Arrow, 1978) described many additional reasons for market failure in the case of health care in general, of which numerous additional reasons apply to prevention goods and services. The conclusion is that government intervention is therefore required to provide prevention goods and services to improve population health as demand is unpredictable and supply is not linked to monetary returns (Arrow, 1978). Thus, the provision of prevention goods and services will not be optimal when left to the market alone meaning alternative approaches are required to inform the allocation of healthcare resources.

[3] In economic theory, such social efficiency can be defined as a situation in which an individual cannot be made better off without making another individual worse off, referred to as a 'pareto optimality'.

1.3 Healthcare resource allocation

The provision of health services within a healthcare system are typically constrained by a resource allocation problem. That is, resources are scarce and the adoption of all potential health interventions is simply not possible. The choice to fund a particular programme, whether that is a new specialist cancer medicine or a targeted primary care screening clinic for infants, means opportunities to use the same resources on an alternative programme are foregone (Drummond et al., 2015). In a resource constrained healthcare system with a finite budget, these difficult decisions are unavoidable.

To address this, economic evaluation informs the resource allocation debate by providing a systematic and transparent framework to understand *how* decisions are made, not just what decisions should be made. Rather than basing decisions on implicit values held by decision makers, economic evaluation makes explicit the decision-making process and increases accountability (Drummond et al., 2015).

This is achieved through a number of steps. First, the costs and benefits of relevant alternative uses of the resources are identified for a specific patient group and situation. Evidence of the costs and benefits ideally inform the economic evaluation (Briggs et al., 2006) as well as the consideration of the relevant perspective (e.g., the NHS). The results then help to identify the amount of additional benefit one alternative produces over another and the additional costs it takes to obtain those benefits. The additional cost should then be compared to a measure of what level of benefit would have been achieved if the funds had been allocated to alternative programmes. This is known as the ‘opportunity cost’.

Second, economic evaluation makes explicit social value judgements of decision makers. That is, explicitly placing a *value* on the benefits produced by the new health intervention relative to the value of the benefits given up owing to the opportunity cost. Not only is valuation in general health economic evaluation challenging, valuation of preventative services are likely to face additional challenges (Watts and Segal, 2009).

1.4 Normative frameworks

The ability to value benefits, both produced by a new programme and those foregone, hinge on normative questions of what the fundamental purpose of healthcare *is* or *should be*. Is it to improve health? Or improve an alternative notion of wellbeing? It is here that approaches to address these questions delineate in terms of what denotes the relevant evaluative space (Gaertner, 1993, Brouwer et al., 2008). The two dominant normative approaches pervading health economic evaluation are *Welfarism* and *Extra Welfarism*.

1.4.1 Welfarism

Welfarism is predicated on the idea that the purpose of healthcare is to improve an overall notion of societal welfare, not just to improve health. This is justified by public spending on non-health interventions and individual consumption opportunities (i.e., spending on goods and services) on things other than health.

Welfare is to be thought of as the ultimate goal and is comprised of individual utility. Judging the 'goodness' of any situation on utility information alone is one of the central tenets of welfare economics (Sen, 1999, Hurley, 1998, Hurley, 2000, Brouwer et al., 2008). In combination with the additional tenets, [4] the welfarist perspective suggests healthcare programmes should be evaluated in terms of the utilities achieved by individuals and that those individuals are themselves the best judges of what contributes to their utility (Sen, 1999, Brouwer et al., 2008).

The predominant approach to interpreting utility is that it represents *preference ordering*. The choices individuals make in the world represent their preferences and in turn the states that maximize their utility and improve welfare. If a healthcare programme improves the welfare of an individual without reducing the welfare of other individuals, (known as a Pareto improvement) this programme can be seen as being efficient, i.e., it improves social welfare. Importantly, the distribution of social welfare gains is not relevant to the decision, rather simply whether overall welfare improves. Important contributions to the literature demonstrated social welfare improvements can still occur if those that 'gain' from a specific state of the world can financially compensate those that 'lose', and still remain better off (Hicks, 1939, Kaldor, 1939).

[4] The four main tenets of welfare economics are: i) The utility principle - individuals are rational and maximise their welfare by ordering the potential options; ii) Individual sovereignty - individuals are the best judges of what contributes to their utility; iii) Consequentialism - utility comes from outcomes not processes themselves; and iv) Welfarism - the 'goodness' of any situation can be judged solely on utility information.

It is this compensation principle that defines *value*. Revealed preferences and the choices that individuals make in the 'market' (i.e., the prices paid) indicate social value i.e., the compensation required for an individual to give something up. In the absence of suitable markets as has been described in the case of healthcare (Arrow, 1978), 'shadow prices' can be used to indicate the price that would be paid in an undistorted market.[5] These are often obtained experimentally through hypothetical scenarios in which individuals make choices to indicate what they would be willing to pay/give up for health (Drummond et al., 2015). The practical application of this approach to evaluative approach in health economic evaluation is known as cost-benefit analysis (CBA).

1.4.1.1 Cost-Benefit Analysis

Cost-benefit analysis is based on the aforementioned compensation principle, in which individuals' willingness-to-pay (WTP) for healthcare programmes (i.e., the shadow price) is used to translate health benefits achieved from a programme (e.g., life years) into monetary terms. The costs required to implement the programme can be compared to the monetary valuation of the health effects gained from the programme, allowing comparison of the costs to benefits in monetary terms. The sum of the costs and benefits indicates whether there is net benefit (loss) from implementing the programme. Subject to a societal budget constraint, a welfarist decision maker will deem those with a net benefit as an efficient use of resources as

[5] Healthcare markets may be distorted due to informational asymmetry, a lack of competition (e.g., due to monopolies), taxation or phenomena such as the principal-agent problem.

implementation improves social welfare. Consideration should however be given to the opportunity cost if the budget constraint is fixed. The health displaced should be valued in terms of its consumption equivalent, in the same way the health gained from the programme is valued (Drummond et al., 2015, Sculpher and Claxton, 2012), i.e., the opportunity cost of the consumption foregone.

In practice CBA has seen limited application in healthcare decision making for a number of reasons. First, equity considerations borne out of basing welfare on WTP could in theory be impacted by an individuals' ability to pay. Even if it is believed the existing income distribution is through individuals maximising their welfare, initial endowment impacts ability to pay and this may not be considered equitable. Second, explicitly valuing improvements in length and quality of life in monetary terms has been seen as problematic (Coast, 2004).

1.4.2 Extra-Welfarism

Extra-welfarism moves away from the strict evaluative space defined by welfarism. Notably, it permits outcomes other than utility to be considered in decision-making; the outcomes need not be preference-based; and valuation can be determined by individuals other than the affected individual (Brouwer et al., 2008). The move came as a result of a number of criticisms of individual utility being too narrow and failing to account for individuals' *capabilities* and *functioning*, amongst other things (Gaertner, 1993, Coast et al., 2008).

In moving away from individual preference, extra-welfarism has largely adopted a 'decision maker's' perspective in which value judgements (including equity

weighting) of public decision makers are deemed important for society (Sugden and Williams, 1978). Further, this move has seen *health* as being identified as important to society (Culyer, 1989, Sugden and Williams, 1978) and the production of health as the fundamental purpose of the healthcare system (Culyer, 1989). Therefore, extra welfarist decision makers can be seen to be maximising health subject to a given healthcare budget constraint. Note, extra welfarism need not require a decision maker's perspective in which health is the maximand, rather it simply denotes the evaluative space in which 'extra' aspects of value can be considered on top of individual utility. This health-maximising decision maker's perspective does, however, predominate health decision making in the UK (Drummond et al., 2015, National Institute for Health and Care Excellence, 2022).

The application of this approach to economic evaluation comes in many forms such as cost-minimisation analysis, cost-consequence analysis, cost-effectiveness analysis (CEA) and cost-utility analysis (CUA). Note, some differentiate between CEA and CUA according to the specific units of health used to evaluate health interventions,[6] however for the purpose of this chapter the term 'CEA' will be used to denote both CEA and CUA hereafter. The predominant approach encountered in the health economic evaluation literature and used in practice is CEA.

[6] Both CEA and CUA assess the benefits of a programme in units of health. The distinction can be made between the two in terms of the specific units of health used. Where a distinction is made, CUA is often used to refer to evaluations in which a generic measure of health is used, e.g., QALYs; and CEA refers to evaluations in which the unit of health is a non-generic measure of health only really valid for that specific health condition e.g., mmHg drop in diastolic blood pressure.

1.4.2.1 Cost-Effectiveness Analysis

Cost-effectiveness analysis assesses the gains in health achieved from a number of relevant and mutually exclusive alternative healthcare programmes and compares those gains to the costs. The results are presented as the ratio of the additional (or 'incremental') cost of one alternative to another and the additional health. The resulting incremental cost-effectiveness ratio (ICER) therefore provides an estimate of the additional cost required per unit of health. To allow comparisons across healthcare programmes in different disease areas or different patient populations, a generic measure of health is preferred which captures improvements in length of life and quality of life. Numerous examples exist of generic measures of health for use in CEA (Whitehead and Ali, 2010), however the most commonly adopted is the quality-adjusted life year (QALY). The QALY weights a year of future life expectancy by the quality of the life lived in that year (Torrance et al., 1982, Williams, 1985). The QALY is the preferred measure of health used to inform economic evaluation of health interventions in England and Wales following the adoption of it in the reference case defined by the National Institute of Health and Care Excellence (NICE) (National Institute for Health Care Excellence, 2022).

The ICER for a programme is then compared to a cost-effectiveness threshold to determine whether it is cost effective. The threshold should represent the opportunity cost, i.e., the health foregone due to the displacement of resources, given the fixed health care budget constraint. A cost-effectiveness threshold representing this approach is known as a 'supply-side threshold' (Culyer, 2016) and the empirical value of such a threshold has been estimated in the UK (Claxton et al., 2015).

Critics of CEA, and in particular the approach adopted in the UK, consider the evaluative space too restrictive as benefits of a programme may well be felt beyond health improvement (Coast et al., 2008); evaluating programmes in QALYs may underestimate the programme benefits. This is particularly apparent in the evaluation of PHIs, including early life interventions. The use of QALYs in CEA has also been criticised on a number of fronts. Firstly, for how well it captures individual preference (Pliskin et al., 1980) and secondly for failing to capture broader aspects of quality of life, for example the ability to form and maintain friendships (Coast et al., 2008).

There are alternative approaches that go beyond health-related quality of life (HRQL) to allow the measurement of a broader QALY. One example is the EQ Health and Wellbeing instrument (EQ-HWB) which captures health and wellbeing for use in healthcare, social care, and public health interventions (Brazier et al., 2022). An alternative example is the ICEpop Capability Measure (ICECAP) that can be used to measure an individual's capability (Al-Janabi et al., 2012, Coast et al., 2008) and like EQ-HWB facilitates evaluations across sectors, e.g. health, social care and education. Other approaches have been described in the literature (Brazier and Tsuchiya, 2015).

1.4.3 Alternative approaches

Despite CEA and CBA dominating the health economic evaluation literature, alternative methods do exist that fall outside of the neat dichotomy of thinking in terms of welfarist and extra-welfarist approaches. Such examples are return on investment (ROI) and social return on investment (SROI).

1.4.3.1 Return on investment

Originally adopted from business and financial analysis, return on investment (ROI) provides estimates of the efficiency of an investment by presenting a ratio of the net benefits of a programme to the costs. Although more frequently encountered in health-adjacent sectors such as education and child development, there are numerous examples of its use in public health decision making (Baxter et al., 2014, Masters et al., 2017).

Return on investment expresses all costs and benefits in monetary terms to allow the estimation of the likely financial returns generated from an investment. It allows the comparison of alternative investments by comparing the ROI generated for each. The evaluation typically takes a narrow perspective, usually from the entity directly paying for the programme, often limiting it to short-term financial costs and benefits (Gargani, 2017). Proponents of the use of ROI in health care decision-making suggest it has merits in reversing political discourse from viewing resources required to fund health care as an expense to an investment (Brousselle et al., 2016).

Critics of the use of ROI in health care decisions cite the limitations of the method in incorporating broader notions of benefit such as those for advancing the public good (Hamelmann et al., 2017, Gargani, 2017). Return on investment also faces criticism due to the inevitable comparisons it engenders with ROI of alternative programmes, and the lack of explicit guidance on how decision making when ROI is available for a number of programmes (Brousselle et al., 2016). Finally, there does not appear to be a consistent approach to deciding on the benefits that should be incorporated in the

calculation and how they should be valued. This lends itself to the idea that ROI could allow ‘cherry picking’ of a programme’s benefits.

1.4.3.2 Social return on investment

To incorporate broader notions of value, SROI appeared from the ROI literature and widened the perspective. SROI was developed by the Roberts Enterprise Development Fund (REDF) and was developed to identify three types of value (economic value, social value and socioeconomic value) created for different stakeholders. It aims to capture the broader social, economic and environmental outcomes (i.e., the triple bottom line) of an investment (Hamelmann et al., 2017). Calculated using the same basic methodology as ROI, SROI attempts to capture the social value of programmes by including both those benefits that can be valued in monetary terms and those intangible benefits that are more difficult to value, such as reducing inequality and improving wellbeing (Nicholls et al., 2009). Guides to using SROI advocate for stakeholder involvement to establish the outcomes of importance; the monetary valuation of all outcomes; and the elimination of those aspects of change that ‘would have happened naturally’ (Nicholls et al., 2009).

There remains some ambiguity regarding what exactly differentiates ROI from SROI. Some definitions state ROI accounts only for value derived from market prices (Hamelmann et al., 2017), however examples of ROI in the public health literature include the monetary valuation of health outcomes (Masters et al., 2017). The line differentiating the two methods may be drawn at the perspective; ROI is used for evaluating programmes from a health care sector perspective, SROI is used for evaluating programmes from a societal perspective.

Social return on investment has been described as a useful tool for evaluating complex PHIs incorporating a variety of levels of implementation and outcomes (Hamelmann et al., 2017, Rauscher et al., 2012). It is this approach that allows it to steer cross-sectoral investment decisions (Hamelmann et al., 2017).

However, SROI (and ROI) in practice fail to explicitly account for a fundamental concept in economic evaluation: opportunity cost. If resources are to be allocated efficiently, then any economic evaluation must account for the benefits foregone. An additional limitation of SROI is the lack of an explicit policy or decision threshold, albeit a policy threshold of greater than £1 per £1 spent could be used to indicate a return greater than the investment. In the same vein as ROI, there is a lack of explicit information for decision makers regarding what decisions should be made with the results of SROI and how to make comparisons with SROI of alternative programmes.

Finally, there does not appear to be an explicit and consistent approach to valuing benefits incorporated in SROI. A wide range of valuation methods appear to be used such as revealed preferences, stated preferences (e.g., contingent valuation such as WTP) and market prices. A lack of consistency also exists with respect to valuing QALYs gained, some value at £70,000 as per Department of Health calculations [7] (HM Treasury, 2024) and some at £20,000 as per NICE guidelines (National Institute for Health Care Excellence, 2022), albeit NICE's policy threshold is a threshold and not a valuation It is in this respect that SROI, although closely aligned to CBA, is not

[7] The value of £60,000 originates from the Department for Transport's research on the value to prevent a fatality (VPF). The research elicited the value of preventing a fatality and calculated the average loss of QALYs due to deaths from road accidents. This resulted in an estimated WTP to be approximately £60,000 per QALY.

classified as a truly welfarist approach to economic evaluation as value is not entirely based on an individual's welfare.

1.5 Challenges in the economic evaluation of early childhood interventions

Evaluating early years interventions (or any healthcare programme) depends simply on the expected benefits accrued at a population level; the costs borne by the payer; and the opportunity cost of allocating resources to that programme. However, in the case of evaluating early years interventions, each of these individual components has the potential to pose substantive challenges.

A number of contributions to the literature have identified challenges when moving beyond the pharmaceutical paradigm to consider the application of methods of economic evaluation to PHIs. Weatherly et al. identified the attribution of effects; measuring and valuing outcomes; identifying intersectoral costs and consequences; and incorporating equity considerations as examples of such challenges (Weatherly et al., 2009). Additional challenges have been identified as the requirement for decision analytic modelling to capture complex relationships and challenges around the generalisability of the often complex and context-dependent evidence (Edwards and McIntosh, 2019).

All of these challenges exist in the context of evaluating early years interventions, however there are areas that require particular consideration over and above those present for general PHIs. Specific challenges relating to evaluating early years interventions have previously been described (Petrou and Gray, 2005) but are outlined below.

1.5.1 Valuing benefits

As described in Section 1.3, valuing the benefits of a health intervention hinges on normative decisions. The predominant approach to decision making in many countries including the UK takes an extra-welfarist health maximising perspective. This relies on QALYs as the unit of health for the purpose of evaluation (National Institute for Health Care Excellence, 2022). However, recent updates to the NICE methods guide have allowed a broadening of the evaluate space to consider approaches such as CBA to account for the specific requirements of PHIs (National Institute for Health Care Excellence, 2022). Deciding on a comprehensive assessment of the true value of a programme hinges on valuing health and non-health benefits to the infant as well as valuing spillover effects on the family.

1.5.2.1 Health benefits

The QALY is a composite measure of health combining length of life and quality of life. The health-related quality of life (HRQL) aspect is captured through patient- or individual-reported health states which are valued using a specific value set. The use of QALYs to capture health benefits fundamentally relies on the notion that '*a QALY is a QALY is a QALY*'. That is, all QALYs are equal and amount to the same quantity of health regardless of the characteristics of the recipient. The use of such a composite measure of health allows comparisons of alternative health interventions irrespective of disease area as well as the consideration of the opportunity cost across the entire health care system. Funding decisions therefore assume a QALY generated as a result of an early years intervention is equivalent to a QALY generated for a programme targeted at those over 80 years old, for instance. This

comparability assumption is fundamental to efficiency and equity of resource allocation. However, Devlin and colleagues (Devlin et al., 2020) provide a framework describing the potential for differences in child and adult QALYs, which tests the assumption of comparability. The framework centres around several key issues.

First, measuring and valuing HRQL. This has the potential to change depending on who is reporting the experienced health i.e., is it the child themselves or a family member/caregiver reporting on behalf of the child? The results may also be impacted by the different valuation methods used and the characteristics of those generating the value set, i.e., is it adults or children.[8] Kwon and colleagues (Kwon et al., 2022) present an overview of the valuation methods used for preference-based measures of child health-related quality of life (HRQL). Despite the existence of valuation methods for child and adolescent populations, guidance on their use in the NICE reference case is limited (National Institute for Health Care Excellence, 2022). Second, the framework highlights challenges around combining elicited utility values with length of life to generate QALYs. In particular, the potential challenges when switching between QALYs estimated and valued using child-specific methods to adult methods when extrapolating QALY gains in the future (Petrou, 2022). Third, the framework raises the question of whether decision makers should value QALYs generated for early life interventions over those for adults. This reflects evidence

[8] The measurement of HRQL is achieved through a number of methods. These are generally classified as directly elicited preference measures (e.g., visual-analogue scale, time trade-off and standard gamble); generic preference-based measures (e.g., EuroQol (EQ)-5D, Short Form 6D (FS-6D) and Health Utilities Index (HUI)); and condition-specific measures (e.g., Asthma Quality of Life Questionnaire). Generic preference-based measures are commonly encountered in economic evaluation due to their routine use in clinical trials. The results of these measures come in the form of a utility score, often between 1 and 0 and are directly obtained from those patients or individuals involved. The generated score is then valued according to a value set obtained from the general public. In elicited preference measures, value is directly elicited. For an overview of HRQL methods used in generating QALYs, see Whitehead and Ali (Whitehead and Ali, 2010b).

suggesting public preference for QALYs gained in infancy and childhood over those gained in later life (Lancsar et al., 2020, Kwon et al., 2022).

If they are to be valued differently, this should be achieved explicitly and transparently in decision-making. The health opportunity cost is the benchmark of value in health decision-making as it reveals the benefits that could have been achieved had the money been spent on alternative interventions.

Equity weights or ‘modifiers’ have been recommended for use in the NICE methods guide to reflect value judgments to attempt to capture those aspects not included in the QALY (National Institute for Health Care Excellence, 2022). In theory, modifiers could be used to modify QALYs generated from early years interventions. To ensure there are no negative impacts to population health (because of implementing programmes that are not cost-effective), equity weights would need to be applied to health benefits and the health foregone, resulting in a new policy threshold with which to assess value for money (Paulden, 2021). This approach, although theoretical, could apply to any subgroup that patients could be assigned to including individual or group-based characteristics. The theory indicates the development of such a weighting approach would be challenging; however, an alternative approach could be to adjust the standard threshold used to estimate cost-effectiveness to ensure positive net health population benefit.

1.5.2.2 Non-health benefits

Early years interventions may have social value beyond just value to the health care system. The fundamental purpose of these programmes may not just be to improve

health but to improve child development, educational attainment, crime avoidance, labour market potential and so on. The purpose of the programme may be even broader still. For example, to improve *wellbeing*, or to lean on Sen's description of capability and wellbeing: to allow a child to have the freedom and capability to flourish in life and participate in the community (Sen, 1993). This may be part of the intrinsic *value* of a health intervention. Deciding on what does and doesn't contribute to the value of a programme is one thing but challenges persist in incorporating these aspects into economic evidence.

From the perspective of economic evaluation, the definition and agreement from stakeholders and decision makers as to what an explicit social welfare function should look like (i.e., a full and explicit function that includes everything that is socially valuable) would be a tremendous challenge and one that may not even be possible given inevitable conflicting claims on what denotes social value (Walker et al., 2019). Short of defining the full social value of a programme, it remains apparent that valuing early years interventions solely in terms of the health outcomes may underestimate the value for money. Value must factor in the costs of the programme as well as the opportunity cost of the programme. Whether the opportunity costs fall on the health sector or results in broader benefits foregone (due to health budget expansion) these opportunity costs should be included in decision making (Sculpher et al., 2017). Questions regarding the nature of the budget raises further challenges in identifying which sector should and indeed does pay for early years interventions given the potential for benefits to be felt beyond health. This will be discussed further in Section 1.5.

There is a lack of agreement as to how to capture benefits beyond just health. The importance of ensuring these benefits are captured is critical to ensure the true reflection of value for money and ultimately the efficient allocation of resources (Jönsson, 2009). Allocation could be based on programmes that impact on the social determinants of health (Marmot et al., 2008), which would require valuation of health and non-health of children and infants throughout the life course (Halfon and Hochstein, 2002, Hertzman and Power, 2004, Cunha and Heckman, 2007, Marmot, 2017).

1.5.2.3 Family benefits

While the focus of early years interventions may typically be the child, there may be benefits that extend to siblings, parents, other relatives and friends (Brouwer et al., 2010). These family effects are thought to be generated as a result of the improvement in health and wellbeing of the child (Brouwer et al., 2010).

Standard methods of economic evaluation do not consider the potential spillover effects. A number of frameworks have been proposed to consider measuring and incorporating such effects. Basu and Meltzer consider the direct and indirect impacts on the welfare of the family (Basu and Meltzer, 2005). Al-Janabi and colleagues' propose a framework, which includes multipliers to capture health spill overs (Al-Janabi et al., 2016). However, despite the existence of these frameworks, there is a lack of standardized methodology regarding their role in decision-making (Lamsal and Zwicker, 2017).

1.5.3 Perspective

The perspective is inherently linked to the breadth of the decision maker's assessment of the social value of the programme. That is, it should be based on the sectors in which the costs and benefits fall. Health technology assessment (HTA) methods, including those recommended in the NICE methods guide (National Institute for Health Care Excellence, 2022), recommend an NHS perspective but this may be deemed too narrow for evaluating early years interventions.

As discussed in Section 1.4.2, there may be considerable value of the programme beyond the health sector. A societal perspective in which the evaluative space is broadened to include social services and other sectors such as education and labour market participation may be deemed more appropriate. Methods for incorporating the totality of the benefits have been discussed in Section 1.4, however one aspect that was not discussed in detail yet remains pertinent to the challenge of broadening the perspective is to consider the funding. It may be appropriate to assume an early years intervention is funded from the public health budget, however if considerable benefits are to be felt in the education sector it may be appropriate to consider funding from both public health and education budgets (Claxton et al., 2007). It has been argued that restricting the perspective will lead to suboptimal resource allocation decisions (Jönsson, 2009). Consideration should be given to the normative approach adopted for the purpose of economic evaluation and the implications this has on budgets: CBA assumes budgets are flexible, efficient and reflect societal preferences, CEA assumes budgets are set based on political considerations. It can be argued the latter is more suitable for decision making in the UK.

1.5.4 Time horizon

The time horizon of any evaluation should be sufficiently long to cover the difference between costs and benefits of the alternative programmes. In the case of early years interventions, this may mean extrapolated time horizons should cover the life course to fully reflect a programme's benefits and costs in terms of health and also education and labour market, for example. Yet, directly observed causal impacts of a programme on these outcomes are unlikely to exist due to the extended time horizon, thus necessitating results to be extrapolated (Drummond et al., 2015).

Extended time horizons have a number of implications for uncertainty, health equity impacts and the discount rate. The extended time horizons render results more uncertain due to the nature of extrapolated (or 'modelled') results. The approach of fitting parametric models to extrapolate patient level data from clinical trials for HTA decision making is well established (Latimer, 2011). But given the long-time horizons and the potential impact of behaviour on the future, it cannot be assumed that extrapolation would follow a parametric distribution. The potential for feedback loops based on changes in behaviour not just in the individual but in their social environment could also impact long term outcomes. This creates challenges in the decision analytic modelling approach used for generating economic evidence (see Section 1.4.6).

Extended time horizons can also impact the effect and cost-effectiveness of early years intervention through equity impacts. That is, the overall effect size of the programme may be diluted through impacts on the socioeconomic distribution of programme effects, which may be subject to poor uptake and high attrition rates over

extended time horizons (Petrou and Kupek, 2005, Petrou and Gray, 2005). More general challenges relating to uncertainty and equity impacts of early years interventions are discussed separately in Section 1.4.6 and Section 1.4.4, respectively.

1.5.*5* Discounting

Related to the extended time horizons is the relationship with discounting future costs and benefits (Brouwer et al., 2005). There is a rich literature discussing the discount rate used in HTA decision making including those recommended by NICE (Attema et al., 2018, Cairns, 1992, Gravelle and Smith, 2001, Gravelle et al., 2007, Paulden et al., 2017, Claxton et al., 2006). Claxton and colleagues summarised the debate and the necessary questions when deciding on an appropriate discount rate, to consider whether a welfarist or extra-welfarist approach is being considered; whether the budget is fixed; and whether the opportunity cost and consumption value of health are likely to change over time (Claxton et al., 2011). Given the extended time horizons of evaluations of early years interventions, each of these components may need specific consideration.

The NICE methods guide outlines costs and benefits should be equally discounted at 3.5% to estimate present value, except in certain circumstances in which differential discounting is permitted (National Institute for Health Care Excellence, 2022). The discount rate can play a significant role in the economic evaluation of early years interventions. By having a high discount rate on costs and benefits, those benefits

felt in the future will be heavily discounted meaning less value is placed on those potential benefits. Further, it is likely that the costs of implementing the programme will be upfront and therefore the impact of discounting will be limited, meaning there will be disproportionately high discounting of benefits relative to the costs. The NICE methods guide allows a discount rate of 1.5% to be applied in circumstances where benefits will be felt in the future (defined as over 30 years) but is reserved for interventions in which patients would 'otherwise die or have a severely impaired life' without intervention (National Institute for Health Care Excellence, 2022). Preventative programmes with benefits expected to be borne in the future, of which early years interventions are perhaps an exemplar, would be heavily influenced by using a 1.5% discount rate on costs but likely do not satisfy the criteria outlined in the NICE methods guide. Evaluations of early years interventions would have to consider the most appropriate discount rate, which can have a considerable impact on the results (Attema et al., 2018).

1.5.6 Equity

Standard methods of economic evaluation, in particular 'conventional' CEA used for decision making in the UK, deals with efficiency i.e., maximising health or other benefits for the available resources (Drummond et al., 2015). This fails to consider those individuals or groups that gain the health (or other benefits) and those that bear the costs; in other words, the social distribution of the impacts of the health intervention. For early years interventions, reducing unfair (or 'inequitable') health inequalities may be a primary objective of the programme (Powell, 2019). Reducing avoidable health inequities starts in early life and can have impacts throughout the life course. As summarised by Marmot: '*High quality early child development sets the*

agenda for everything that follows: better educational performance, better job, higher income, better living conditions and, as a result, better health'. (Marmot, 2017) Yet, the introduction of a programme can increase health inequalities as socially advantaged individuals are better able to seek, co-invest and benefit from them (Cookson et al., 2021a).

Identifying those health interventions that minimise inequitable health inequalities may be important for decision making purposes and would not be considered in conventional economic evaluation. Defining what is equitable is no mean feat. As described by Cookson (Cookson, 2017) explicitly defining the social inequality reduction objective can prevent radically different measures of equity. The three key questions raised by Cookson regarding the objective are: i) Equality of what? ii) Equality of whom? iii) How is equality measured? However, it may be challenging for decision makers to agree on what the equity objective of early years interventions are.

The efficiency impacts of the programme may need to be included alongside the equity impacts and potentially traded-off if programmes are inefficient and simultaneously improve inequalities or vice versa (Williams and Cookson, 2006). Defining the efficiency impacts may prove challenging for early years interventions as although the full costs and benefits of the programme throughout the life course should be included in the decision, local public health decision-makers (of which early years interventions fall under their funding consideration) may have short 3-5 year budget cycles and may be concerned with cost savings within those budgets cycles (see Section 1.5).

A number of general approaches have been outlined to allow the incorporation of equity concerns in decision making. (Cookson et al., 2009) Recently several methodological contributions to the economic evaluation literature have included the explicit incorporation of such equity considerations, including distributional cost-effectiveness analysis (DCEA) and extended cost-effectiveness analysis (ECEA) (Cookson et al., 2017a). These methods have been used in healthcare decision making, however given uncertainty in how to value the benefits of early childhood interventions (see Section 1.4.2), the non-health benefits may require incorporation and there may be challenges in achieving this.

1.5.7 Modelling

Decision-making cannot rely on clinical trials alone. This is particularly true for early childhood interventions given the challenges of conducting a trial that spans the length of the participants life to understand effectiveness and value for money. Further, even if such a trial was feasible the results will likely be outdated and answering a question that is no longer relevant to the population. Decision analytic modelling provides an explicit analytical framework for the synthesis of evidence and for use in decision-making. It does this through the inclusion of all the relevant evidence of the full range of options and provides a quantification of uncertainty (Briggs et al., 2006).

There is an extensive literature of the array of modelling approaches for health economic evaluation (Briggs et al., 2006, Drummond et al., 2015, Karnon, 2003, Barton et al., 2004). These detail the many strengths and limitations of individual approaches. This brief overview therefore intends to introduce some of these

modelling approaches and outline challenges specific to early childhood interventions.

The literature divides modelling approaches into two categories: cohort models and simulation models. Cohort models characterise the 'average' patient thereby assuming patients share the same characteristics. This may be problematic for modelling early childhood interventions given the importance of incorporating equity considerations. By estimating the average, heterogeneity in costs and outcomes according to individual characteristics (e.g., ethnicity or income) will be ignored. Capturing such heterogeneity is important in minimising uncertainty and to evaluate distributional outcomes and assess equity impacts.

Cohort models are typically separated into decision trees and Markov models. Decision trees are a simple form of decision model which provide expected costs and outcomes weighted by pathway probabilities,[9] the methods of which are discussed in detail elsewhere (Briggs et al., 2006, Drummond et al., 2015). Decision trees are generally inflexible when it comes to incorporating time. They do not differentiate between when events occur in time; have problems with recurring events; and are generally not equipped to attribute events to certain time points impacting the discounting of health and outcomes. This may be problematic when considering early years interventions given the extended time horizons over which events may occur. Markov models are structured as a set of mutually exclusive

[9] Pathways are based on mutually exclusive sequences of events and these pathways form the branches of the tree. Branches are made up of any number of decision nodes and chance nodes and where there are sequential chance nodes in a single pathway, pathway probabilities are calculated as the conditional probability i.e., the probability of the second event happening at the second chance node given the first event happened at the first chance node.

disease states and transitions among states occurs over a number of cycles or discrete time periods. A potentially important limitation of Markov models is that they are 'memoryless'.[10] That is, all individuals in a specific state are considered homogenous, regardless of the time spent in that state or previous states. This again may not be appropriate for modelling early years interventions as it may be important to consider how outcomes differ for those that have spent a long time in poor health, education or derivation compared to a shorter time.

Simulation modelling differs from cohort modelling as rather than modelling an entire homogenous cohort, individuals are tracked though the model allowing the estimation of an individual patient history and the resulting accumulated costs and HRQoL through time. By allowing time dependency and heterogeneity (e.g., in baseline characteristics, prognosis, risks of events amongst other things) simulation models may be more appropriate for modelling early years interventions. This additional flexibility, however, comes with additional data requirements.

There are a number of specific techniques that fall under the umbrella of simulation modelling. Discrete event simulation (DES) allows the modelling of the time spent in certain states by considering the time to the next event. This requires the specification of the 'rules' for the individuals themselves. Agent-based modelling (ABM) allows the assessment of interactions and spatial relationships. It considers the inputs and outputs (e.g., costs and outcomes) for individuals but does so by specifying the rules of the 'system' rather than the rules for individuals. It can consider dynamic feedback loops which can be used to test hypotheses; however

[10] The Markov assumption can be relaxed through adding in additional 'tunnel states'. This is known as a semi-Markov process.

they are considered the most complex of the simulation models and required the most complexity of data. Finally, microsimulation, although loosely defined often refers to something that is neither DES or ABM and is based on probability of moving from one health state to another. It is considered a good option for incorporating individual characteristics and generating distributional inputs and outcomes.

Finally, systems dynamic modelling (SDM) is a cohort-style model but is often considered distinct from ‘traditional’ cohort approaches. It relies on differential equations based on stocks and flows, which map out causal loops. SDM considers the entire complex system and tends to ignore the fine details, rather focusing on the interaction of the system as a whole. This approach has its strengths in considered the broader social determinants of health but it is difficult for looking at individual patient groups. Decisions around which approach to modelling early years interventions will need to consider the strengths and weaknesses of the various approaches and weigh these up with those aspects of value that are considered important to capture in the evidence.

1.6 Early childhood PHI decision-making

Health economic evidence forms an integral part of resource allocation decisions. The generation of the evidence is subject to many positive and normative challenges as outlined in Section 1.5. Challenges faced by those making national-level decisions on whether a health technology is value for money, by bodies such as NICE in England and Wales, may face different requirements of the methods and evidence compared to those making local-level public health decisions. Resource allocation decisions at a national level are transparent with a clearly defined value

assessment framework (National Institute for Health Care Excellence, 2022). At a local level, where public health resources are allocated, decision-maker's assessments of value are less transparent and face policy-objective pressures and budgetary restrictions (Wenzel and Robertson, 2019). Recent literature describes the disconnect between the nature and use of economic evidence when comparing the national and local decision-makers (Hinde et al., 2022, Howdon et al., 2022). Studies by Eddama and Coast (Eddama and Coast, 2008, Eddama and Coast, 2009) have shown the limited use of economic evaluation evidence at a local decision-making level which may be down to political, cultural and methodological factors.

A tool provided by Public Health England (now replaced by UK Health Security Agency and Office for Health Improvement and Disparities) brought together the health economic literature which was commonly used by Public Health England (Public Health England, 2019a). It described a number of interventions or policies for all age ranges alongside the results of the economic evaluation. Limited evidence was identified in the early childhood category. It was therefore considered pertinent to identify the nature of the health economic evidence available to public health decision-makers. A systematic review was conducted to identify the breadth of the economic evaluation methods and approaches used in the literature as well as the assessment of value for money of early childhood public health interventions conducted in a UK context available in the literature. This is described in Chapter 2.

Chapter 2: Economic evaluations of UK-based early childhood PHIs: A systematic literature review

A condensed version of this Chapter has been published in the *British Medical Bulletin*:

> **Murphy P**, Hinde S, Fulbright H, Padgett L, Richardson G. Methods of assessing value for money of UK-based early childhood PHIs: a systematic literature review. *British Medical Bulletin*. 2023 Mar;145(1):88-109.

The overview of the literature presented in the previous chapter demonstrated the vast range of methods and approaches to economic evaluation available in the literature. The current chapter identifies the evidence base regarding UK-based early childhood PHIs, and considers the methods and results of the evaluations.

2.1 Introduction

2.1.1 Background

There is a strong economic case for prevention in early childhood (Marmot, 2010, OECD and Organization, 2015). Yet, it is important that decisions to fund early childhood PHIs are based on systematic and robust assessments of clinical and economic evidence (Drummond et al., 2015). Chapter 1 outlined a number of the challenges of their evaluation as the concept of health may be broadened to consider fairness and the social determinants of health (Marmot et al., 2008). Given this complexity, there remains limited agreement on the most appropriate economic evaluation methods (Mathes et al., 2017). Methods are becoming more established (National Institute for Health Care Excellence, 2022, Edwards and McIntosh, 2019) but are far from reaching a consensus akin to those observed in health technology assessment. The lack of established methods and the complexity may well play a role in the challenges of decision making around early childhood PHIs.

Recent evidence presented in a House of Commons Briefing (Powell et al., 2021) highlighted the gap between the evidence available in the peer-reviewed literature and the decisions made regarding early childhood interventions.

Questions have previously been raised of the appropriateness of the methods used to capture costs and benefits of large-scale early childhood interventions (Rutter, 2006).

2.1.2. Why is it important to do this systematic literature review?

The UK government's Office for Health Improvement and Disparities (OHID) launched in October 2021 and has outlined its aims to reduce unacceptable health disparities across the country by tackling health conditions before they develop (Department of Health and Social Care, 2021). Early childhood remains a crucial period for achieving such goals. As identified in Sir Michael Marmot's seminal contributions, inequalities in early life have lifelong consequences and interventions targeting the early life are most effective at disrupting such health inequalities (Marmot, 2010, Marmot et al., 2020). Targeting this period of life has been highlighted further in the UK Government's *The Best Start for Life* report (HM Government, 2021) which outlines the importance of identifying the best and most cost-effective interventions. Given the lack of consensus regarding methods and approaches, this review aims to collate the breadth of the existing evidence; outline the methods and approaches; and critically appraise the evidence. More broadly this systematic review of economic evaluation will aim to summarise the available evidence in a way that is meaningful for decision-makers; to help justify and contextualise the evidence used in decision-making; to determine if the published evidence is sufficiently reliable that further analysis is not required; and to reduce error and bias in the abstraction and adjustment of results.

It is hoped this will help researchers and policy-makers in the UK and elsewhere to minimize opportunity costs (and the associated potential for sub-optimal resource allocation) from decisions based on an incomplete or misleading evidence base. For individual researchers interested in early childhood public health, a systematic review of health economic evaluations may help inform the development of a new decision model, identify the most relevant studies to inform a particular decision in a jurisdiction, and identify the key economic trade-offs implicit in a given intervention. Furthermore, well-reported systematic reviews of health economic evaluations play a crucial role in empowering patients and the public to make informed decisions, understand healthcare value, and participate in shaping healthcare policy.

2.1.3 Objectives of the systematic review

With the aim of trying to shed light on these issues, this systematic review was conducted to collate the available evidence regarding the economic evaluation of early childhood PHIs in the UK. Specific objectives include:

- To systematically identify the breadth of existing economic evaluation evidence of early childhood public health interventions conducted in a UK context
- To summarise the methodological approaches and the evaluative frameworks used in the generation of economic evidence
- To assess what the recommendation was for the specific interventions identified and/or if they were deemed value for money
- To critically appraise the quality of the evidence

- To help inform discussions around the determinations of value for money for those generating evidence or making decision regarding similar interventions

The presented systematic review will also inform the foundations for the subsequent chapters in this PhD thesis.

2.2. Methods

2.2.1. Overall Approach

The protocol for the systematic literature review was written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines (Shamseer et al., 2015) and was registered with PROSPERO, the International Prospective Register of Systematic Reviews (CRD42021270751). The systematic review was conducted and reported in accordance with PRISMA guidelines (Moher et al., 2009) and the Cochrane Handbook for Systematic Reviews (Higgins et al., 2023).

2.2.2. Types of Economic Evaluations

Given the anticipated breadth of economic studies in the literature, the boundaries of the types of studies to be included were set to limit the evidence to those in which costs and outcomes were combined into a single evaluative framework. This, in part, aligns with the distinction between full and partial economic evaluations (Rabarison et al., 2015). Full economic evaluation is considered to be the comparative evaluation of distinct courses of action, which includes both costs and outcomes,

combined into a single evaluate framework (Drummond et al., 2015). Examples of such frameworks include cost-effectiveness analysis (CEA) (which will be referred to as ‘non-QALY-based CEAs’), cost-utility analysis (CUA) (which will be referred to as ‘QALY-based CEAs’), cost-benefit analysis (CBA), cost-consequence analysis (CCA), and cost minimization analysis (CMA). Partial economic evaluation is considered to be the evaluation of a single intervention or course of action without comparison to the relevant alternatives and does not link costs to outcomes (Drummond et al., 2015, Rabarison et al., 2015). Under the umbrella of partial economic evaluations, frameworks can be separated into those that do and do not necessitate a link between costs and outcomes, and those that do and do not necessitate a comparative evaluation. Social return on investment (SROI) and return on investment (ROI) are examples of frameworks in which costs and outcomes are combined but a comparative evaluation of multiple interventions is not mandatory. As such, they may be considered ‘performance measures’. Despite not including a comparative analysis they were included in this systematic review, owing to their inclusion in Public Health England’s Health Economic Evidence Resource (HEER) tool (Public Health England, 2019a).

Other partial economic evaluation frameworks include: comparative evaluations in which only costs are included, for example cost analysis; non-comparative evaluations in which only costs are included, for example cost-of-illness studies; comparative evaluations in which only outcomes are included, for example efficacy analysis; and non-comparative outcomes in which only outcomes are include, for example outcomes descriptions. The distinction between the various frameworks can be seen in the matrix presented in Table 1. The shaded cells in the matrix highlight

those economic evaluation frameworks in which costs and outcomes are combined and therefore those included in the presented review. All other methods of economic evaluation are excluded. For a discussion of the aforementioned types of economic evaluation and the underlying principles informing each type, see Section 1.1.

Table 1 Description of economic evaluation frameworks

	Costs and outcomes included	**Costs included**	**Outcomes included**
Comparative evaluation necessary	Non-QALY-based CEA QALY-based CEAs CBA CCA CMA	Cost analysis	Efficacy analysis
Comparative evaluation not necessary	ROI SROI Cost-outcome description	Cost-of-illness studies	Outcomes description

Abbreviations: CBA, cost benefit analysis; CCA, cost-consequence analysis; CEA, cost-effectiveness analysis; CMA, cost-minimisation analysis; QALY, quality-adjusted life year; ROI, return on investment; SROI, social return on investment

It is worth noting that non-QALY-based CEAs, QALY-based CEAs, CBA and CCA are all frameworks that are recommended as being applicable to the economic evaluation of PHIs in NICE's public health guidance. (Edwards and McIntosh, 2019) Cost minimisation analysis has largely been criticised as inappropriate for the separate analysis of costs and effects and failing to consider the uncertainty around the point estimate of the effects (Briggs and O'Brien, 2001). As a result, it does not feature in NICE guidance. However, as the presented review is concerned with methods and approaches used when generating economic evidence, CMA were included as the use of such methods is considered a relevant finding. In addition, ROI and SROI do not feature in NICE's public health guidance but they are included

as a recent systematic review identified numerous ROI studies present in the public health literature (Masters et al., 2017).

Given economic evaluation is not a research method rather it is a framework, evidence is required to inform the evaluation. The presented review therefore includes economic evaluations conducted alongside experimental studies, including randomised controlled trials and studies with a quasi-experimental design. In addition, those based on decision analytic models are also included.

2.3.4. Population

The age group of interest was birth to five years to align with those interventions targeting the important pre-school years that play a critical role in emotional and physical health, social skills, and cognitive-linguistic capacities (Center on the Developing Child, 2010). The presented review therefore included economic evaluations of interventions for infants and children with a mean age of five years or under at baseline. Economic evaluations of interventions that included ages beyond five years of age were considered for inclusion if the economic evaluation explicitly included a subgroup analysis and separate decision/recommendation for infants and/or children of five years or under. Those aimed at pregnant women were excluded. Those evaluating interventions in infants, children and family members with existing medical conditions were also excluded. This was to help differentiate between PHIs which stress the prevention of disease, and therapeutic interventions which are for treatment, mitigation or postponing the effects of disease once it is

underway (Smith et al., 2015). Within these excluded interventions, were those for post-natal depression and management strategies for the care of preterm infants.

2.3.5. Interventions

The distinction of what defines a public health intervention does require definition as it is important for the scope of the presented review. Broadly, public health is defined as '*the science and art of preventing disease, prolonging life and promoting health through the organized efforts of society'* (Acheson, 1998). Public health seeks to reduce health inequalities and promote and protect health by targeting those at increased risk of ill health. PHIs are therefore any active measure or policy enacted to improve health on a population level delivered in a range of settings by various personnel. Records were included if they reported economic evaluations of public health interventions in the UK. Public health was defined using terms that broadly reflected interventions of health improvement and included terms for wider social determinants of health (see search strategy in the appendix).

2.3.5.1. Intervention

The broad and complex nature of PHIs (Edwards and McIntosh, 2019) meant that precisely capturing the types of interventions to be included presented challenges. Broadly, interventions with the aim of health improvement were considered for inclusion. However, the complex interplay between health, development, education and socioeconomic status (Gibb et al., 2012, Shonkoff, 2012, McCrory et al., 2010, Shonkoff et al., 2009, Blackburn et al., 2013, Grossman, 1972) meant that health improvement may be the result of an intervention that targets child development, for

example. To avoid missing these studies, this review included interventions with the rationale of improving a number of health or health-adjacent outcomes, including wellness; welfare; lifestyle; development; diet and nutrition; oral health; safety; immunity; weight; and exercise. As public health is concerned with the prevention of ill health and reducing health inequalities, health protection programmes in the form of screening and vaccination programmes for eligible infants and children were included. Clinical guidelines and disease management guidelines were excluded.

2.3.5.2. Setting

Interventions delivered in a number of settings including, the community, home, general practice, and childcare settings were included.

2.3.5.3. Comparator

There were no restrictions on the type of comparator used in the evaluation, meaning non-intervention control groups, usual care, and those head-to-head comparisons comparing active interventions were all included. Further, as described above, a number of partial economic evaluations were included meaning economic evaluations in which the intervention has no comparator were also included.

2.3.5.4. Intervention personnel

PHIs may be delivered by a wide range of personnel, including community health care workers, primary care physicians, researchers, public health practitioners, and

nursery/pre-school workers. Therefore, there were no restrictions on the personnel delivering the interventions.

2.3.6. Outcome Measures

As described above, a number of different study types were included. The resulting outcome measures vary according to the common numeraire adopted by the specific economic evaluation framework and are used to evaluate an intervention's value. Examples include: the quality adjusted life year (QALY) and number of infants diagnosed with a specific condition. The former is used in QALY-based CEA and the latter in non QALY-based CEA. In addition, monetary outcomes are considered as this forms the maximand in CBA, ROI and SROI. As a result, there were no restrictions on the outcomes included.

2.3.7. Location and perspective

Only economic evaluations in which the perspective of the evaluation was located in the UK were included. This was to identify the economic evidence relevant to UK public health decision makers. Given the numerous positive and normative reasons why results of economic evaluations may differ across jurisdictions (Drummond et al., 2015) focussing solely on the UK avoids the potential for heterogeneity across the methods identified.

The perspective defines the boundaries of the economic evaluation. It is used to represent the point of view of the decision maker therefore limiting it to include only those costs and outcomes relevant to the decision maker (Drummond et al., 2015,

Edwards and McIntosh, 2019). Examples of included perspectives include the NHS, personal social services, societal and local government (Drummond et al., 2015, National Institute for Health Care Excellence, 2022). There were no restrictions on the location of the experimental studies informing the UK-focussed economic evaluation.

2.3.8. Additional Context

In order to produce a contemporary description of the approaches used, studies published prior to the year 2000 were excluded. There were no restrictions on the language in which the study was published. Systematic reviews and scoping reviews identified in the database searches were not included in the evidence synthesis but were selected and checked for relevant economic evaluations. Within the reviews, grey literature was considered for inclusion as it was deemed to be reported in the literature. A formal search of the grey literature databases was not conducted owing to time limitations. A summary of the eligibility criteria can be seen in Table 2.

Table 2 Summary of eligibility criteria

	Inclusion	***Exclusion***
Population	All children and infants of 5 years and under at baseline	Children over 5 years and pregnant women
Intervention	Any public health intervention	Pharmaceutical interventions, diagnostics, medical technologies, and devices.
Comparator	Any or no comparator	n/a
Outcome	Any outcome resulting from the economic evaluation of the intervention	No outcome recorded

Study design	Any full economic evaluation and partial economic evaluations in which costs and outcomes are included: QALY-based CEAs Non-QALY-based CEAs Cost-benefit analysis Cost-minimisation analysis Cost-consequence analysis Return on investment Social return on investment	Partial economic evaluations which only consider costs or outcomes: Cost analysis Cost-of-illness study Efficacy analysis Outcomes description
Country	United Kingdom	Non-UK countries
Language	All languages	n/a
Year of publication	2000 - present	Pre 2000
Publication type	Articles published in peer-reviewed journals and recorded in an online bibliographic database. Articles included in systematic reviews, scoping reviews and literature reviews that are in the published literature.	Conference abstracts

2.4. Search methods for identification of studies

2.4.1 Electronic searches

A search strategy was developed in Ovid MEDLINE in conjunction with an Information Specialist and included input from the review team. PICO (described above) was used to define the concepts of the topic and the structure of the searches. The strategy included terms for the population: children aged 0-5; and terms that broadly reflected the interventions targeting health and development improvement, which was a difficult area to capture precisely. Each concept used a choice of subject headings and free-text terms as this reflects best practice in information retrieval. The MEDLINE search also used an economics search filter and a geographical filter to limit to the UK. No language restrictions were applied to the

searches, but animal studies were removed. A date limit of 2000 onwards was applied to the searches.

The following sources were searched between August 16 and 23, 2021:

1. MEDLINE(R) ALL (Ovid): 1946 to August 13, 2021.
2. Embase (Ovid): 1974 to August 17, 2021.
3. Econlit (Ovid): 1886 to August 5, 2021.
4. Health Management Information Consortium (HMIC) (Ovid): 1979 to July 2021.
5. Cochrane Central Register of Controlled Trials (Wiley): 2021, Issue 8 in the Cochrane Library.
6. Cochrane Database of Systematic Reviews (Wiley): 2021, Issue 8 in the Cochrane Library.
7. Health Technology Assessment (CRD): Inception to March 2018.
8. Economic Evaluations Database (CRD): Inception to March 31, 2015;
9. Science Citation Index Expanded (Web of Science): 1900 to August 16, 2021.

All of EndNote 20's default settings for deduplication were used to deduplicate the records, with those marked as duplicates checked by eye. Following this, various combinations of EndNote fields were compared against each other in a further manual process of deduplication, with records marked as duplicates checked by eye. Details of the full search strategies are contained in Appendix 1.

2.4.2. Searching other resources

Supplementary searches of additional sources were undertaken. This was necessary to compensate for the fact that the intervention was difficult to capture precisely in the search terms. Therefore, reference checking and backwards citation searching of the identified systematic reviews identified through the database search were checked for relevant economic evaluations that were conducted within the time frame and would have been eligible for inclusion had they been picked up in the database search. (Hinde and Spackman, 2015). These searches were conducted on October 15, 2021.

2.5.1. Data collection and analysis

2.5.1.1. Selection of studies

Two review authors (PM and WR) independently conducted title and abstract screening of a random sample of 10% of the retrieved records. A kappa statistic for assessing inter-rater agreement (McHugh, 2012) was calculated to assess the strength of the agreement between the two reviewers for the initial 10%. Upon the achievement of a Kappa statistic of 0.8 or above (which was considered to be 'strong agreement' for the purpose of the presented review), one reviewer (PM) screened the remaining titles and abstracts. Failure to achieve the required kappa statistic meant a further 10% would be screened by both reviewers until the required score was achieved. Reviewers screened 20% (two screening rounds) before the sufficient kappa statistic was achieved. This process was applied at both the title and abstract

screening stage and the full text screening stage. Discrepancies were resolved by discussion between the two review authors.

All titles and abstracts were assessed in duplicate using the web-based screening tool RAYYAN (Ouzzani et al., 2016). For records potentially meeting the inclusion criteria, the full text of the article was retrieved for eligibility screening. Differences in opinion and uncertainty were resolved through a process of discussion.

2.5.2. Data Extraction

This review sought to identify the literature and assess the methodological approaches used in the relevant economic evaluations. The empirical results of the economic evaluations were extracted. A *de novo* data extraction pro-forma was developed as to our knowledge there were no previous systematic reviews with the same aims as the presented review. The extracted information was based on a number of central characteristics of the include studies: general; intervention; economic evaluation; modelling; equity; recommendation; uncertainty; and the empirical results. Further detail is provided below:

1) *General information*: author, year, target population, targeted or universal intervention
2) *Intervention*: intervention, comparator, study design, study location, length of follow up of the study, intervention setting, results of the effectiveness evidence,
3) *Economic evaluation*:

- *General*: evaluative framework, perspective, discount rate, time horizon
- *Costs*: health and non-health resource use and costs, source of the cost data, opportunity cost
- Outcomes: health and non-health outcomes captured, source of the utility measure if QALYs are the health outcome

4) *Modelling*: the presence of decision analytic modelling, model category, model structure
5) *Equity*: Approach to formally incorporate equity consideration in the economic evaluation (defined as the reporting of distributional outcomes of the economic evaluation by a social variable such as socioeconomic position, or the formal incorporation of an equity-informative method of economic evaluation such as distributional cost-effectiveness analysis, extended cost-effectiveness analysis, multicriteria decision analysis, equity-based weighting or SROI), general equity consideration
6) *Recommendation*: recommendation on cost-effectiveness (or value for money), incorporation of cross-sectoral outcomes and equity outcomes in the decision and the approach to trade-off of the alternative outcomes
7) *Characterisation of uncertainty*: exploration of structural and parameter uncertainty, distributions used around parametric extrapolations; use of probabilistic sensitivity analysis, presentation of uncertainty and the influence on the recommendation
8) *Empirical results*: result of the evaluation

The full data extraction template can be found in the appendix. Data extraction was performed by one review author (PM) due to resource limitations but the potential for errors in the extraction and bias in the results should be considered as best practice recommends extraction is conducted by two reviewers (Higgins et al., 2023). Note, extracted costs are inflated to 2023 prices using data from the Office for National Statistics (Office for National Statistics, 2024) to allow comparison.

2.5.3. Critical appraisal of included studies

Critical appraisal of the methodological quality of the included studies was conducted through the use of the Drummond checklist (Drummond et al., 2005). The checklist allows the appraisal of the underlying assumptions and potential biases in the reporting of full and partial economic evaluations. Although relevance of the economic questions, interventions, populations and outcomes being studied are important they were not formally recorded in the systematic review. Study inclusion was not based on the results of quality appraisal or relevance. The checklist used in the review can be found in the appendix.

2.5.4. Synthesis

Quantitative synthesis of the results of economic evaluations is usually considered inappropriate given heterogeneity in populations, the counterfactual, perspectives, health outcomes and costs (Shields and Elvidge, 2020). To address this, a narrative synthesis was used to compile the results of the eligible studies. The narrative approach to synthesis lends itself to grouping of key discussion points identified in the methodological approaches used and the types of interventions evaluated. The

aims of the synthesis are aligned with those of the systematic review in general, which are:

- To systematically identify the breadth of existing economic evaluation evidence of early childhood public health interventions conducted in a UK context
- To summarize the methodological approaches and the evaluative frameworks used in the generation of economic evidence
- To assess what the recommendation was for the specific interventions identified and/or if they were deemed value for money
- To critically appraise the quality of the evidence
- To help inform discussions around the determinations of value for money for those generating evidence or making decision regarding similar interventions

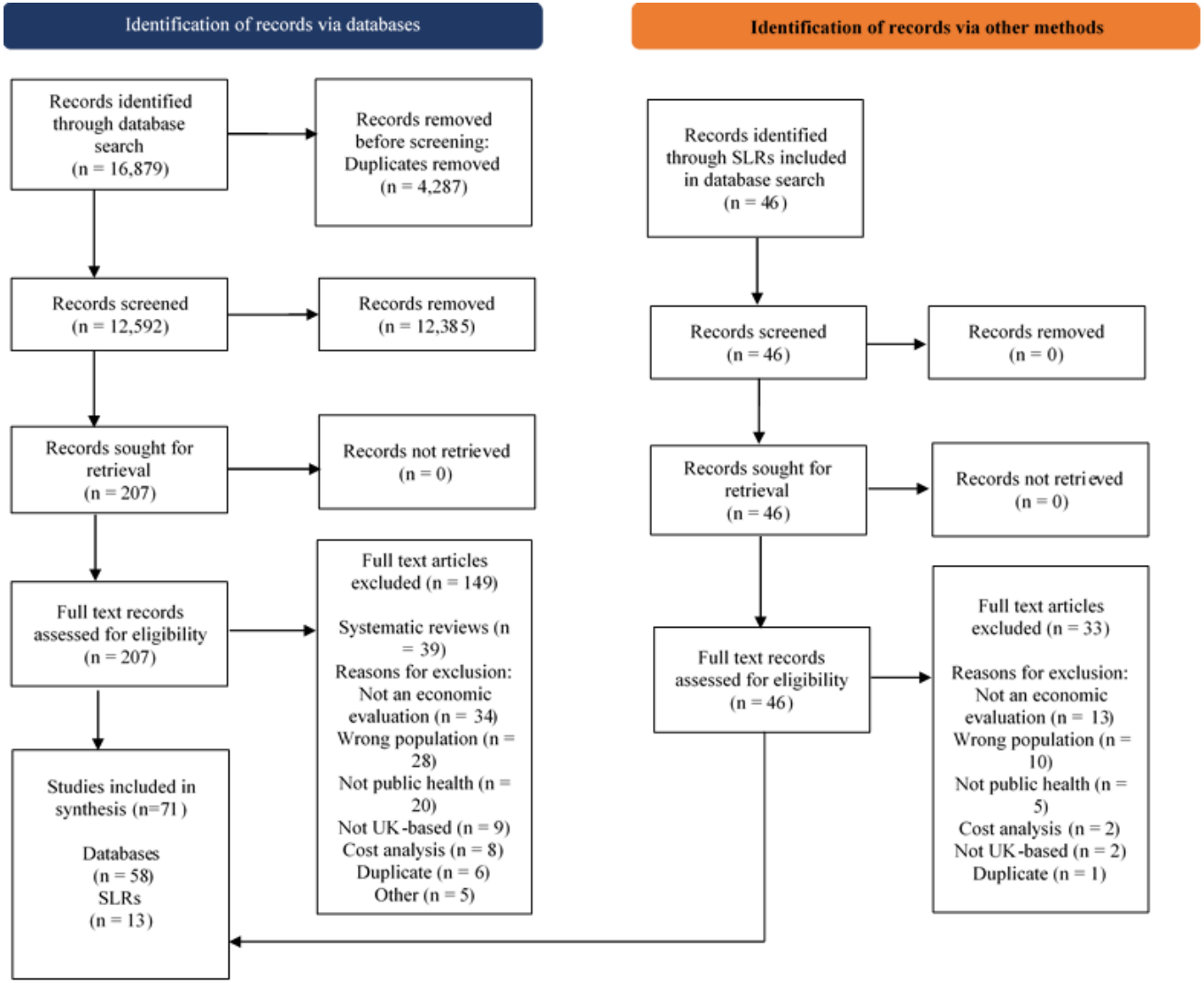
2.6. Results

2.6.1 Review profile

The database search retrieved 16,879 records in total, resulting in 12,592 unique records following deduplication. Of these, 207 full text articles were screened and 58 met the eligibility criteria for inclusion in this systematic review. Although identified systematic reviews (Aballea et al., 2013, Abu-Omar et al., 2017, Ades et al., 2000, Anopa and Conway, 2020, Ashton et al., 2020, Banke-Thomas et al., 2015, Batura et al., 2015, Bayer et al., 2009, Boonacker et al., 2011, Buckle et al., 2017, Camacho and Hussain, 2020, Charles et al., 2011, Clemison et al., 2014, Craig et al., 2011, Dalziel and Segal, 2012, Davenport et al., 2003, Duncan et al., 2017, Fenwick et al.,

2013, Furlong et al., 2012, Grosse et al., 2017, Institute of Health Economics, 2012a, Institute of Health Economics, 2012b, Institute of Health Economics, 2012c, Kotirum et al., 2017, Law et al., 2012, McDaid and Park, 2011, Nargesi et al., 2020, National Institute for Health and Care Excellence, 2008, Nkonki et al., 2017, Renfrew et al., 2008, Rheingans et al., 2006, Rogers et al., 2019, Sharma et al., 2019, Shiri et al., 2019, Yong et al., 2020, Zanganeh et al., 2019, Zechmeister et al., 2008) were excluded from the inclusion criteria, the economic evaluations described in the systematic reviews were checked for potential inclusion. Extraction of the papers identified in the database search yielded an additional 46 records for screening, of which 13 met the inclusion criteria. In total, 71 articles were included in the synthesis. See Figure 1 for the PRISMA flow diagram (Page et al., 2021).

Figure 1 - PRISMA diagram of the flow of included and excluded studies



2.6.2 Retrieved studies

The searches yielded 71 individual papers describing economic evaluations of early childhood interventions. In the case of three economic evaluations, the same evaluation was described in two separate papers and was therefore considered to be one evaluation for the purpose of the results. This was the case for the evaluations described in Morrell et al. 2000 (Morrell et al., 2000b) and Morrell et al. 2000 (Morrell et al., 2000a); Pandor et al. 2004 (Pandor et al., 2004) and Pandor et al. 2006 (Pandor et al., 2006); and Jacklin et al. 2007 (Jacklin et al., 2007) and NICE 2008 (Jacklin et al., 2006). One paper (Kendrick et al., 2017) included the results of six separate economic evaluations that all met the inclusion criteria. However, five of the six were based on one master economic model and the one additional economic evaluation was based on a separate approach. Therefore, for the purpose of the evidence synthesis it was assumed there were two distinct economic evaluations in Kendrick et al. (Kendrick et al., 2017). The results of this systematic review are therefore based on 69 individual economic evaluations.

The full results are presented in Table 3 and Table 4. The sections presented below provide given an overview of the results of the evidence synthesis.

2.6.4 Table of results

Table 3 Results – author, year, intervention and approach to economic evaluation

Author, Year	Intervention category	Universal or targeted	Intervention (comparator)	Population	Evidence	Evaluative framework	Perspective	Time Horizon	Discount rate	Extent of costs captured
Achana 2016 (Achana et al., 2016)	Injury prevention	Targeted	Six intervention combinations of education, equipment, home inspection and fitting (usual care)	Under 4 years	NMA	CUA & CEA	NHS & PSS	100 years	3.5%	NHS & PSS
Anokye 2020 (Anokye et al., 2020)	Breast feeding	Universal	Nourishing Start for Health , (usual care)	Newborn	RCT	CEA	NHS	1 year	No discounting	NHS
Atkins 2012 (Atkins et al., 2012)	Health protection	Universal	RotaTeq (no vaccination)	Under 6 months	RCT	CUA	NHS	50 years	3.5%	NHS
Baguelin 2015 (Baguelin et al., 2015)	Health protection	Universal	LAIV, (no vaccination)	2-4 years	SLR	CUA	NHS	10 years	3.5%	NHS
Bamford 2007 (Bamford et al., 2007)	Hearing/vision screening	Universal and targeted	Alternative SES programmes (no SES)	4-5 years	Survey; SLR	CUA	NHS, education services, patients and family	11 years	3.5%	Healthcare, social care, education
Barber 2015 (Barber et al., 2015)	Health promotion	Universal	Preschoolers in the Playground, (usual care)	1-4 years	RCT	CUA	NHS	1 year	No discounting	NHS & PSS
Barlow 2019 (Barlow et al., 2019)	Reducing risk of abuse/maltreatment	Targeted	Parents under Pressure, (treatment as usual)	Under 2 years	RCT	CUA	NHS & PSS (scenario analysis of societal perspective)	1 year	No discounting	Health & PSS, legal services and costs borne directly by parents
Barnardo's 2012a (Salisbury et al., 2012)	Parenting support	Universal and targeted	Barnardo's Children's Centre service: Stay and Play (unclear)	Under 2 years	Qualitative data	SROI	Societal	5 years	No discounting	Council costs and parent/carer

										contributions
Barnardo's 2012b (Salisbury et al., 2012)	Parenting support	Targeted	Barnardo's Children's Centre service: Family Support Worker (unclear)	Under 5 years	Qualitative data	SROI	Societal	5 years	No discounting	Council costs, Barnardos and School (venue) costs
Beck 2021(Beck et al., 2021)	Health protection	Universal	4CMenB vaccination (no vaccination)	Under 1 year	Case-control study; SLR	CUA	NHS + (scenario analysis of societal perspective)	100 years	3.5%	NHS, special educational needs costs, productivity losses
Bessey 2019 (Bessey et al., 2019)	Newborn screening	Universal	Severe combined immunodeficiency screening (no screening)	Newborn	SLR	CUA	NHS & PSS	5 years	3.5%	NHS
Bessey 2018 (Bessey et al., 2018)	Newborn screening	Universal	X-ALD screening (no screening)	Newborn	SLR	CUA	NHS & PSS	Lifetime	3.5%	NHS & PSS, special education costs
Boyd 2016 (Boyd et al., 2016)	Reducing risk of abuse/maltreatment	Targeted	New Orleans-Glasgow model (existing Glasgow model)	Under 5 years	Pre-post study; literature; expert opinion	CCA	Societal	5 years	3.5% (costs)	NHS, social services, legal system and birth parents productivity losses
Brisson 2003 (Brisson and Edmunds, 2003)	Health protection	Universal	VZV vaccination (no vaccination)	12 - 15 months	Epidemiological model	CUA	NHS & societal	80 years	3%	Direct medical costs. The societal perspective includes all medical and productivit

										y loss costs as well as household expenditures
Burke 2012 (Burke et al., 2012)	Newborn screening	Universal	i) Universal newborn hearing screening & ii) One-stage universal screening (selective screening)	Newborn	Literature	CEA	NHS + (scenario analysis of societal perspective)	Unclear	No discounting	Health costs, travel time and lost productivity due to symptom-related work absence
Carlton 2008 (Carlton et al., 2008)	Hearing/vision screening	Universal	Amblyopia and stabismus screening (no screening)	3-5 years	SLR	CUA	NHS and "other government departments"	100 years	3.5%	NHS
Chance 2013 (Chance, 2013)	Parenting support & health promotion	Targeted	Cambridgeshire's Funded Two-year-old Childcare (unclear)	2 years	Questionnaire	SROI	Societal	5 years	3.5% (costs)	Local authority costs
Christensen 2013 (Christensen et al., 2013)	Health protection	Universal	New 'MenB' vaccine (no vaccination)	2 months to 4 years	SLR	CUA	NHS & PSS	100 years	3.5% for the first 30 years, 3.0% in years 31–75 and 2.5% in years 76–99	NHS
Christensen 2014 (Christensen et al., 2014)	Health protection	Universal	Bexsero (no vaccination)	2 months to 1 year	SLR	CUA	NHS & PSS	100 years	3.5%	NHS & PSS, litigation costs falling on the NHS
Craig 2011 (Craig et al., 2011)	Short stature screening	Universal	Grote strategy for short stature screening (UK strategy)	Under 3 years	SLR	CUA	NHS & PSS	12 years	3.5%	NHS
Davenport 2003	Oral health	Universal	3-, 6-, 12-, 18-, 24- and 36-month dental check recall policies (unclear)	3 months	SLR	CEA	NHS (not explicit)	6 years	6% (costs)	NHS

(Davenport et al., 2003)										
Davies 2000 (Davies et al., 2000)	Newborn screening	Universal and targeted	Neonatal screening nurse follow-up (targeted screening)	Newborn	SLR	CEA	NHS (not explicit)	Unclear	6% (costs)	NHS
Davies 2003 (Davies et al., 2003)	Oral health	Targeted	The provision of free toothpaste and toothbrushes to 3-month (doing nothing)	1 year	RCT	CEA	NHS	4 years	5% (costs)	Interventio n
Edmunds 2002(Edmunds et al., 2002)	Health protection	Universal	Acellular pertussis booster (no vaccination)	4 years	Literature; HES data	CEA	NHS + (scenario analysis of societal perspective)	lifetime	3%	NHS and prodctivity losses
Edwards 2007 (Edwards et al., 2007)	Parenting support	Targeted	The Webster-Stratton Incredible Years basic parenting programme (waiting list)	3-4 years	RCT	CEA	Societal	1 year	No discounting	NHS & PSS and special educationa l services
Ewer 2012 (Ewer et al., 2012)	Newborn screening	Universal	Pulse oximetry screening (clinical examination)	Newborn	Diagnostic accuracy study	CEA	NHS	1 year	3.5% (costs)	NHS
Fayter 2007 (Fayter et al., 2007)	Short stature screening	Universal	Short stature screening (no monitoring)	5 years	SLR	CUA	NHS	Lifetime	3.5%	NHS
Fortnum 2016 (Fortnum et al., 2016)	Hearing/vision screening	Universal	Hearing screening (no screening)	4-5 years	Case-control study; SLR	CUA	NHS & the family	4 years	3.5%	NHS and transporta tion costs for family
Gardner 2017 (Gardner et al., 2017)	Parenting support	Targeted	IY Basic parenting programme (no intervention)	5 years	MA	CEA & ROI	Public sector	25 years	3.5% (costs)	NHS, social services departme nts, Departme nt for Education, voluntary sector, criminal justice system, health

										impacts of crime and benefits payments
Griebsch 2007 (Griebsch et al., 2007)	Newborn screening	Universal	Congenital heart defect screening (clinical examination)	Newborn	SLR + observational study	CEA	NHS	1 year	No discounting	NHS
Grill 2006 (Grill et al., 2006)	Hearing/vision screening	Universal	Hospital earing screening (community)	Newborn	SLR	CEA	NHS	10 years	6% costs, 1.5% outcome	NHS
Hoddinott 2012 (Hoddinott et al., 2012)	Breast feeding	Targeted	FEeding Support Team (reactive telephone support)	Newborn	RCT	CEA	NHS (not explicit)	6-8 weeks	No discounting	NHS
Hodgson 2020 (Hodgson et al., 2020)	Health protection	Universal and targeted	RSV vaccination (status quo)	Under 5 years	Literature search	CUA	NHS & PSS	10 years	3.5%	NHS & PSS
Hollingworth 2012 (Hollingworth et al., 2012)	Health promotion	Targeted	Obesity/overweight interventions (no/minimal intervention)	4-5 years	SLR	CEA	NHS	Lifetime	3.5%	NHS
Jacklin 2007, NICE 2008 (Jacklin et al., 2006, Jacklin et al., 2007)	Breast feeding	Targeted	Breast feeding peer support (unclear)	Newborn	Pre-post study	CUA	NHS (not explicit)	Unclear	3.5% (only QALYs stated)	NHS and costs of running the sevice
Jit 2007 (Jit and Edmunds, 2007)	Health protection	Universal	Rotavirus vaccination (no vaccination)	2-4 months	RCT	CUA & CEA	NHS	Unclear	3.5% (both) for the first 30 years, 3.0% thereafter	NHS and lost productivity for the care giver
Jit 2009 (Jit et al., 2009)	Health protection	Universal	Rotavirus vaccination (no vaccination)	2-4 months	Literature	CUA	NHS + (scenario analysis of societal perspective)	5 years	3%	NHS. Societal costs included NHS, lost productivity for carers and out-of-

										pocket expenses
Jit 2010 (Update of 2009 paper with new efficacy evidence) (Jit et al., 2010)	Health protection	Universal	Rotavirus vaccination (current care)	2-4 months	RCT	CUA	NHS + (scenario analysis of societal perspective)	5 years	3%	NHS. Societal costs included NHS, lost productivity for carers and out-of-pocket expenses
Kay 2018 (Kay et al., 2018)	Oral health	Targeted	Supervised tooth brushing (no intervention)	5 years	RCT	CUA	States 'public sector' but appears to be NHS	3 years	1.5%	NHS
Kendrick 2017 I (Kendrick et al., 2017)	Injury prevention	Targeted	a) Functional smoke alarm (usual care) b) Safe hot tap water temperature (usual care) c) Promoting safety gate possession and use (usual care) d) Promoting the safe storage of medicines (usual care) e) Promoting the safe storage of household and other products (usual care)	Under 5 years	NMA	CUA	Public sector	100 years	3.5%	NHS & PSS and other public sector costs
Kendrick 2017 ii (Kendrick et al., 2017)	Injury prevention	Targeted	IPB with or without facilitation (usual care)	Under 3 years	RCT	CEA	Societal	1 year	No discounting	Children's centre; fire and rescue service; other agencies

										including local councils; family costs
Knerer 2012 (Knerer et al., 2012)	Health protection	Universal	Pneummococcal vaccination (PCV-13)	Under 2 years	Literature	CUA	NHS (not explicit)	94 years	3.5%	NHS
Knowles 2005 (Knowles et al., 2005)	Newborn screening	Universal	Congenital heart defect screening (clinical examination)	Newborn	SLR	CEA	NHS	1 year	6%	NHS
Kowash 2006	Oral health	Targeted	Out-reach education programme (unclear)	Under 1 year	RCT	CBA & CEA	NHS	3 years	No discounting	NHS
Lorgelly 2007 (Lorgelly et al., 2008)	Health protection	Universal	Rotavirus vaccination programme (no vaccination)	Newborn	Literature	CEA	NHS & societal	5 years	3.5%	NHS. Societal costs included NHS, lost productivity and OTC medicines
Martin 2009 (Martin et al., 2009)	Health protection	Universal	Rotarix (no vaccination)	Under 6 months	Literature	CEA	NHS	Lifetime	3.5%	NHS
McAuley 2004 (McAuley et al., 2004)	Parenting support	Targeted	Home Start support (no Home Start support)	Under 5 years	Interview (naive comparison)	CEA & CCA	Children and their families	1 year	No discounting	Education and child care service use, hospital inpatient service use, community health service use, mental health service use,

McIntosh 2003 (McIntosh et al., 2003)	Health protection	Universal	Pneumococcal vaccination (no vaccination)	Under 6 months	RCT	CEA	NHS (includes scenario with lost labour costs to families of children)	10 years	6% (costs)	NHS. Included a scenario which incorporated parent's lost productivity
Melegaro 2004 (Melegaro and Edmunds, 2004)	Health protection	Universal	Pneumococcal vaccination (no vaccination)	2 months to 2 years	RCT	CEA	NHS	Lifetime	3.5% costs, 1.5% benefits	NHS
Morell 2000a & Morell 2000b (Morrell et al., 2000a, Morrell et al., 2000b)	Parenting support	Universal	Postnatal support from a community midwifery support worker (no support worker)	Newborn	RCT	CCA (some ambiguity as one SLR referred to it as a cost-analysis but they do report costs and outcomes separately. Could also be a cost-minimisation assuming both have same effect)	NHS	6 months	5% costs	NHS
Mujica Mota 2006 (Mujica Mota et al., 2006)	Parenting support & health promotion	Targeted	Means-tested access to full-time or part-time day care at the Hackney Early Years	6 months to 3.5 years	RCT	CEA	Societal	18 months	6% costs after 12 months	Early years education and care,

			Centre (childcare secured themselves)							NHS, productivity gains and other contributions relating to mothers and their partners. Out-of-pocket costs to parents for travel to health care and child education services and medications
O'Neill 2017 (O'Neill et al., 2017)	Oral health	Universal	Caries prevention (advice only)	2-3 years	RCT	CEA	Public payer	3 years	No discounting	NHS and lost productivity
Pandor 2004 (Pandor et al., 2004)+ Pandoor 2006(Pandor et al., 2006)	Newborn screening	Universal	Inborn errors of metabolism screening (screening for phenylketonuria only)	Newborn	SLR	CEA	Health and other public sector providers within the UK'	80 years	6% (costs)	NHS & PSS, education sector costs
Phillips 2011 (Phillips et al., 2011)	Injury prevention	Targeted	Scald prevention (waiting list)	Under 5 years	RCT	CEA & CBA (but not stated)	Public sector	1 year	No discounting (the discussion did include a back of the envelope calculation which used 3.5% rate for outcomes)	Public sector costs

Pitman 2013 (Pitman et al., 2013)	Health protection	Universal	Influenza vaccination (no vaccination)	2-4 years	Observational study	CUA	NHS	200 years	3.5%	NHS
Pokhrel 2015 (Pokhrel et al., 2015)	Breast feeding	Targeted	Breast feeding support (no breast-feeding support)	Newborn	SLR; observational study	Not explicit but costs and QALYs are presented albeit doesn't appear to be incremental. Could call it a CCA	NHS	For three acute conditions (GI, LRTI and AOM), analysis was limited to the first year of life; maternal BC took a lifetime horizon; NEC focussed on the stay in a neonatal unit	3.5%	NHS
Renwick 2018 (Renwick et al., 2018)	Health promotion	Targeted	Smoking home intervention (usual care)	Under 5 years	RCT	CEA	NHS & PSS	12 weeks	No discounting	NHS
Roberts 2012 (Roberts et al., 2012)	Newborn screening	Universal	Congenital heart defect screening (clinical examination)	Newborn	RCT	CEA	NHS	1 year	No discounting	NHS
Saramago 2014 (Saramago et al., 2014)	Injury prevention	Universal	Fire injury prevention interventions (usual care)	Under 5 years	MA	CUA	Public sector, including the NHS and PSS	100 years	3.50%	NHS & PSS. Scenario which includes law

										enforcement and fire and rescue costs
Siddiqui 2011 (Siddiqui et al., 2011)	Health protection	Universal and targeted	HBV programme (current vaccination practice)	Under 6 months	Literature	CUA	NHS	99 years	3.50%	NHS
Simkiss 2013 (Simkiss et al., 2013)	Parenting support	Targeted	The Family Links Nurturing Programme (no screening)	2-4 years	RCT	CUA	NHS & PSS	10 years	No discounting	NHS & PSS
Simpson 2005 (Simpson et al., 2005)	Newborn screening	Universal	Cystic Fibrosis screening (no screening)	Newborn	Literature	CUA	NHS	Lifetime	6% costs; 2% outcomes	NHS
Thomas 2018 (Thomas, 2018)	Health protection	Targeted	RSV vaccination (no vaccination)	Under 2 years	Observational study	CBA	Societal	Lifetime	3.5% (costs)	NHS and lost productivity
Tickle 2016 (Tickle et al., 2016)	Oral health	Universal	NIC-PIP caries prevention (prevention advice alone)	2-3 years	RCT	CEA	NHS	3 years	No discounting	Dental services
Trotter 2002 (Trotter and Edmunds, 2002)	Health protection	Universal	Meningitis C vaccination (no vaccination)	Under 4 years	Literature + observational study	CEA	NHS	Lifetime	3%	NHS
Trotter 2006a (Trotter et al., 2006)	Health protection	Universal	Meningococcal vaccination (no vaccination)	Under 1 year	Literature + observational study	CUA & CEA	NHS	100 years	3%	NHS
Trotter 2006b (Trotter and Edmunds, 2006)	Health protection	Universal	Meningococcal vaccination (current schedule)	Under 2 years	Literature + observational study	CEA	NHS	75 years	3.50%	NHS
Tudor Edwards 2016 (Edwards et al., 2016)	Parenting support	Targeted	IY BASIC parenting programme (waiting list)	3-4 years	RCT	CEA	Public sector multi-agency	6 months	No discounting	NHS & PSS and special education services
Uus 2006 (Uus et al., 2006)	Newborn screening	Universal	Newborn Hearing Screening Programme (	Newborn	Literature	CEA	Societal	10 years	No discounting	NHS and costs to the family

Abbreviations: CBA, cost-benefit analysis; CCA, cost consequence analysis; CEA, cost-effectiveness analysis; CUA, cost utility analysis; IY, incredible years; NHS, national health service; NMA, network meta-analysis; PSS, personal social services; RCT, randomised controlled trial; ROI, return on investment; SLR, systematic literature review; SROI, social return on investment.

Table 4 Results – outcomes, equity, modelling approach, uncertainty and results

Author, Year	Outcomes captured (HRQL measure/utility instrument for QALY estimation)	Formal incorporation of equity¶	General equity consideration	Modelling approach	Author recommended?	Structural uncertainty	PSA	Reporting of uncertainty in the results	Result of the economic evaluation
Achana 2016 (Achana et al., 2016)	QALYs (health state HRQL values from the literature) & Numbers of poison cases avoided	Yes. Sensitivity analysis of increasing the rate of unintentional poisoning to the rate observed in the 4th and 5th most deprived quintiles.	Model for under 5-year-olds from socio-economic disadvantaged groups whom the evidence suggest are at increased risk of unintentional injury compared to those from a well-off family background.	Decision tree + markov model	CUA: No interventions were considered cost-effective. CEA: No interventions were considered cost-effective.	No	Yes	CE-plane (PSA); CEAC; DSA.	CEA: Compared with usual care, the intervention with the lowest ICER was education at £2888 per poison avoided. CUA: Compared to usual care, the ICER was lowest for education at £41,330 per QALY gained.
Anokye 2020 (Anokye et al., 2020)	Proportion baby breast fed at 6 weeks	No	Intervention focussed in area with low breastfeeding prevalence.	n/a	Not stated. Threshold analysis.	No (trial based evaluation)	Yes	CEAC; DSA	Compared to usual care, the ICER was £974 per additional baby breast fed baby
Atkins 2012 (Atkins et al., 2012)	QALYs (health state HRQL values from the literature)	No	No	Dynamic transmission model	Yes	No	Yes	CE-plane (PSA); CEAC; DSA	Compared to no vaccination, the ICER using the dynamic model was £27,133 per QALY gained; using the static model was £34,728 per QALY gained. Other scenarios presented.

Baguelin 2015 (Baguelin et al., 2015)	QALYs (health state HRQL values from the literature)	No	No	Dynamic transmission model	Yes	No	Yes	CE-plane (PSA); DSA	Compared to no vaccination, the ICER is £2,613 per QALY gained
Bamford 2007 (Bamford et al., 2007)	QALYs (HUI)	No	No	Decision tree	Yes	No	Yes	CEAC	Compared with no SES, the NMB is £4867
Barber 2015 (Barber et al., 2015)	QALYs ((EQ-5D and PedsQL)	No	Intervention implemented in Bradford due to area's ethnic diversity and social deprivation	n/a	Borderline	No (trial based evaluation)	Yes	CEAC	Compared to usual practice, the ICER is £19,588 per QALY gained
Barlow 2019 (Barlow et al., 2019)	QALYs (EQ-5D-5L)	No	Intervention for substance misusing parents	n/a	Borderline	No (trial based evaluation)	Yes	Probability of being cost effective; DSA	Compared to treatment as usual, the ICER is £34,095 per QALY gained (NHS & PSS perspective); £56,269 per QALY gained (societal perspective)
Barnardo's 2012a (Salisbury et al., 2012)	Monetary outcomes	No	Stay and Play is considered to be a useful gateway for in need families to access more targeted services.	n/a	Yes - positive SROI	No	No	DSA	Approximately £2 for every £1 invested
Barnardo's 2012b (Salisbury et al., 2012)	Monetary outcomes	No	The FSW service makes provision for families who are just above the threshold at which social services would intervene.	n/a	Yes - positive SROI	No	No	DSA	£4.50 for every £1 invested
Beck 2021(Beck et al., 2021)	QALYs (health state HRQL values from the literature)	No	No	Dynamic transmission model	Yes	No	Yes	CEAC; DSA	Compared to no vaccination, the ICER is £18 645 per QALY gained

Bessey 2019 (Bessey et al., 2019)	QALYs (EQ-5D-3L)	No	No	Decision tree	Not stated	No	Yes	CE-plane (PSA); DSA. Conducted VOI analysis in the form of EVPI and EVPPI.	Compared to no screening, the ICER is £18,222 per QALY gained
Bessey 2018 (Bessey et al., 2018)	QALYs (EQ-5D-5L)	No	No	Decision tree	Yes	No	Yes	CE-plane (PSA); DSA	Compared to no screening, screening dominates (positive QALYs, negative costs)
Boyd 2016 (Boyd et al., 2016)	Probability of one and two episodes in care	No	No	n/a	Not stated	No	No	n/a	Compared to the existing Glasgow model, the New Orleans model has a reduced probability of two episodes in care (incremental reduction of 0.41) and reduced mean cost per child in the model (incremental difference of £6,820). Other outcomes differ in magnitude and direction.
Brisson 2003 (Brisson and Edmunds, 2003)	QALYs (HUI-2)	No	No	Dynamic transmission model	No	No	Yes	CEAC; DSA	Compared to no vaccination, the VZV infant vaccination strategy is dominated as it results in a significant QALY loss.

Burke 2012 (Burke et al., 2012)	Cases detected	No	No	Decision tree	Unclear for NHS perspective, cost saving for societal perspective	No	No	n/a	Compared to selective screening, the ICER is £36,181 per case detected.
Carlton 2008 (Carlton et al., 2008)	QALYs (health state HRQL values from the literature)	No	No	Markov model	Unlikely to be cost-effective	No	Yes	CEAF (frontier); DSA. Conducted VOI analysis in the form of EVPI.	Compared to no screening, screening at 3 years without autorefraction was the most cost-effective with an ICER of £527,375 per QALY gained.
Chance 2013 (Chance, 2013)	Monetary outcomes	No	This was targeted at disadvantaged families	n/a	Positive SROI	No	No	DSA	£8.40 for every £1 invested.
Christensen 2013 (Christensen et al., 2013)	QALYs (health state HRQL values from the literature)	No	No	Cohort model & dynamic transmission model	No	No	Yes	CEAC	Compared to no vaccination, the ICERs for the various infant strategies ranged from £162,800 to £290,000 per QALY gained (cohort model); and between £91,800 to £97,600 per QALY gained (dynamic model)
Christensen 2014 (Christensen et al., 2014)	QALYs (EQ-5DY)	No	No	Dynamic transmission model	No recommendation. Results were presented as the price the vaccine would have to be to be deemed cost-effective at a threshold of £20,000	No	No	Not presented	Compared to no vaccination, the ICERs for the various infant strategies ranged from £163,100 to £221,000 per QALY gained.

Craig 2011 (Craig et al., 2011)	QALYs (health state HRQL values from literature and expert opinion)	No	No	Decision tree	Yes	No	Yes	CE-plane (PSA); CEAC; DSA	Compared to the UK strategy, the ICER is £1144 per QALY gained
Davenport 2003 (Davenport et al., 2003)	Number of teeth free from decay, fillings or extraction	Yes. The cost-effectiveness was evaluated across two groups: those using manual toothbrushing and those using non-manual toothbrushing. These were used as proxies to categorise participants into socioeconomic status.	Key risk factor was used for the present study: socioeconomic background (manual versus nonmanual)	Markov model	Not stated	No	No	n/a	No ICERs reported.
Davies 2000 (Davies et al., 2000)	SCD cases identified	No	Access issues relating to haemoglobinopathy screening, particularly as they relate to race.	Unclear	For areas where there are 16 sickle cell traits and 0.5 sickle cell disease cases per 1000 births, the data suggest that universal screening is cost-effective	No	No	n/a	Compared to targeted screening, range of ICERs reported for various disease incidence rates. For example, prevalence of 0.1 or 0.3 per 1000 births, results in ICERs in the range £25,000–£100,000 per case identified
Davies 2003 (Davies et al., 2003)	Decayed, missing and filled teeth	No	The intervention was for children living in deprived, non-	n/a	Not stated	No	No	n/a	Compared to doing nothing, ICERs are £80.83

	reduction by one unit; child kept free of caries experience; child kept free of extraction experience		fluoridated areas of North-West England.						per tooth saved from carious attack; £424.38 per child kept free of caries experience; £679.01 per extraction avoided
Edmunds 2002(Edmunds et al., 2002)	Life-years gained; general practitioner consultation; and hospitalisation averted	No	No	Dynamic transmission model	Not possible to draw any strong conclusions regarding the cost-effectiveness of acellular booster doses from the perspective of the health care provider	No	Yes	No probabilistic results presented graphically; DSA	Compared to no vaccination the range of ICERs reported for various booster doses ranges from £8,463 to ££49,511 per life year gained from the health perspective; £2,489 to £36,941 per life year gained from a societal perspective.
Edwards 2007 (Edwards et al., 2007)	ECBI-I	No	The intervention was given to families who were mostly socially and economically disadvantaged compared with the mean values for the UK.	n/a	Likely to be cost effective for a ceiling ratio of £100 per point increase in intensity score. Threshold analysis.	No (trial based evaluation)	Yes	CE-plane (PSA); CEAC; DSA	Compared to a six-month waiting list, the ICER is £71 per 1 point change in the ECBI-I score
Ewer 2012 (Ewer et al., 2012)	Detection of CHD	No	No	Decision tree	If society's WTP would be £50,000 then the probability that pulse oximetry as an adjunct to clinical examination' is cost-effective is >90%. Threshold analysis.	No	Yes	CE-plane (PSA); CEAC	Compared to clinical examination alone, the ICER is £24,900 per timely diagnosis

Fayter 2007 (Fayter et al., 2007)	QALYs (health state HRQL values from literature)	No	No	Decision tree	Yes	No	Yes	CE-plane (PSA); CEAC. Planned to do VOI analysis but it was not undertaken.	Compared to no monitoring, the ICER is £9500 per QALY gained
Fortnum 2016 (Fortnum et al., 2016)	QALYs (health state HRQL values from literature)	No	No	Decision tree	Unlikely to be cost-effective	No	No	n/a	Compared to no screening, the SES programme is dominated
Gardner 2017 (Gardner et al., 2017)	ECBI-I	No	The study was concerned with distributional impacts across groups. However, there were no differential effects of IY on disruptive behaviour in families with different levels of social/socioeconomic disadvantage or differential effects for ethnic minority families, families with different parenting styles, or for children with comorbid ADHD or emotional problems or of different ages.	Markov model	No recommendation but does indicate a WTP of £109 per point improvement on the ECBI-I is 50%. This increases to 99% at a WTP of £145. Threshold analysis.	No	Yes	CEAC; DSA	Compared to no intervention, a WTP of £109 per point improvement on the ECBI-I is 50% probability of being cost-effective. In the 'high-cost' scenario, the return on investment is substantial, with average net savings of between £5000 and £7000 per child.
Griebsch 2007 (Griebsch et al., 2007)	Timely diagnosis of life-threatening congenital heart defects	No	No	Decision tree	Pulse oximetry 'appears cost-effective'	No	Yes	CEAC; DSA. Conducted VOI analysis in the form of EVPI and EVPPI.	Compared to clinical examination alone, the ICER for pulse oximetry is £4,894 per additional timely diagnosis; for screening echocardiography

									it is £4,496,666 per additional timely diagnosis.
Grill 2006 (Grill et al., 2006)	Quality weighted detected child months	No	No	Markov model	Not stated. Threshold analysis.	No	Yes	CE-plane (PSA); CEAC; DSA	Compared to community, the ICER is £2423 per detected child; £25 per quality weighed detected child month
Hoddinott 2012 (Hoddinott et al., 2012)	Any breastfeeding; exclusive breastfeeding	No	Intervention targeted at women living in SIMD 1–3 postcode areas.	N/a	Not stated	No (trial based evaluation)	No	n/a	Compared to reactive only telephone support, the ICER is £87 per additional woman any breastfeeding; £91 per additional woman exclusively breast feeding
Hodgson 2020 (Hodgson et al., 2020)	QALYs (EQ-5D)	No	No	Dynamic transmission model	No recommendation. Results presented as the maximum purchasing price per course for programmes to be cost-effective. Threshold analysis.	No	Yes	Equivalent of CEAC with maximum purchase price for vaccine and box plots (sensitivity analysis)	Results presented as the maximum purchasing price per course for programmes to be cost-effective (compared to status quo). For: MAB-VHR-S (£4342.97); MAB-HR-S (£201.15); MAD; MAB-HR-S+ (£87.03); VAC-INF-S (£94.76).
Hollingworth 2012 (Hollingworth et al., 2012)	Life years gained	No	No	Microsimulation model	Yes	No	No	n/a	Compared to no/minimal intervention, the ICER is £66,567 per life year gained (BMI standard deviation score reduction of

									0.03); £13,589 per life year gained (0.13 BMI standard deviation score reduction)
Jacklin 2007, NICE 2008 (Jacklin et al., 2006, Jacklin et al., 2007)	QALYs (unclear); premenopausal breast cancer averted; infant infections averted	No	Intervention targeted at the poorest areas of Sheffield	Unclear	Yes	Unclear	No	DSA	No ICER reported. Investment of £20,000 in a peer support scheme of this type produces net societal savings of £5,500. In addition the model suggests that the scheme would avert 0.057 cases of pre-menopausal breast cancer in mothers (2.7 cases per 10,000) and almost 6 cases (285 cases per 10,000) of infections requiring hospitalisation in the first year of life.
Jit 2007 (Jit and Edmunds, 2007)	QALYs (HUI-2 and EQ-5D)	No	No	Cohort model	No	No	Yes	CE-plane (PSA); CEAC; DSA	Compared to no vaccination, the ICER is £79,905 per QALY gained; £525 per episode prevented; £3,803 per hospitalisation prevented (vaccination using RotaTeq). £60,928 per QALY gained; £391 per episode

									prevented; £3,647 per hospitalisation prevented (vaccination using Rotarix).
Jit 2009 (Jit et al., 2009)	QALYs (HUI-2 and EQ-5D)	No	No	Cohort model	No	No	No	Not presented	Compared to current care, the ICER is EUR110,000 per QALY gained (Rotarix vaccination programme) and EUR160,000 per QALY gained (RotaTeq vaccination programme)
Jit 2010 (Update of 2009 paper with new efficacy evidence) (Jit et al., 2010)	QALYs (HUI-2 and EQ-5D)	No	No	Cohort model	No	No	No	Not presented	Compared to current care, the ICER is EUR110,000 per QALY gained (Rotarix vaccination programme) and EUR150,000 per QALY gained (RotaTeq vaccination programme)
Kay 2018 (Kay et al., 2018)	QALYs (health state HRQL values from literature)	No	The intervention was targeted at those at high risk of oral disease (children in the most deprived quintile in England).	Modelling of relative risk reduction of caries	Range of costs given for the interventions to be deemed cost-effective	No	No	Not presented	Compared to no intervention, spending less than £55 per child on supervised tooth brushing is cost-effective; spending less than £100 on varnish would be cost-effective over 3 years

Kendrick 2017 I (Kendrick et al., 2017)	QALYs (health state HRQL values from literature)	No	Interventions were aimed at people in social housing and in the most deprived areas	Markov model	Not really stated. Threshold analysis. Note, intervention e) was deemed not to be cost-effective	No	Yes	CEAC; DSA	a) Compared to usual care, the ICER for education + equipment is £34,200 per QALY gained. Note, this was the only non-dominated intervention. b) Compared to usual care, the ICER for education is £40,271 per QALY gained. Note, this was the lowest ICER. c) Compared to usual care, the ICER for education is £284,068 per QALY gained. Note, this was the lowest ICER. d) Compared to usual care, the ICER for education is £41,330 per QALY gained. Note, this was the lowest ICER. e) All interventions were more costly and less effective than usual care

Kendrick 2017 ii (Kendrick et al., 2017)	Probability of having a fire escape plan	No	The children's centres provide community-based integrated services, information and support for families with young children. They aim to improve outcomes for young children and their families, with a particular focus on the most disadvantaged, to reduce inequalities in health.	n/a	IPB only dominates (cost saving and better outcomes)	No	No	CEAC; DSA	Compared to usual care, the ICER for injury prevention briefing only is £1260 per additional fire escape plan; the ICER for injury prevention briefing + is £616.13 per additional fire escape plan
Knerer 2012 (Knerer et al., 2012)	QALYs (health state HRQL values from literature)	No	No	Markov model	Yes	No	Yes	DSA	Compared to PCV-13, the pneumococcal conjugate vaccine dominates (positive QALYs, negative costs).
Knowles 2005 (Knowles et al., 2005)	Timely diagnosis	No	No	Decision tree	Not stated. Threshold analysis.	No	Yes	CE-plane (PSA); CEAC; DSA. Conducted VOI analysis in the form of EVPI.	Compared to clinical examination, the ICER is £4,894 per timely diagnosis
Kowash 2006	Monetary and decayed, missing or filled tooth or tooth surface	No	The intervention is targeted at women living in a deprived area of Leeds	n/a	Unclear	No	No	n/a	The benefit/cost ratio is 5.6. Cost-effectiveness ratio is 1.8.
Lorgelly 2007 (Lorgelly et al., 2008)	Gastroenteritis episode avoided; GP visit avoid; hospitalisation	No	The authors argued that the societal perspective provides important equity information: differing	Decision tree	Yes (but they use that to mean cost saving)	No	No	DSA	Compared to no vaccination programme, the ICER is £60.41 per episode

	visit avoided; life years saved		cost-effectiveness across perspectives reflects the fact the rotavirus gastroenteritis is a significant burden on parents and families.						avoided; £177,212 per life year saved.
Martin 2009 (Martin et al., 2009)	QALYs (EQ-5D)	No	No	Markov model	Yes	Yes	Yes	DSA, PSA	Compared to no vaccination, the ICER is £23 298 per QALY gained.
McAuley 2004 (McAuley et al., 2004)	Parenting Stress Index; Edinburgh Postnatal Depression Scale; Rosenberg Self-Esteem; Brief Infant–Toddler Social and Emotional Assessment Scale; Maternal Social Support Index	No	The Study families were referred by Home-Start organisers or health visitors. The predominant reason for referral for all the families in the study fell within the five categories: maternal mental/physical health, social isolation, multiple births/young children and a child/children with special needs. A quarter of families were in council housing, 7% in housing association housing, 85 per cent of single-parent families	n/a	No	No	No	n/a	Compared to no home start support, the intervention was assumed to be dominated (no effect difference and increases costs in the Home Start arm)
McIntosh 2003 (McIntosh et al., 2003)	Life years saved	No	No	Unclear	Unclear	No	No	n/a	Compared to no vaccination, the ICER is £31,512 per life year saved
Melegaro 2004 (Melegaro and Edmunds, 2004)	Life years gained; QALYs	No	No	Cohort model	Not likely to be deemed cost-effective from the NHS perspective	No	Yes	CEAC; DSA	Compared to no vaccination, the ICER is £70,699 per life year

									gained; £31,021 per QALY gained. Other scenarios presented all with higher ICERs.
Morell 2000a & Morell 2000b (Morrell et al., 2000a, Morrell et al., 2000b)	SF-36; Duke functional social support; Edinburgh postnatal depression scale; number breastfeeding only; number formula milk feeding only	No	No	n/a	Not stated	No	No	n/a	No evidence of differences in health status scores (SF-36, Edinburgh postnatal depression scale, and Duke functional social support scale) and rates of breast feeding between the two groups. The difference in total NHS costs between the groups was £178.61.
Mujica Mota 2006 (Mujica Mota et al., 2006)	Proportion of mothers in paid employment or education at 18 months	No	The centres in the intervention are established in areas of high levels of deprivation	n/a	The societal costing was estimated to be cost saving. The public sector evaluation didn't report as there was no specified WTP. Threshold analysis.	No	Yes	CEAC; DSA	Compared to childcare secured by the participants themselves, the ICER was £38,550 per additional woman in paid Societal perspective shows it to be cost saving.
O'Neill 2017 (O'Neill et al., 2017)	Proportion caries free; number of carious surfaces; number of episodes of pain	No	No	n/a	Only for carious surfaces at £1,000 per carious surface avoided. Only carious surfaces considered as this was the only	No	Yes	CE-plane (PSA); CEAC; DSA	Compared to advice only, the ICER is £2,092.59 per caries free person; £250.58 per carious surface; £259.07

					statistically significant result. Threshold analysis.				per number of pain episodes
Pandor 2004 (Pandor et al., 2004)+ Pandoor 2006(Pandor et al., 2006)	Life years gained; cases of inborn error of metabolism detected	No	No	Unclear	Probably cost-effective when used for phenylketonuria (PKU) and medium-chain acyl-coenzyme A dehydrogenase (MCAD) but not likely for PKU alone. Not likely with the addition of other metabolic diseases	No	Yes	CE-plane (PSA); CEAC. Conducted VOI analysis in the form of EVPI.	Compared to screening for PKU only, the ICER for PKU+MCAD is –£7,359 per case of inborn error of metabolism detected; ICER for cost per life year gained are not reported.
Phillips 2011 (Phillips et al., 2011)	Risk reduction (scalds)	No	This intervention is for families with children under 5 years of age living in accommodation provided by the Glasgow Housing Association.	n/a	Cost saving	No	No	n/a	Compared to a waiting list, the scald prevention intervention results in net savings of £7273 per scald avoided (NHS perspective); £53 949 per scald avoided (lifetime perspective). The net benefit (cost) per £1 spent is £1.41 for an NHS perspective and (£0.47) for a lifetime perspective.

Pitman 2013 (Pitman et al., 2013)	QALYs (health state HRQL values from literature)	No	No	Dynamic transmission model	Not stated. TIV dominated; LAIV cost saving	No	Yes	CEAC; DSA	Compared to current policy, TIV in 2-4 year olds is dominated. Compared to current policy, LAIV in 2-4 year olds is cost saving (with positive QALYs).
Pokhrel 2015 (Pokhrel et al., 2015)	Cost savings. This includes a cost derived using NMB (assuming 20,000/QALYs) for the breast cancer benefits).	No	Infants of parents from low-income backgrounds, who are young, white, with fewer educational qualifications and who were themselves formula fed, are least likely to be breastfed.	Markov model	Yes	Unsure	No	DSA	Report outcomes using 3 different types of policies,: policy A, B and C (impacts on actue diseases (GI, LRTI and AOM)); Policy D (impacts NEC) and Policy E (impacts BC). Results not combined. Policy A2 saves £11.04m; policy D2 saves £6.12m and policy E2 saves £31.42m (this includes QALYs gained)
Renwick 2018 (Renwick et al., 2018)	Average 16–24 h levels of particulate matter of < 2.5 μm diameter ($PM_{2.5}$) ; the number of quitters	No	Intervention targeted at deprived communities in Nottingham City and County in England. Caregivers aged 18 and over, with a child aged under five living in their household, reported smoking tobacco inside their home and were not willing to quit	n/a	Not stated	No	Yes	CE-plane (PSA); DSA	Compared to usual care, the ICER is £131 per additional 10μg/m3 reduction of 16-24 h PM2.5; £71 per additional quitter

Roberts 2012 (Roberts et al., 2012)	Case of timely diagnosis	No	No	Decision tree	Yes	No	Yes	CEAC; DSA	Compared to clinical examination alone, the ICER is £24,900 per timely diagnosis of significant congenital heart defects
Saramago 2014 (Saramago et al., 2014)	QALYs (health state HRQL values from literature)	No	Social inequalities exist in the possession of functioning smoke alarms in families with children under 5 in the UK	Decision tree	Not stated	No	Yes	CEAC; DSA	Compared to usual care, the only non-dominated interventions are education plus low cost/free safety equipment with an ICER of £34,200 per QALY gained; Education plus low cost/free safety equipment plus fitting plus home inspection has an ICER of £3,466,635 per QALY gained.
Siddiqui 2011 (Siddiqui et al., 2011)	QALYs (health state HRQL values from literature)	No	No	Markov model	No	No	No	DSA	Compared to current vaccination practice, the ICER is £263,000 per QALY gained (for universal infant vaccination programme); £90,000 per QALY gained (for the selective infant programme)
Simkiss 2013 (Simkiss et al., 2013)	QALYs (SF-6D, PedsQL)	No	The intervention was implemented in early years centres in four	n/a	No evidence of value for money	No	Yes	Threshold analysis; DSA	Compared to a waiting list, the

			deprived areas of South Wales						ICER is £34,913 over 5 years and £18,954 over 10 years
Simpson 2005 (Simpson et al., 2005)	QALYs (QWB)	No	No	Decision tree + markov model	Not stated	No	No	DSA	Compared to no screening, the ICER is £6,864 per QALY gained
Thomas 2018 (Thomas, 2018)	Costs	No	No	n/a	For certain subgroups (BD, EI and PN)	No	No	DSA	Compared to no vaccination procedure, the benefit/cost ratio is: 7.726 for bronchopulmonary dysplasia; 0.694 for congenital heart disease; 1.391 for extreme immaturity; 1.426 for premature babies; 0.465 for all other RSV admissions. All results for year of 2012/2013.
Tickle 2016 (Tickle et al., 2016)	Caries-free person; carious surfaces; episodes of pain	No	The study did look at the effects of the intervention across IMD quintile groups but didn't consider these groups in the economic evaluation, and the discussion included a discussion of the uptake and effect of a universal intervention across SE groups.	n/a	No (not for the outcomes of caries avoided)	No	Yes	CEAC; DSA	Compared to prevention advice alone, the ICER is £2092.59 per proportion caries free; £250.58 per number of carious surfaces; £259.07 per episode of pain
Trotter 2002 (Trotter and Edmunds, 2002)	Life years saved	No	No	Cohort model	Modelling of the cost effectiveness of the campaign supports the	No	No	DSA	Compared to no vaccination, the ICER is £14,630

					introduction of the vaccine				per life year saved for 0-4 month programme, £9,493 per life year saved for the 5-11 month programme, £5,826 per life year saved for the 1-4 year programme.
Trotter 2006a (Trotter et al., 2006)	Life years gained and QALYs (health state HRQL values from literature)	No	No	Dynamic transmission model	Not stated	The paper was exploring the differences in modelling with dynamic model compared to previous paper with static model. But not difference in model structure in the paper	No	DSA	Compared to no vaccination, the ICER for the 2, 3, 4 months programme is £38,164 per life year saved; £31,152 per QALY gained.
Trotter 2006b (Trotter and Edmunds, 2006)	Life years gained	No	No	Dynamic transmission model	Not stated	Two models were explored. The base case and then an additional model to consider the assumptions around the waning of duration of protection	No	Not presented	Compared to the current schedule, the ICER for Strategy 2 is £4,498,000 per life year gained; Strategy 3a (2,4,13 months) -£ 2,000 per life year gained; Strategy 3ab (3, 13 months) - £4,811,000 per life year gained;

						against carriage acquisition			Strategy 4 - £16,419,000 per life year gained
Tudor Edwards 2016 (Edwards et al., 2016)	Strengths and Difficulties Questionnaire (SDQ) and Eyberg Child Behaviour Inventory (ECBI), and the Arnold-O'Leary Parenting Scale (APS).	No	No	n/a	Not stated. Threshold analysis.	No	Yes	CE-plane (PSA); CEAC; DSA	Compared to waiting list, the ICER is £1,295 per one point improvement in SDQ; £237 per one point improvement in ECBI-I; £9,477 per one point improvement in APS
Uus 2006 (Uus et al., 2006)	Cases detected	No	No	n/a	Results compared favourably' - not explicitly stated	No	No	n/a	Compared to infant Distraction Test Screening, the ICER is £12,527 per case detected

Abbreviations: CBA, cost-benefit analysis; CCA, cost consequence analysis; CEA, cost-effectiveness analysis; CEAC, cost-effectiveness acceptability curve; CUA, cost utility analysis; DSA, deterministic sensitivity analysis; EQ-5D, EuroQol 5 dimension; EQ-5DY, child friendly EuroQol 5 dimension; EVPI, expected value of perfect information; EVPPI, expected value of partial perfect information; HUI, health utilities index; ICER, incremental cost-effectiveness ratio; IY, incredible years; NHS, national health service; NMA, network meta-analysis; PedsQL, pediatric quality of life inventory; PSA, probabilistic sensitivity analysis; PSS, personal social services; QWB, quality of wellbeing scale; RCT, randomised controlled trial; ROI, return on investment; SF-6D, short form 6 dimensions; SLR, systematic literature review; SROI, social return on investment; VOI, value of information.

2.6.3 Summary of the evidence

Health protection programmes were the most common intervention category (32%; 22/69) (Atkins et al., 2012, Baguelin et al., 2015, Beck et al., 2021, Brisson and Edmunds, 2003, Christensen et al., 2013, Christensen et al., 2014, Edmunds et al., 2002, Hodgson et al., 2020, Jit and Edmunds, 2007, Jit et al., 2009, Jit et al., 2010, Knerer et al., 2012, Lorgelly et al., 2008, Martin et al., 2009, McIntosh et al., 2003, Melegaro and Edmunds, 2004, Pitman et al., 2013, Siddiqui et al., 2011, (Thomas, 2018, Trotter and Edmunds, 2002, Trotter et al., 2006, Trotter and Edmunds, 2006). The remaining interventions were newborn screening (16%; 11/69) (Bessey et al., 2019, Bessey et al., 2018, Burke et al., 2012, Davies et al., 2000, Ewer et al., 2012, Griebsch et al., 2007, Knowles et al., 2005, Pandor et al., 2004, Pandor et al., 2006, Roberts et al., 2012, Simpson et al., 2005, Uus et al., 2006), parenting support (12%; 8/69) (Edwards et al., 2007, Salisbury et al., 2012, Gardner et al., 2017, McAuley et al., 2004, Morrell et al., 2000a, Morrell et al., 2000b, Simkiss et al., 2013, Edwards et al., 2016) , injury prevention (7%; 5/69) (Achana et al., 2016, Kendrick et al., 2017, Phillips et al., 2011, Saramago et al., 2014), health promotion (4%; 3/69) (Barber et al., 2015, Hollingworth et al., 2012, Renwick et al., 2018), oral health (9%; 6/69) (Davenport et al., 2003, Davies et al., 2000, Kay et al., 2018, Kowash et al., 2006, O'Neill et al., 2017, Tickle et al., 2016), childhood screening (9%; 6/69) (Bamford et al., 2007, Carlton et al., 2008, Craig et al., 2011, Fayter et al., 2007, Fortnum et al., 2016, Grill et al., 2006), breast feeding (6%; 4/69) (Anokye et al., 2020, Hoddinott et al., 2012, Jacklin et al., 2006, Pokhrel et al., 2015), reducing the risk of maltreatment (3%; 2/69) (Barlow et al., 2019, Boyd et al., 2016) and finally, interventions that

cover both parenting support and health promotion (3%; 2/69) (Salisbury et al., 2012, Chance, 2013)

A little under half of the evaluations were QALY-based CEAs (46%; 32/69) (Jacklin et al., 2006, Jacklin et al., 2007, Bamford et al., 2007, Carlton et al., 2008, Craig et al., 2011, Fayter et al., 2007, Fortnum et al., 2016, Barber et al., 2015, Atkins et al., 2012, Baguelin et al., 2015, Beck et al., 2021, Brisson and Edmunds, 2003, Christensen et al., 2013, Christensen et al., 2014, Hodgson et al., 2020, Jit and Edmunds, 2007, Jit et al., 2009, Jit et al., 2010, Knerer et al., 2012, Martin et al., 2009, Pitman et al., 2013, Siddiqui et al., 2011, Achana et al., 2016, Kendrick et al., 2017, Saramago et al., 2014, Bessey et al., 2019, Bessey et al., 2018, Simpson et al., 2005, Kay et al., 2018, Simkiss et al., 2013, Barlow et al., 2019) The majority of evaluations were non-QALY-based CEAs (49%; 34/69), with the health outcomes used including life years gained/saved (29%; 10/34) (Edmunds et al., 2002, Hollingworth et al., 2012, Lorgelly et al., 2008, McIntosh et al., 2003, Melegaro and Edmunds, 2004, Pandor et al., 2004, Pandor et al., 2006, Trotter and Edmunds, 2002, Trotter et al., 2006, Trotter and Edmunds, 2006), oral health outcomes such as dental caries detected or number of teeth free from decay (15%, 5/34) (Davenport et al., 2003, Davies et al., 2003, Kowash et al., 2006, O'Neill et al., 2017, Tickle et al., 2016) and cases of a specific disease or condition detected (12%, 4/34) (Burke et al., 2012, Davies et al., 2000, Ewer et al., 2012, Griebsch et al., 2007). See Table 4 for the list of outcomes. One evaluation (1%) was a CCA (Boyd et al., 2016) and one (1%) a CCA alongside a CEA. (McAuley et al., 2004) Of the studies reporting outcomes in monetary terms, the evaluations identified were SROI (4%; 3/69) (Salisbury et al., 2012, Chance, 2013), CBA (3%; 2/69) (Thomas, 2018) with one of

the CBAs being conducted alongside a CEA (Kowash et al., 2006). Finally, four (4%) were not explicit about the type of evaluation used; however, detailed inspecting suggested two of them could be classified as CCA (Morrell et al., 2000a, Pokhrel et al., 2015) and two as ROI analysis (Phillips et al., 2011, Gardner et al., 2017).

For the QALY-based CEAs, half (50%, 16/32) did not directly measure and value health states rather HRQL weights were extracted from the literature (Achana et al., 2016, Atkins et al., 2012, Baguelin et al., 2015, Beck et al., 2021,

Carlton et al., 2008, Christensen et al., 2013, Craig et al., 2011, Fayter et al., 2007, Fortnum et al., 2016, Kay et al., 2018, Kendrick et al., 2017, Knerer et al., 2012, Pitman et al., 2013, Saramago et al., 2014, Siddiqui et al., 2011, Trotter et al., 2006). Five studies (16% 5/32) used EQ-5D (Barlow et al., 2019, Bessey et al., 2018, Bessey et al., 2019, Hodgson et al., 2020, Martin et al., 2009), five (16% 5/32) used the health utilities index (HUI) (Bamford et al., 2015, Brisson and Edmunds, 2003, Jit and Edmunds, 2007, Jit et al., 2009, Jit et al., 2010) and one (3%, 1/32) used the quality of wellbeing (QWB) score (Simpson et al., 2005). Two studies (6%, 2/32) used the child-specific paediatric quality of life instrument (PedsQL) (Barber et al., 2015, Simkiss et al., 2013) and one study (3%, 1/32) used the child version of EQ-5D, referred to as EQ-5D-Y (Christensen et al., 2014). It was unclear where the HRQL weights used in the economic evaluation came from in two studies (6%, 2/32) (Jacklin et al., 2006, Jacklin et al., 2007).

Randomised controlled trials (RCTs) upon which the economic evaluations were embedded were the most common source of evidence of effectiveness (35%; 24/69) (Anokye et al., 2020, Atkins et al., 2012, Barber et al., 2015, Barlow et al., 2019,

Edwards et al., 2007, Hoddinott et al., 2012, Jit and Edmunds, 2007, Jit et al., 2010, Kay et al., 2018, Kendrick et al., 2017, Kowash et al., 2006, McIntosh et al., 2003, Melegaro and Edmunds, 2004, Morrell et al., 2000a, Morrell et al., 2000b, Mujica Mota et al., 2006, O'Neill et al., 2017, Phillips et al., 2011, Renwick et al., 2018, Roberts et al., 2012, Simkiss et al., 2013, Tickle et al., 2016, Edwards et al., 2016) used to inform the economic evaluations. Regarding the remaining sources, literature searching for evidence (16%; 11/69), systematic literature reviews (12%; 8/69) (Baguelin et al., 2015, Beck et al., 2021, Bessey et al., 2019, Bessey et al., 2018, Carlton et al., 2008, Christensen et al., 2013, Christensen et al., 2014, Craig et al., 2011, Davenport et al., 2003, Davies et al., 2000, Fayter et al., 2007,and meta-analysis including network meta-analysis (6%; 4/69) played a role in informing effectiveness estimates (Achana et al., 2016, Gardner et al., 2017, Kendrick et al., 2017, Saramago et al., 2014). In almost all of these cases, the identified literature results informed parameter estimates for decision models. Literature searching combined with observational data/survey data (7%; 5/69) (Bamford et al., 2007, Pokhrel et al., 2015, Trotter and Edmunds, 2002, Trotter et al., 2006, Trotter and Edmunds, 2006) and the use of a model (largely in the form of epidemiological models) (6%; 4/69) were used to generate effectiveness evidence (Brisson and Edmunds, 2003, Hodgson et al., 2020, Thomas, 2018, Pitman et al., 2013).

Qualitative data was used to estimate effectiveness in two (3%) associated economic evaluations (Salisbury et al., 2012) a questionnaire informed the effectiveness in the economic evaluation presented in Chance et al. 2013 (Chance, 2013). In two studies (3%) (Jacklin et al., 2006, Jacklin et al., 2007, Uus et al., 2006) it was unclear as to what effectiveness evidence was informing the economic

evaluation. Of those remaining, an observational study (Thomas, 2018), a pre-post analysis (Boyd et al., 2016) and a naïve comparison (McAuley et al., 2004) were all identified.

The most commonly reported perspective was the NHS or NHS and personal social services (PSS) (55%, 38/69) (Achana et al., 2016, Anokye et al., 2020, Atkins et al., 2012, Baguelin et al., 2015, Barber et al., 2015, Bessey et al., 2019, Bessey et al., 2018, Christensen et al., 2013, Christensen et al., 2014, Craig et al., 2011, Davies et al., 2003, Ewer et al., 2012, Fayter et al., 2007, Griebsch et al., 2007, Grill et al., 2006, Hodgson et al., 2020, Hollingworth et al., 2012, Jit and Edmunds, 2007, Knowles et al., 2005, Kowash et al., 2006, Martin et al., 2009, Melegaro and Edmunds, 2004, Morrell et al., 2000a, Morrell et al., 2000b, Pitman et al., 2013, Pokhrel et al., 2015, Renwick et al., 2018, Roberts et al., 2012, Saramago et al., 2014, Siddiqui et al., 2011, Simkiss et al., 2013, Simpson et al., 2005, Tickle et al., 2016, Trotter and Edmunds, 2002, Trotter et al., 2006, Trotter and Edmunds, 2006), which is consistent with the latest NICE methods guidance (National Institute for Health Care Excellence, 2022). A considerable number were defined as having a societal perspective in the base case (13%; 9/69) (Salisbury et al., 2012, Boyd et al., 2016, Chance, 2013, Edwards et al., 2007, Kendrick et al., 2017, Mujica Mota et al., 2006, Thomas, 2018, Phillips et al., 2011, Uus et al., 2006) or presenting a societal perspective alongside an NHS or NHS and PSS perspective (13%; 9/69) (Barlow et al., 2019, Beck et al., 2021, Brisson and Edmunds, 2003, Burke et al., 2012, Edmunds et al., 2002, Jit et al., 2009, Jit et al., 2010, Lorgelly et al., 2008, Edwards et al., 2016),. The breadth of the incorporated costs and outcomes in the societal perspectives, however, differed across evaluations. These included costs borne by

the family/caregiver (72%; 13/18) (Barlow et al., 2019, Salisbury et al., 2012, Fortnum et al., 2016, Boyd et al., 2016, Brisson and Edmunds, 2003, Burke et al., 2012, Fortnum et al., 2016, Gardner et al., 2017, Jit et al., 2009, Jit et al., 2010, Kendrick et al., 2017, Mujica Mota et al., 2006, Uus et al., 2006), lost wages (61%, 11/18) (Beck et al., 2021, Boyd et al., 2016, Brisson and Edmunds, 2003, Burke et al., 2012, Edmun ds et al., 2002, Jit and Edmunds, 2007, Jit et al., 2009, Jit et al., 2010, Lorgelly et al., 2008, McIntosh et al., 2003, Mujica Mota et al., 2006), household expenditure (28%, 5/18) (Brisson and Edmunds, 2003, Fortnum et al., 2016, Kendrick et al., 2017, McIntosh et al., 2003, Mujica Mota et al., 2006, travel time (11%, 2/18) (Burke et al., 2012, Fortnum et al., 2016), the local authority/council (22%, 4/18) (Salisbury et al., 2012, Gardner et al., 2017, Kendrick et al., 2017), legal costs (11%, 2/18) (Christensen et al., 2014, Gardner et al., 2017, Saramago et al., 2014) and education costs (17%; 3/18) (Salisbury et al., 2012, Beck et al., 2021, Edwards et al., 2007). The outcomes captured in the societal perspective were solely health in 11 evaluations (61%; 11/18) (Boyd et al., 2016, Edwards et al., 2007, Kendrick et al., 2017, Uus et al., 2006, Barlow et al., 2019, Beck et al., 2021, Brisson and Edmunds, 2003, Edmunds et al., 2002, Gardner et al., 2017, Jit et al., 2009, Jit et al., 2010) including QALYs (33%; 6/18) (Kendrick et al., 2017, Barlow et al., 2019, Beck et al., 2021, Brisson and Edmunds, 2003, Jit et al., 2009, Jit et al., 2010) or another measure of health (28%; 5/18) (Boyd et al., 2016, Edwards et al., 2007, Uus et al., 2006, Edmunds et al., 2002, Gardner et al., 2017). Outcomes were captured in monetary units in four evaluations with a societal perspective (22%; 4/18) (Salisbury et al., 2012, Chance, 2013, Pokhrel et al., 2015, Thomas, 2018). A small number were more prescriptive with the definition of the perspective. For example, describing the perspective as that of the ‘NHS & the family’ (Fortnum et al., 2016), ‘NHS,

education services, patients and family' (Bamford et al., 2007), 'NHS and other government departments' (Carlton et al., 2008) or children and their families (McAuley et al., 2004). Finally, eight economic evaluations failed to explicitly state the perspective (Davenport et al., 2003, Davies et al., 2000, Hoddinott et al., 2012, Jacklin et al., 2006, Jacklin et al., 2007, Knerer et al., 2012, Kay et al., 2018, Kendrick et al., 2017). The extracted intervention and comparator costs are reported in the Appendix. Although they are inflated to 2023 costs using the consumer price index, they are difficult to compare as there is a mix of studies reporting population costs (Atkins et al., 2012, Bessey et al., 2019, Bessey et al., 2018, Boyd et al., 2016, Christensen et al., 2013, Fayter et al., 2007, Griebsch et al., 2007, Knowles et al., 2005, McIntosh et al., 2003, Pitman et al., 2013, Roberts et al., 2012, Trotter and Edmunds, 2002) and individual costs (Bamford et al., 2007, Craig et al., 2011, Davenport et al., 2003, Edwards et al., 2007, Hoddinott et al., 2012, Kendrick et al., 2017, Martin et al., 2009, Phillips et al., 2011, Simkiss et al., 2013, Tickle et al., 2016). In addition, the variation in the perspectives adopted makes cost comparison challenging.

The time horizons over which the costs and outcomes of the interventions were captured were predominantly one of two categories: those with a short time horizon, i.e. 0–10 years (54%, 37/69) (Anokye et al., 2020, Baguelin et al., 2015, Barber et al., 2015, Barlow et al., 2019, Salisbury et al., 2012, Bessey et al., 2019, Boyd et al., 2016, Chance, 2013, Davenport et al., 2003, Davies et al., 2003, Edwards et al., 2007, Ewer et al., 2012, Fortnum et al., 2016, Griebsch et al., 2007, Grill et al., 2006, Hoddinott et al., 2012, Hodgson et al., 2020, Jit et al., 2009, Jit et al., 2010, Kay et al., 2018, Kendrick et al., 2017, Knowles et al., 2005, Kowash et al., 2006, Lorgelly et al., 2008, McAuley et al., 2004, McIntosh et al., 2003, Morrell et al., 2000a, Morrell et al., 2000b, Mujica Mota et al., 2006, O'Neill et al., 2017, Phillips et al., 2011, Renwick

et al., 2018, Roberts et al., 2012, Simkiss et al., 2013, Tickle et al., 2016, Edwards et al., 2016, Uus et al., 2006) or those with a lifetime horizon that was categorized as 76 years and over (32%, 22/69) (Achana et al., 2016, Beck et al., 2021, Bessey et al., 2018, Brisson and Edmunds, 2003, Carlton et al., 2008, Christensen et al., 2013, Christensen et al., 2014, Edmunds et al., 2002, Fayter et al., 2007, Hollingworth et al., 2012, Kendrick et al., 2017, Knerer et al., 2012, Martin et al., 2009, Melegaro and Edmunds, 2004, Pandor et al., 2004, Pandor et al., 2006, Pitman et al., 2013, Saramago et al., 2014, Siddiqui et al., 2011, Simpson et al., 2005, Thomas, 2018, Trotter and Edmunds, 2002, Trotter et al., 2006, Trotter and Edmunds, 2006). The exact number of years over which the costs and outcomes were evaluated was unclear in the case of four evaluations (6%; 4/69) (Burke et al., 2012, Davies et al., 2000, Jacklin et al., 2006, Jacklin et al., 2007, Jit and Edmunds, 2007).

Decision analytic modelling was used in the majority of evaluations (67%; 46/69). Of these, the adopted approaches were decision trees (28%; 13/46) (Bamford et al., 2007, Bessey et al., 2019, Bessey et al., 2018, Burke et al., 2012, Craig et al., 2011, Ewer et al., 2012, Fayter et al., 2007, Fortnum et al., 2016, Griebsch et al., 2007, Knowles et al., 2005, Lorgelly et al., 2008, Roberts et al., 2012, Saramago et al., 2014) dynamic transmission models (22%; 10/46) (Atkins et al., 2012, Baguelin et al., 2015, Beck et al., 2021, Brisson and Edmunds, 2003, Christensen et al., 2014, Edmunds et al., 2002, Hodgson et al., 2020, Pitman et al., 2013, Trotter et al., 2006, Trotter and Edmunds, 2006), Markov models (20%; 6/46) (Carlton et al., 2008, Davenport et al., 2003, Gardner et al., 2017, Grill et al., 2006, Kendrick et al., 2017, Knerer et al., 2012), and a decision tree followed by a Markov model (4%; 2/46) (Achana et al., 2016, Simpson et al., 2005). Five economic evaluations (11%) (Jit

and Edmunds, 2007, Jit et al., 2009, Jit et al., 2010, Melegaro and Edmunds, 2004, Trotter and Edmunds, 2002) described the modelling approach as a 'cohort model', but the exact approach was unclear. Four evaluations (9%) were based on decision models, yet little information on the approach was provided (Davies et al., 2000, Jacklin et al., 2006, Jacklin et al., 2007, McIntosh et al., 2003, Pandor et al., 2004, Pandor et al., 2006). The overwhelming majority of evaluations did not formally incorporate equity considerations (97%; 67/69), see Table 4. Two evaluations (3%) considered the cost-effectiveness results across two different social groups. Achana et al. (Achana et al., 2016) presented sensitivity analysis which considered the impact on the cost-effectiveness results of increasing the rate of unintentional poisoning to the rate observed in the 4th and 5th most deprived quintiles. In the economic evaluation presented by Davenport et al. (Davenport et al., 2003), the cost-effectiveness was evaluated across two groups: those using manual toothbrushing and those using non-manual toothbrushing, which were used as proxies to categorise participants into socioeconomic status. Despite the lack of formal inclusion of equity considerations, a number of the included economic evaluations had what was termed for the purpose of this review a general equity consideration in the decision problem (39%; 27/69). Examples of this include Edwards et al. (Edwards et al., 2007) which included an economic evaluation of an intervention given to socially disadvantaged families; most were socially and economically disadvantaged compared with the mean values for the UK. Mujica et al. (Mujica Mota et al., 2006) conducted an economic evaluation of centres which were established in areas with high levels of deprivation. The economic evaluations presented by Tickle et al. (Tickle et al., 2016) and Gardner et al. (Gardner et al., 2017) did consider whether there were effects of the intervention observed across

social groups but did not consider these groups in the economic evaluation. Finally, Lorgelly et al. (Lorgelly et al., 2008) argued that the results of the societal perspective in their economic evaluation, in which parental productivity was included, provided important equity information. A brief summary of the approaches is provided in Table 5.

Table 5 – Brief summary of approaches

	Category	Total	%
Type of evaluation[1]	QALY-based CEA	32/77	42
	Non-QALY-based CEA	34/77	44
	CCA	4/77	5
	CBA	2/77	3
	SROI	3/77	4
	ROI	2/77	1
Outcomes used in CEA	Life years	10/34	29
	Multiple oral health outcomes	5/34	15
	Cases detected	4/34	12
	ECBI-I	3/34	9
	Timely diagnosis	3/34	9
	Multiple breastfeeding outcomes	2/34	6
	Poison cases avoided	1/34	3
	Quality weighted detected child months		
	Probability of having a fire escape plan	1/34	3
	Proportion of mothers in paid employment or education at 18 months	1/34	3
	Risk reduction (scalds)	1/34	3
	PM2.5 level and the number of quitters	1/34	3
	Unclear	1/34	3
Perspective	NHS or NHS and PSS	38/69	55
	Societal	9/69	13
	NHS (scenario analysis of societal)	9/69	13
	Public sector	6/69	9
	NHS, education services, patients and family	1/69	1
	Public payer	1/69	1
	Health and other public sector providers	1/69	1
	NHS and the family	1/69	1
	NHS and ‘other government departments’	1/69	1
	Children and their families	1/69	1
	NHS (includes scenario with lost labour costs to families of children)	1/69	1
Incorporation of equity considerations in analysis?	Yes	2/69	3

	No	67/69	97
Use of decision modelling?	Yes	46/69	67
	No	23/69	33

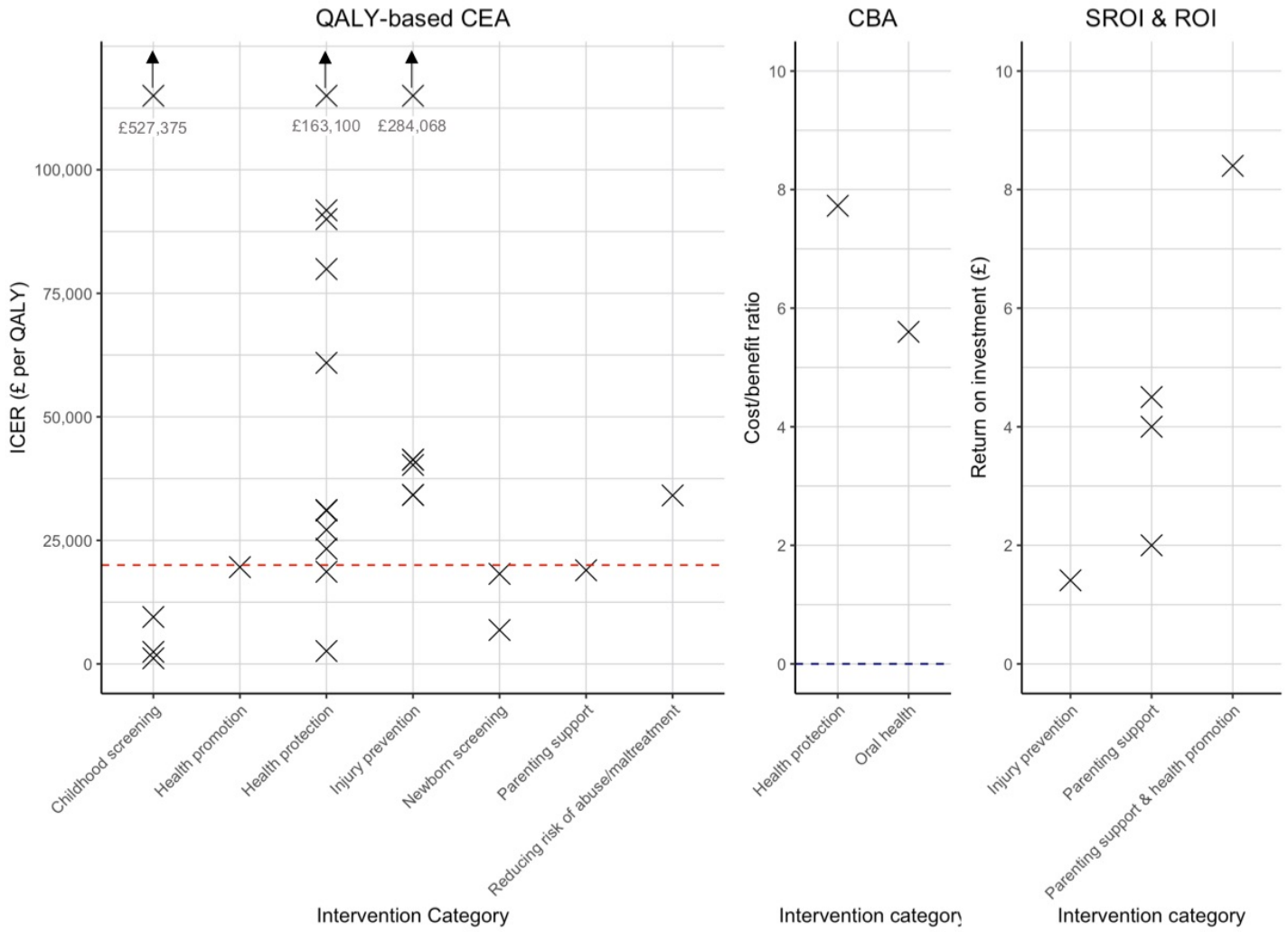
[1]For the purpose of the summary of results, the number of evaluations was considered to be 77 as eight evaluations presented the results of two types of evaluation.

Abbreviations: ECBI, Eyberg Child Behaviour Inventory; PM, particulate matter.

2.6.4 Reported value for money of the interventions

Figure 2 presents the reported results from each study, grouped by the framework used and the intervention group. For QALY-based CEAs, 26 evaluations reported an incremental cost per QALY result. In Figure 2, the NICE-adopted policy threshold of £20 000 per QALY is represented by the dashed red line in the QALY-based CEA plot. Six additional interventions were not included in Figure 2: three were considered to be dominant and three were considered to be dominated. See Table 3 and Table 4 for further details. Two evaluations presented the results in Euros per QALYs and were therefore excluded from Figure 2. The results of the non-QALY-based CEAs and the CCAs are not included as the outcomes of the results differ across evaluations.

Figure 2 - Results of the QALY-based CEAs, CBAs and SROI and ROI by intervention category.



Both of the CBAs reported a benefit to cost ratios above 0 (the point at which the intervention is considered value for money). The study by Thomas (Thomas, 2018) presented the results by disease category, only those results for bronchopulmonary dysplasia are included in Figure 2 as this disease had the highest benefit/cost (B/C) ratio. The other disease category B/C ratios reported in Thomas can be seen in Table 4. All of the identified SROIs and ROIs indicated that for every pound spent on the intervention, a return of >£1 would be generated (Figure 2). For four of the five SROIs and ROIs, the evaluations were conducted without a comparator arm.

2.6.5 Quality assessment

The included studies were appraised for quality and reporting of the economic evaluation by applying the Drummond checklist. Given three of the economic evaluations were each reported in two separate papers, the quality appraisal was conducted for one of the two studies only. This was the case for the evaluations described in Morrell et al. 2000a (Morrell et al., 2000a) and Morrell et al. 2000b (Morrell et al., 2000b); Pandor et al. 2004 (Pandor et al., 2004) and Pandor et al. 2006 (Pandor et al., 2006); and Jacklin et al. 2007 (Jacklin et al., 2007) and NICE 2008 (Jacklin et al., 2006).

A well-defined question was posed for the majority of economic evaluations. As part of this, the time horizon was generally well-reported albeit the time horizon was not clearly described in three economic evaluations and the perspective was not explicitly stated in eight economic evaluations. All economic evaluations reported the competing interventions.

The reporting of the effectiveness of the intervention was generally well reported, however in two of the economic evaluations, the source of the effectiveness evidence was unclear. The reporting of whether all of the relevant costs and consequences of each alternative intervention were present was again relatively well described, yet in eight of the economic evaluations it was unclear whether all relevant costs and consequences had been described as the perspective of the evaluation had not been stated.

The measurement of the costs and consequences was reported in all economic evaluations yet the value of the costs and consequences was unclear or not reported in 16 economic evaluations. The latter was due to the evaluative framework used in which the value of the health gains was not made explicit.

The reporting of the discount rate was only deemed relevant to those economic evaluations with a time horizon beyond 1 year. Of those deemed relevant, the discount rate for costs and outcomes was not reported in 20 economic evaluations. In 13 of these no discount rate was reported and in the remaining seven, there was only a discount rate reported for the costs. Eight of the economic evaluations failed to adequately report uncertainty, that is there was no uncertainty analysis reported. Finally, only 29 of the economic evaluations were deemed to have covered all of the issues of concern in the presentation and discussion of results. Of these, the vast majority based the conclusions on overall index or ratio but only 15 alluded to other important factors such as the distribution of costs and outcomes or ethical considerations, 24 discussed the feasibility of adopting the intervention, and only 21 reported the exploration of uncertainty and he need for future research. The results of the detailed Drummond checklist are presented in the appendix. The Drummond

checklist was used for quality appraisal in this chapter but it should be noted there are more recent checklists such as the CHEERS 2013 checklist (Husereau et al., 2013) and CHEERS 2022 checklist (Husereau et al., 2022). The Drummond checklist covers 10 criteria and provides a high-level assessment of whether the key aspects of an economic evaluation have been reported. The CHEERS checklists were developed to standardise reporting of economic evaluations with the 2013 version covers 24 items and the 2022 version covering 28 items and reflect new methods and developments in the field, as well as reflecting the increased role of stakeholder involvement including patients and the public (Husereau et al., 2022). As the results of the quality appraisal did not influence inclusion in the synthesis, the use of the older Drummond checklist is considered adequate for this work.

2.7 Discussion

2.7.1 Main Findings

The results show the breadth of UK-focussed economic evaluations of early childhood public health interventions reported or discussed in the published literature. The methods adopted in the demonstration of value for money showed a lack of consistency across many aspects including the type of economic evaluation, the health outcomes captured and the perspective adopted. Fourteen papers reported on all aspects of the Drummond Checklist meaning 55 (80%) were lacking elements required of a well-reported economic evaluation.

Many of the evaluated interventions were deemed value for money from the perspectives taken. Twelve (38%) of the QALY-based CEAs are cost-effective

against the NICE policy threshold of £20 000 per QALY. However, the interpretation of some of the results may require particular consideration given the health, economic, political and social context of these studies may have changed between 2000 and present day.

Because of the evaluative framework chosen for many of the other studies a robust statement of value for money of the intervention is not always possible. For example, in non-QALY-based CEAs, an explicit statement of cost-effectiveness is challenging when the outcome is a metric other than a generic measure of health such as the QALY as it is not possible to compare across different health dimensions. Much has been made of the limitations and challenges of using QALYs for paediatric populations (Petrou, 2022, Rowen et al., 2020) but their use does allow the comparison of interventions across diseases areas as well as the consideration of the displaced resources (or the 'opportunity cost').

All of the interventions evaluated using SROI, ROI or CBA frameworks could be considered value for money as they were deemed to generate more monetary benefits than the costs (having a ratio of >£1 of benefit per £1 of cost in the case of the SROI and ROI). Yet, caution is required when considering these results. None of the SROI or ROI evaluations incorporated the opportunity cost and it was made explicit in only one CBA (Thomas, 2018). The exclusion of such a fundamental aspect of economic evaluations results in an overestimation of the value of the intervention and risks doing more harm than good to the public by neglecting the health foregone through the net effect of spending. Furthermore, four out of five of the SROI and ROI evaluations were conducted without a comparator. The lack of the

inclusion of the opportunity cost or a comparator may feed into the previously reported challenges of allocation decision using ROI (Brousselle et al., 2016).

The broad range of the types of evaluation and outcomes may reflect the diverse nature and needs of the decision-makers relevant to such interventions. Public health commissioning decisions in the UK are often the responsibility of local commissioners of services, such as local authorities and integrated care boards (ICBs), previously called clinical commissioning groups (CCGs), not national decision-makers such as NICE. Although NICE's public health approach allows for flexibility in the methods, evaluations conducted using the NICE methods guide may fall short of reflecting the challenges faced by ICBs (Hinde et al., 2020). A paper by Frew et al. (Frew and Breheny, 2020) detailed the context of local authority health economic decision making. It highlighted numerous challenges including the shortcomings of using QALYs, the importance of including wider societal outcomes and the incorporation of multiple budgets. Such perceived shortcomings of 'traditional' CUA could in part explain the range of evaluative frameworks and outcomes identified in this review.

Although only a minority, a number of evaluations attempted to incorporate the wider social value of the intervention beyond the value to the health care system. A total of 18 evaluations adopted a 'societal perspective' but the results identified a lack of consistency in the included aspects of value. The inclusion of lost productivity to the parent or caregiver (in the form of wages lost) featured heavily in the evaluations, as did incorporating costs falling on special education services and legal services, yet none featured consistently. The implication of such inconsistencies is that value judgements about what 'should' count are falling on the researchers rather than

socially legitimate decision-makers (Williams, 1991). Public health guidance issued by NICE (National Institute for Health Care Excellence, 2022) does allow for flexibility in the costs and outcomes considered in an economic evaluation, but the lack of explicit value judgements may facilitate inconsistencies. Certain decision-making organisations including NICE have specified their value preferences by defining reference cases. In the case of the NICE public health methods guidance, it states that health effects should be measured and valued using QALYs, but it also stipulates that non-health effects should be measured and valued on a case-by-case basis (National Institute for Health Care Excellence, 2022). The lack of explicit value judgements in health economic guidance may be the cause of inconsistencies in those aspects included in the studies identified in this review.

Even in the presence of consistency of the included aspects of value, the identified costs and outcomes falling on each sector need to be assigned weights to be traded-off. Such trade-offs may be implicit or made explicit through the expression of a social welfare function or through budget allocations (Paulden and Claxton, 2012). A rigid definition of all aspects deemed to be socially valuable to all early childhood public health decisions is undoubtably challenging. However, analysts and decision makers alike would benefit from more explicit messages regarding the most important aspects that require inclusion. Those aspect could then be incorporated consistently across evaluations into a framework such as the one proposed by Walker et al. (Walker et al., 2019).

The results showed the most common time horizons were either 0–5 years or those that extended beyond 76 years. Reasons for this appear to be based around whether an intervention was a trial-based evaluation or those that incorporated

decision modelling to model the long-term costs and outcomes. Guidance in the economic evaluation literature indicates that time horizons should be long enough to reflect all of the important differences in costs and outcomes between comparators (Drummond et al., 2015, National Institute for Health Care Excellence, 2022). Such horizons may be well defined for patient-focussed health technologies but not for population-focussed interventions that aim to change behaviour, education, housing and so on. Given the evidence linking the social determinants of health and life expectancy (Ingleby et al., 2021), it stands that a lifetime horizon may be more appropriate.

One aspect of relative consistency in the methods was the lack of the formal incorporation of equity considerations. Interventions implemented in early life have considerable potential to disrupt existing inequalities and remain a fundamental reason for targeting these important years. Yet, the formal incorporation of equity does not appear to be common practice in economic evaluation in this setting. There are now a number of approaches to formally incorporate equity considerations into CEAs (Cookson et al., 2017a).

The focus of this review was to identify interventions relevant to UK decision-makers. However, there may be important information available in an international context to aid learnings around the use of methods and approaches relevant to the UK. Future research may consider describing the methods and approaches adopted in the global evidence base to highlight consistencies in the demonstration of value for money in those economic evaluations developed for an international context.

Learning lessons

The presented systematic review reiterates the plentiful methodological challenges when evaluating childhood interventions (Petrou and Gray, 2005). The challenges may account for the prior experience of evaluating a number of large-scale early childhood and/or parenting interventions, which have failed to demonstrate cost-effectiveness (or more broadly value for money) in the UK (Edwards and McIntosh, 2019). The impact of such challenges are likely to impact on the results of the economic evaluation. The subsequent chapters in this thesis will attempt to build a more extensive framework to allow the consideration of these methodological challenges and demonstrate the impact on the determination of value for money.

2.7.2 Strengths and limitations

The comprehensive and robust search strategy used to identify the evidence is a real strength of this review. This is evidenced through the almost 17,000 records retrieved from the searched databases. There does always remain the possibility that studies may have been missed. However, given the high number of systematic literature reviews identified in this review and the approach to retrieving all studies included in such reviews, it is hoped this review provides a comprehensive overview of the relevant economic evaluations.

The focus on UK-specific economic evaluations provides a further strength. The review aimed to determine the methodological approaches used in economic

evaluations and given the numerous positive and normative reasons why results of economic evaluations may differ across jurisdictions (Drummond et al., 2009) focussing on one jurisdiction (i.e., the UK) avoids the potential for heterogeneity across the methods identified. This review therefore considers the range of methodological approaches across a relatively homogenous combination of evaluations, which should all be adhering to capturing value for money in a similar way.

Despite the review being based on a comprehensive search of the published literature, a limitation is that there may be relevant and yet uncaptured evaluations in the grey literature. It is feasible that government and charitable organisations have produced health economic evidence. This is evidenced through the identification of economic evaluations produced by NICE (Jacklin et al., 2006), Social Value UK (Chance, 2013), Barnardo's (Salisbury et al., 2012) and the Joseph Rowntree Foundation (McAuley et al., 2004) which were not identified in the database search but rather through the identified literature reviews. The search strategy included the HMIC database and lists grey literature amongst its coverage, hence the decision to include relevant grey literature in the reference searches of systematic reviews. The inclusion of the grey literature identified though the supplementary reference searching does in part explain the high number of studies identified in this way (5 of the 13). We considered it important to include grey literature as it is included in the HEER tool (Public Health England, 2019a), yet a pragmatic decision was made for the purpose of this review. Future literature reviews may consider searching and identifying a wider range of grey literature sources.

A further potential limitation was the difficulty posed in defining the interventions to be included in this review. As the focus of the review was the rather broad early childhood PHIs, there were difficulties in defining the extent of 'public health' and 'early childhood' for the purpose of the search strategy. There may have been eligible studies that fell outside of the broad list of search terms included in the review. The review focussed on interventions that aimed to improve the health of the infant or child yet health improvement in early childhood may be dependent on lifestyle and environment not merely based on biology and genetics (Marmot, 2013). It stands that a social model of health may have generated different results. A pragmatic decision was made to include health terms and terms to capture the wider determinants of health in the search strategy.

2.7.3 Comparison to previous literature reviews

The literature has seen a number of reviews of economic evaluations of childhood interventions conducted in the past, albeit few have focused on health and even fewer have presented economic evidence directly relevant to the UK context. This literature review identified a number of systematic literature reviews and scoping reviews as part of the screening process and a handful of these are discussed below.

Of the literature reviews aiming to identify health economic evaluations in early childhood, two have focused on weight management schemes. A systematic review by Döring et al. (Döring et al., 2016) identified 6 relevant studies conducted in various countries around the world. The results showed the majority were estimated using cost-effectiveness analysis (CEA). Interestingly, the majority of studies failed to

demonstrate an effect size yet were still deemed cost-effective. The study authors concluded that the existing evaluations were of limited use for decision making purposes. None of the eligible studies were conducted in the UK, echoing the findings of a previous systematic review (Bond et al., 2009).

Dalziel and Segal (Dalziel and Segal, 2012) conducted a review of cost-effectiveness evidence of home visiting programmes for the prevention of child maltreatment. The study showed a wide range in the costs of interventions but again showed the majority were cost-effective. However, all cost-effectiveness results were presented from an Australian perspective and only two of the 33 identified studies originally conducted in the UK.

A number of literature reviews have been conducted with the aim of capturing a broader definition of preventative interventions for early childhood, departing from the simple remit of health to consider development, behavioural problems, education and social care. A literature review conducted by Bennett (Bennett, 2008) identified interventions to improve education and care in early childhood. The study considered interventions conducted in any OECD country. Sixteen economic studies were presented with the inclusion of one UK-based educational study. Reynolds and Temple (Reynolds and Temple, 2008) conducted a review of predominantly US-based early childhood development programmes delivered in preschool/kindergarten. No formal economic evaluations were described but the evidence in terms of the economic returns to investments were described. Karoly (Karoly, 2012) conducted a review of 19 US-based interventions designed to improve health, development and education and presented the cost-benefit ratios of these interventions.

A recent systematic review by El-Banna and colleagues (El-Banna et al., 2021) identified the economic evidence of children's social care interventions. The review included interventions for children and adolescents defined as 'in need' with no restriction on the location of the study. The identified studies were all conducted as non QALY-based CEA or QALY-based CEA. The inclusion criteria, however, limited evaluations to those with a comparator. The review highlighted the majority of interventions were cost-effective but with outcomes rarely expressed in a generic measure of health (such as the quality-adjusted life year (QALY) comparison of interventions was challenging. The majority of included studies were conducted in the UK.

A study conducted by Stevens (Stevens, 2014) identified the evidence of the cost-effectiveness of UK parenting programmes for preventing behavioural problems in children. The evidence indicated the potential for interventions to be cost-effective (and even cost saving) yet the authors concluded there were considerable gaps in the literature. Finally, a number of studies have identified economic evidence of education interventions in early childhood. A study conducted by Dalziel et al. (Dalziel et al., 2015) identified the economic evidence of education interventions for disadvantaged children. The results show considerable uncertainty around the outcomes generated from investments in early childhood education. Only one of the 13 identified studies was conducted in the UK.

Previous literature reviews of the economic evidence (described above) have focused on specific health interventions or those delivered in global settings making comparative analysis difficult owing to evident heterogeneity. In addition, there has been little attention paid to the diversity of methods used. It is hoped the presented

review can provide evidence to assist analysts and decision makers tasked with the important role of improving population health and health equity among those in the early years of life and beyond.

2.7.4 Research and policy implications

The gap between the evidence available in the peer-reviewed literature and the decisions made in the UK regarding early childhood interventions has been highlighted (Powell et al., 2021). Questions have been asked of the appropriateness of the methods used to capture the value for money of such interventions (Rutter, 2006). The results of this systematic review reveal the methods used in the literature to date may not be appropriate. This appears to be for two reasons. First, the literature highlights the lack of an explicit recognition of just what the aspects of value are. Normative questions of value outline the outcomes that influence decision making and their relative worth. The literature is rich with descriptions of the importance of the early childhood period throughout the life course (see Chapter 1). It is clear many of these aspects do indeed have value to local public health decision makers (Frew and Breheny, 2019), yet this review shows that these are not necessarily captured in economic evaluations. The literature would benefit from a clearer statement regarding the normative aspects of value when it comes to early childhood PHIs. However, this would inevitably stop short of defining a full social welfare function (i.e., all aspects of social value defined *ex ante*), not least due to the fact that not every local decision maker will have the same health goals and therefore may not value the same costs and outcomes.

Second, within those aspects of value, there needs to be consistency in the way in which analysts incorporate these. For example, the results showed a considerable number adopting a societal perspective, but the inconsistencies in those included aspects were apparent. The health economic literature could benefit from a taxonomy of the types of societal perspectives available. This is due not only to the breadth of the potential aspects but the ambiguity regarding exactly what societal costs and outcomes means. Furthermore, future analyses must adhere to the principles of internal consistency and apply the corresponding outcomes along with the costs.

This review has discussed a series of issues that will be helpful to consider for those generating and using future economic evaluations of similar interventions. These were detailed as: the choice of evaluative frameworks and the incorporation of the opportunity cost, the decision-making context, the perspective adopted, the incorporation of equity considerations, the choice of time horizon and the inclusion and interpretation of decision uncertainty. If the outlined issues are considered, this will help decisions makers make informed decisions regarding which intervention are most likely to produce certain outcomes.

Finally, this systematic review should provide decision makers in the UK with the first comprehensive collation of the published health economic evidence available to them. Local public health decision makers tasked with spending a budget can incorporate the results identified in this review along with the methods available to them, whether that is the Public Health England's Prioritisation Framework tool (Public Health England, 2019b) or alternative approaches, to make spending decisions across public health programmes.

2.8 Conclusion

This systematic review provides the first summary of the UK-specific health economic evidence for early childhood PHIs. In addition to identifying the breadth of evidence available in the published literature, this review provides an overview of the methodological approaches used. The lack of consistency identified in the methods has highlighted a number of issues that may require consideration in the future generation of economic evaluations of similar interventions. It is hoped the results of this systematic review can provide a foundation to help improve decision-making and provide a starting point for methodological developments in the early childhood public health context.

Chapter 3: Framework and Case Study

The systematic literature review presented in Chapter 2 demonstrates how the evidence base addresses a number of the previously described methodological challenges in making resource allocation decisions about early childhood PHIs. Amongst these challenges were (i) the incorporation of health equity, (ii) the extrapolation of the results to incorporate the life course of the child and (iii) the incorporation of non-health costs and benefits.

There are a number of additional challenges over and above the three highlighted however these three elements have been selected for exploration throughout this thesis for a number of reasons. First, Public Health England (now known as the UK Health Security Agency and Office for Health Improvement and Disparities) published a report in 2019 entitled 'What Good Children and Young People's Public Health Looks Like' (Pearson et al., 2019). The report advocates 'taking a life course approach to children's public health' and that all policies should have the 'aim of impacting positively on social determinants that we know have an impact on health and wellbeing' (Pearson et al., 2019). Second, the three areas of consideration have been highlighted as important to public health decision-makers. A Delphi panel of public health decision-makers in England, Wales and Ireland conducted by Frew et al. (Frew and Breheny, 2019) found high agreement across decision makers that evaluations should: incorporate wellbeing and broader outcomes in decision making; formally weight outcomes by population subgroup; and ensure time horizon captures long term costs and outcomes, including consideration of the individual's lifetime. The Delphi panel were reviewing decisions based on all public health economic evidence and not just childhood decisions. Public health decisions, whether child or adult, are the purview of clinical commissioning groups within local authorities. The

outcomes of the Delphi panel are therefore assumed to reflect the values of public health decision makers for childhood interventions.

This chapter will outline the methods available for researchers and policy-makers considering (i) incorporating equity; (ii) extending the time horizon; and (iii) broadening the perspective of an early childhood PHI evaluation. The thesis will leverage methods and show the impact of incorporating them on an assessment of value for money. In order to do this a case study will be used throughout the thesis. The identification of the case study will be described which may then help think about which of the methods are relevant to the decision problem of the case study. Following the case study description, the methods available in the literature will be described.

3. 2 Identification of the case study

To demonstrate the impact of incorporating the aspects outlined in Section 3.1 on assessments of value, an early childhood public health intervention was sought to act as a case study. Identification of potential case studies occurred through a number of approaches, including searching the results of the systematic review presented in Chapter 2; searching the York Trials Unit for completed trials and evaluations; and through discussion with my PhD supervisors and thesis advisory panel. A short list of interventions was compiled and the appropriateness of the interventions to act as a case study for the purpose of exploring those aspects outlined in Section 3.1 was discussed (see appendix for the short list). Principal investigators and primary authors of corresponding manuscripts were contacted to

further discuss the appropriateness of the interventions and ease of access to the individual participant data from the corresponding trial.

3.2.1 The E-SEE Steps Trial

Following screening, the E-SEE Steps trial (Blower et al., 2021b) was identified as the most appropriate case study. E-SEE Steps is a multi-layer intervention for parents designed to prevent mental health and behavioural difficulties of very young children by enhancing social and emotional wellbeing. Positive social and emotional wellbeing in the early years of life is associated with positive health and development outcomes later in life. The parent-child relationship plays a crucial role in the development of child social and emotional wellbeing meaning parenting knowledge and skills as well as parental mental health may impact the child.

The E-SEE Steps intervention aims to target this by providing three elements of the Incredible Years (IY) programme, given to the families of young children. The elements are provided in a proportionate universal (PU) approach. That is, the intervention is provided universally with differing degrees of intensity depending on need or deprivation. Proportionate universalism was first proposed in the seminal work by Marmot et al. (Marmot, 2010) in which it was stated “greater intensity of action is likely to be needed for those with greater social and economic disadvantage, but focusing solely on the most disadvantaged will not reduce the health gradient, and will only tackle a small part of the problem”.

The IY programme delivered as part of the multi-layer intervention is a parenting programme designed to enhance the social and emotional wellbeing of children

(Pidano and Allen, 2015). The universal aspect of E-SEE Steps is the Incredible Years Babies Book (IY-B), which is provided to all families. The targeted aspects are IY Infant (IY-I) and Toddler (IY-T) programmes, for 0-1 and 1-3-year-olds respectively. The IY-I and IY-T are provided as groups sessions delivered by trained professionals to 10 to 12 parents for two hours a week over a period of 10-14 weeks.

The primary aim of ESEE-Steps was to assess whether the E-SEE Steps programme enhanced child social and emotional wellbeing at 20 months of age compared to service as usual.

3.2.1.1 E-SEE Steps Trial Design

The E-SEE Trial was conducted as a community-based, pragmatic, two-arm randomised controlled trial. A total of 341 mothers were block-randomised to E-SEE Steps or service as usual. Randomisation occurred on a 5:1 (intervention to control) ratio. Stratified randomisation was used and divided participants using the following variables: baseline PHQ-9, child ASQ:SE-2 scores, child and parent sex, and research site. Participants, IY leaders and process evaluators were not blinded to the allocation. The trial was conducted over a 30-month time horizon across four research sites based on local authority areas made up of two from the North of England, one from the Midlands of England and one from the South of England. For further information on the E-SEE Steps trial design, see Bywater et al. (Blower et al., 2021b, Blower et al., 2021a).

3.2.1.2 Population

The trial population was formed of parents of infants less than 8 weeks old. Participants were identified by health visitors, family and child services, as well as self-referral if participants had heard about the E-SEE Trial via other channels.

3.2.1.2 Interventions

All intervention parents received the IY-B, which was considered the universal level stage of E-SEE Steps. The IY-B is a guide and journal designed to promote the physical, social and emotional development of the baby (Pidano and Allen, 2015). The IY-B is sent to participants and is designed to be conducted at home. Selected parents were then offered IY-I and/or IY-T for parents of children aged 0–1 and 1–3 years of age, respectively. IY-I is a group-based programme in which parents and infants attend for two-hour sessions, once a week for 10 weeks. The sessions are facilitated by health professionals to support training and allow discussion amongst parents with the aim of encouraging physical and social development. IY-T is a further group-based programme in which parents and toddlers attend for two-hour sessions, once a week for 12 weeks. The sessions are again facilitated by health professionals to promote social and emotional development and to help toddlers feel loved and secure. Eligibility for IY-I and IY-T was based on the parent's level of depression as measured using Patient Health Questionnaire (PHQ-9) and/or the child's level of emotional and social wellbeing as measured by Ages and Stages Questionnaire: Social Emotional, Second Edition (ASQ:SE-2) (Squires et al., 2015). Pre-defined thresholds were set for eligibility for IY-I and IY-T and decisions on

which participants were eligible was made at 2- and 9-months post baseline during data collection.

The comparator intervention was service as usual (SAU). SAU did not include IY interventions but did include the potential for alternative early childhood parenting programmes offered in the local authority. Participants were randomly allocated on a 5:1 ratio to the IY or SAU arms of E-SEE Steps.

3.2.1.3 Outcomes

The primary outcome of the E-SEE Steps Trial was child social and emotional well-being as measured using ASQ:SE-2 (Squires et al., 2015). ASQ:SE-2 is a screening tool for social and emotional development of infants and toddlers measuring: self-regulation, compliance, social communication, adaptive functioning, autonomy, affect and interaction with people. Multiple versions of ASQ:SE-2 exist for a range of ages from 1 to 72 months. Measurement of the infant's ASQ:SE-2 score was completed by the parent.

There were multiple secondary outcomes for both parent and child. The child's secondary outcomes included child behaviour, as measured by Strengths and Difficulties Questionnaire (SDQ) 2-4 version (Goodman, 1997). SDQ is a 25-item questionnaire completed by the parents of children aged 2 to 4 years old. It is based on 6 sub-group scores including: emotional problems; conduct problems; hyperactivity; peer problems; prosocial problems and an impact sore. The child's cognitive development and health-related quality of life (HRQL) were measured using the Pediatric Quality of Life Inventory (PedsQL) Infant Scale (Varni et al.,

1999). The PedsQL Infant Scale is a 45-item questionnaire completed by the parents of children aged 13 to 24 months old.

The parent's secondary outcomes included screening for depression using the PHQ-9 tool (Kroenke et al., 2001). PHQ-9 is a self-completed 9-item questionnaire and provides an index of depression severity. Parent HRQL was measured using the five-dimension EuroQol instrument, EQ-5D-5L (van Reenen et al., 2019), which is a self-completed measure covering five dimensions of self-reported quality of life: mobility, ability to self-care, ability to undertake usual activities, pain and discomfort, and anxiety and depression. Parent and child attachment and interaction was measured using the self-reported Maternal Post-Natal Attachment Scale (MPAS) (Condon and Corkindale, 1998) and Paternal Post-Natal Attachment Scale (PPAS) (Condon et al., 2008), which comprises 19 self-reported items. Finally, parenting skill was assessed using the Parenting Sense of Competence tool (PSoC) (Johnston and Mash, 1989) which is self-completed questionnaire covering 17 items. The final effectiveness outcome was based around an assessment of the child-parent dyad. Assessment was measured using the CARE Index Infant/Toddler instrument (Crittenden, 1981) which is based on independent observation of three to five minutes of play. CARE Index Infant/Toddler is considered to be suitable for infants aged 1–48 months. Primary parent and child service use was captured by the parent by completing a Client Service Receipt Inventory (CSRI).

ASQ:SE-2, PHQ-9, MPAS, PPAS, PSoC, EQ-5D5L and CARE Index Infant/Toddler were all measured at all time-points: baseline, follow-up 1 (FU1, 2 months post-baseline), follow-up 2 (FU2, 9 months post baseline) and follow-up 3 (FU3, 18 months post-baseline). SDQ and PedsQL were measured at FU3 only.

3.2.1.4 Resource use

The perspective of the evaluation was that of the public health sector (i.e. NHS and Personal Social Services). Parental and child resource use was recorded throughout. Resource use and costs were grouped as follows: intervention-related; primary care; secondary care; mental health care; community service; social service; childcare; and absent workdays. For a detailed description of the costs, see Cox et al. (Cox et al., 2022).

3.2.1.4 Trial Results

The results of the E-SEE Steps randomised controlled trial showed a borderline statistically significant higher ASQ: SE-2 score in the IY arm compared to SAU indicating the IY arm had a detrimental effect on children's outcomes (3.02, 95%CI: -0.03, 6.08). PHQ-9 scores showed improvements in the IY arm, although not statistically significant (-0.61, 95%CI: -1.34, 0.12). Parent EQ-5D showed a statistically significant improvement for the primary caregiver in the IY arm compared to SAU (0.02, 95%CI: 0.00, 0.04). The infant CARE index and PCOS failed to show any signal of difference between arms.

The difference between the arms for the outcomes measured at 18-months only showed no significant difference. SDQ was higher in the IY arm (0.64, 95%CI: =0.64, 1.91), PEDSQL was lower in the IY arm (-0.60, 95%CI: -3.22, 2.01) and MPAS was higher in the IY arm (0.94, 95% CI, -0.76, 2.64).

The trial results are summarised in Table 6. The results have been colour coded to highlight the measures in which there was an improvement (referred to as 'better') in the IY arm outcome (green) and those that had a detrimental impact (referred to as 'worse') on the IY arm outcome (red). As Table 6 shows, there is considerable variation in whether IY was shown to have a beneficial or detrimental impact on the trial participants compared to SAU.

Table 6 - E-SEE Steps results

Measure	**Difference (IY – SAU)**	**Better/worse in the IY arm**
ASQ:SE-2	3.02 (-0.03, 6.08)	Worse
PHQ-9 (primary care giver)	-0.61 (-1.34, 0.12)	Better
Infant CARE-Index	-0.25 (-1.09,0.59)	Worse
PSOC	0.07 (-1.74, 1.87)	Worse
EQ-5D	0.02* (0.00, 0.04)	Better
SDQ	0.64 (-0.64, 1.91)	Worse
PEDSQL	-0.60 (-3.22, 2.01)	Worse
MPAS	0.94 (-0.76, 2.64)	Better
*indicates statistical significance		

3.2.1.5 Economic Evaluation Results

For the purpose of the economic evaluation, adult and child trial outcomes were mapped to QALYs. The EQ5D-5L of the parents was mapped to an EQ5D-3L value set to generate HRQL values (van Hout et al., 2012). A more recent validated mapping function has been developed by the NICE Decision Support Unit (Hernandez et al., 2020) however this was not implemented in the published economic evaluation of E-SEE Steps (Cox et al., 2022). The HRQL values for the children were estimated by mapping the SDQ score at FU3 onto the Child Health Utility (CHU9D) questionnaire, which was used to derive HRQL values (Furber et al., 2014). As SDQ score was only captured at FU3, baseline HRQL was assumed to be the same across arms at baseline.

The results of the published within-trial economic evaluation of E-SEE Steps (Cox et al., 2022) showed the E-SEE Steps programme had an incremental cost-effectiveness ratio (ICER) of £13,011 per QALY compared to service as usual for the adult costs and outcomes. The ICERs for the child and overall (adult-child dyad) were dominated [11] and £20,061 per QALY, respectively. The results are summarised in Table 7. The following results have not been generated by myself and I was not involved in the within-trial economic evaluation of E-SEE Steps, rather they are the results that were reported in the literature (Cox et al., 2022).

[11] An intervention or strategy is considered dominated if it has higher costs than the comparator and lower effects.

Table 7 - Cost-effectiveness results of the E-SEE Steps trial

	Costs	QALYs	Inc. costs	Inc. QALYs	ICER	NHB*
Child						
SAU	£1,000.28 (£164.27)	1.27420 (0.0039)	-	-	-	-
E-SEE Steps	£1,177.33 (£83.20)	1.26957 (10.0016)	£177.05 (£157.04)	-0.00463 (0.0040)	Dominated	-0.016
Adult						
SAU	£942.44 (£264.63)	1.31392 (0.0192)	-	-	-	-
E-SEE Steps	£1,388.26 (£128.03	1.34818 (0.0079)	£445.82 (£226.73)	0.03427 (0.0217)	£13,010.68	0.0045
Dyad						
SAU	£1,988.61 (£319.82)	2.58680 (0.0176)	-	-	-	-
E-SEE Steps	£2,609.46 (£174.28)	2.61775 (0.0084)	£620.85 (£340.75)	0.03095 (0.0204)	£20,061.02	-0.0104

*****NHB is estimated using £15,000 as the policy threshold (λ) (Martin et al., 2020). NHB = inc. QALYs – (inc. costs / λ)
Abbreviations: ICER, incremental cost-effectiveness ratio; NHB, net health benefit; QALYs, quality-adjusted life years; SAU, service as usual.

3.1 Introduction to potential methods

The methods available for considering incorporating equity, extending the time horizon and broadening the perspective are outlined below.

3.1.1 Equity

Chapter 1 described the various evaluative frameworks and their normative underpinnings used in resource allocation decisions. Cost-effectiveness analysis is the most commonly used framework in the evidence base (see Chapter 2) and therefore the methods of incorporating equity into CEA are first considered. This is followed by alternative evaluative frameworks.

Cost-effectiveness analysis

As described in Chapter 1, CEA is borne out of extra-welfarism and is predicated on health being the maximand, which is subject to the budget constraint. A number of contributions to the literature have identified how CEA can address equity concerns and the respective limitations of the methods (Cookson et al., 2017a, Ward et al., 2022, Avanceña and Prosser, 2021). A systematic review by Ward et al. (Ward et al., 2022) groups results into the following: distributional cost-effectiveness analysis (DCEA), extended cost-effectiveness analysis (ECEA), multi-criteria decision analysis (MCDA), equity-based weighting (EBW) methods and mathematical programming (MP). These categories will be briefly described below.

DCEA (Asaria et al., 2016) is based on the measurement of the distribution of health pre- and post-intervention across subgroups. The post-intervention health gains (e.g., in quality-adjusted life years (QALYS)) are summed with the baseline level of health (e.g., quality-adjusted life expectancy (QALE)) to assess whether social gradients in health have changed. The framework then facilities the calculation of how much improvement in health efficiency a decision maker would be willing to trade off to improve health equity.

ECEA (Verguet et al., 2016) extends traditional cost-effectiveness analysis by incorporating an additional consideration, commonly financial risk protection (FRP). The health impacts of an intervention for each subgroup of the stratified population are reported alongside the FRP impacts for each subgroup. Thus, decision makers can consider both in resource allocation decisions.

MCDA (Jit, 2018) involves the specification of weights to apply to multiple dimensions to allow the incorporation of several objectives into the decision. Cost-effectiveness analysis may form one dimension, but other dimensions may be specified such as severity of the disease being targeted, size and characteristics of the population likely to benefit from the intervention. It is at this point that equity-relevant dimensions can be included. The dimensions are then assigned weights and the various interventions are ranked or scored. The result of an MCDA provides a ranking of the interventions that maximised the multiple criteria.

EBW simply applies weights to QALYs, costs and/or the decision threshold with which to compare an incremental cost effectiveness ratio (ICER). This allows greater weight to be applied to interventions for specific groups of the population, based on specified characteristics. The weights may be elicited or specified by the decision makers.

MP (Stinnett and Paltiel, 1996) optimises a set of interventions to maximise health (e.g., QALYs) subject to constraints. The constraints likely include the budget (meaning a traditional CEA approach is used i.e., maximising QALYs s.t. the budget) but can also include equity-relevant criteria. MP therefore is not based on equity outcomes rather it considers equity constraints on outcomes.

Cost-consequence analysis

Cost-consequence analysis (CCA) is an alternative to CEA. In a CCA, costs and outcomes are disaggregated and summarised. The stratification could be along the lines of equity-relevant characteristics meaning the costs and outcomes are reported

by equity-relevant groups. This could be considered akin to an equity-impact analysis, which quantifies the distribution of costs and outcomes by an equity-relevant variable (Cookson et al., 2017a). CCA does not necessitate the incorporation of the health opportunity cost (see Chapter 1) meaning it diverges from the equity-impact stage of a DCEA in this regard.

Cost-benefit analysis

As detailed in Chapter 1, CBA reports health outcomes and costs in a common numeraire (i.e., monetary units). Its use is justified on Kaldor-Hick's hypothetical compensation grounds (Hicks, 1983) in which society benefits if those that gain from the policy can in theory compensate those that do not gain. Thus, advocates may argue that the choice to apply weights or alter the values of costs and outcomes is 'value-laden' or that distributional concerns should be handled through taxes and transfer. However, CBA has been criticized for being insensitive to distributional concerns and the literature suggests equity weights as a method of addressing these concerns (Adler and Posner, 1999, Adler, 2016).

This involves applying weights to the social benefits and costs depending on equity-relevant characteristics. The Treasury's Green Book (HM Treasury, 2023) recommends 'distributional weighting' when considering social CBA which states weights are based on the concept of diminishing marginal utility of income. Health equity concerns can be elicited using willingness-to-pay (WTP) of such non-market goods e.g., improvements in health for certain groups based on equity-relevant characteristics and improvements in social determinants of health. Thus, the value of

health equity improvements can be included alongside the costs (Roldós and Breen, 2021).

Social return on investment and return on investment

Finally, social return on investment (SROI) and return on investment (ROI) are closely related to CBA (Edwards and Lawrence, 2021) and therefore approaches to incorporating equity considerations can be as those described for CBA. With SROI, value is not however restricted to measurement through WTP or contingent valuation (as in CBA) meaning social value estimates of improvements in health equity may be readily sought and applied in an analysis. Alternatively, as SROI can be considered a localised CBA for a given population or geographical location (Tudor-Edwards and Lawrence, 2021) a SROI could be estimated for each group of the population based on equity characteristics. An important distinction between CBA and SROI is that CBA is almost always done prospectively evaluating new policies whereas SROI is often retrospective, although the latter can be prospective and can be referred to as ‘forecast SROI’.

Choice of equity method for exploration in this thesis

For the exploration of equity in this thesis, DCEA was selected. DCEA is a method of CEA which is grounded in extra-welfarist theory (see Chapter 1). Extra-welfarism is the predominant approach used for health resource allocation in England and Wales (National Institute for Health Care Excellence, 2022), therefore it was felt that it may be easier to impact policy if the preferred normative approach forms the basis of the evidence. Of the equity-informative CEA methods available (Ward et al., 2022,

Cookson et al., 2017a) DCEA represents a method that allows trade-offs between equity and efficiency to be considered. ECEA can in theory consider trade-offs however the incorporation of financial risk protection (which is commonly included in ECEA) was not considered a relevant concern given healthcare in England and Wales is publicly funded. DCEA also provides the opportunity to consider an equity-impact assessment (i.e. prior to trade-off analyses DCEA presents which groups the costs and outcomes fall on). Reporting the results as an equity impact analysis may also facilitate the incorporation of broader costs and outcomes. One of the challenges with DCEA is the considerable data requirements not least in the estimation of baseline data, or the 'baseline distribution'. Should a relevant baseline distribution not exist then it requires estimation.

3.1.2 Extending the time horizon

The time horizon of an economic evaluation should cover the life course to fully reflect a programme's benefits and costs. Yet, directly observed causal impacts of a programme on these outcomes are unlikely to exist due to the extended time horizon, thus necessitating results to be extrapolated (Drummond et al., 2015, Briggs et al., 2006). Chapter 1 describes the overarching modelling approaches that can be used to extrapolate costs and outcomes over an individual's lifetime. This section will therefore introduce a handful of models in the literature that model the life course or periods of it whilst capturing dynamic interacting outcomes over time. They are categorised as microsimulation models and agent-based models. This is not intended to be an exhaustive list of models, rather it hopes to highlight models available in the literature that could be useful in future chapters.

Microsimulation models

LifeSim (Skarda et al., 2021) is a dynamic microsimulation model that uses data from the Millennium Cohort Study (Centre for Longitudinal Studies, 2023) to model the life course. It models dynamic clustering and compounding of multiple outcomes over time and includes the parental characteristics of the child as well as cognitive and behavioural scores for the child. It reports lifetime health and healthcare costs as well as lifetime social, economic and wellbeing outcomes.

The ELSI model (Salonen et al., 2021) is a dynamic microsimulation model that models the life course of individuals based on Finnish data. It captures mortality as well as labour market and education dynamics and reports economic outcomes such as employment and earnings. The Lifetime INcome Distributional Analysis (LINDA) model (Van de Ven, 2016) presents is a dynamic microsimulation that captures lifetime health status, mortality, career status, education status and migration status. The Modelling the Early life-course (MELC) model (Milne et al., 2015) is an early life dynamic microsimulation model based on the New Zealand census. It captures family circumstances and early education and reports health service use, early literacy, and conduct problems up to age 13 years. HealthPaths (Wolfson and Rowe, 2014) models dynamic patterns of functional health based on data from the National Population Health Survey of Canada. It models health trajectories using select health determinants, namely health status, education, smoking and obesity to model health adjusted life expectancy. The POpulation HEalth Model (POHEM) (Hennessy et al., 2015) is a cardiovascular disease model that captures a number of social and health determinants of health such as ethnicity, income, education, smoker, nutrition, physical activity and presence of hypertension, diabetes, depression.

A systematic review by Li & O'Donoghue (Li and O'Donoghue, 2013) published in 2013 identified 66 dynamic microsimulation models that capture the distributional impacts of public policy that can report outcomes in multiple sectors.

Agent-based models

A model by Caucutt and Lochner (Caucutt and Lochner, 2019) models multigenerational ability and considers investments in human capital production with a focus on early childhood. A model developed by Attanasio and colleagues (Attanasio et al., 2020) used data from a cohort of children and families in Hyderabad to model the impact of parental investments in human capital production for children up to age 12 years.

A number of contributions to the literature have modelled dynamic determinants of child development. Del Boca et al. (Del Boca et al., 2014) modelled the child cognitive development process as a function of household labour decisions e.g., time and money inputs. Gayle (Gayle et al., 2018) modelled the impact of social determinants such as parental education, income and time on child development and educational outcomes. Finally, Bernal (Bernal, 2008) use data from National Longitudinal Survey of Youth in America to model the dynamic effects of child care and parental employment child cognitive ability.

Choice of model for considering the life course evaluation of E-SEE Steps

The models available in the literature and described above offer the potential to consider longer-term horizons. Of the models available, the LifeSim model (Skarda

et al., 2021, Skarda et al., 2022) was selected for use in this thesis. It captures the complex interacting nature of many determinants of health. Furthermore, the LifeSim model utilises SDQ scores (as captured in the Millennium Cohort Study) as an input to model future life events. SDQ was a reported outcome of E-SEE Steps meaning there is the potential to link the E-SEE Steps data to LifeSim.

3.1.3. Broadening the perspective

As discussed in Chapter 1, there may be considerable value of an intervention beyond the health sector. The perspective defines the boundaries of the economic evaluation and determines which costs and outcomes are to be included. Traditionally decision making in England and Wales under the purview of NICE has been based on an NHS and personal social services perspective, referred to as a 'healthcare' perspective. A broader perspective, sometimes referred to a 'societal perspective', considers the costs and benefits beyond the healthcare sector. There is generally a lack of agreement over what defines a societal perspective but additions to the literature have outlined the pillars forming a societal perspective (Drost et al., 2020).

A systematic review conducted by Kim et al. (Kim et al., 2020) categorised the perspectives used in HTA as: *healthcare payer*; *healthcare sector*; *limited societal* and *societal*. According to Kim healthcare payer and healthcare sector differ in that the healthcare payer is limited to the health costs and consequences falling on the health payer whereas healthcare sector includes out-of-pocket (OOP) payments falling on individuals. Limited societal includes costs and outcomes beyond those captured by the healthcare sector perspective; societal includes all resources that

could be used for other purposes. For the purpose of this Chapter, the term ‘broader’ perspective is used to denote healthcare sector; limited societal and societal perspectives.

The methods of incorporating broader costs and outcomes into an evaluative framework are categorized as follows: frameworks and analytical approaches facilitating the incorporation of broader costs and outcomes in CEA; outcomes measures that move beyond simply capturing health in CEA; and non-CEA frameworks.

Frameworks and analytical approaches facilitating the incorporation of broader costs and outcomes in CEA

Several frameworks in the literature have described ways in which CEA can consider outcomes other than health in decision-making. The Second Panel on Cost-Effectiveness in Health and Medicine (Sanders et al., 2016) recommend the use of an impact inventory to clarify the scope of the economic evaluation and to detail the costs and consequences falling on the health sector and those falling on other domains. Walker and colleagues (Walker et al., 2019) built on this approach to capturing the societal perspective by including and making explicit the opportunity cost in each of the dimensions included in the inventory. The framework then facilitates aggregating the results by domain or by group. Vallejo-Torres (Vallejo-Torres, 2023) build upon the concepts introduced in the Walker framework (Walker et al., 2019) by further incorporating differential weights to outcomes (which can be considered equity weights) paying attention to the differential health opportunity costs as a result of differential equity weights (Paulden and McCabe, 2021).

MCDA is an alternative analytical approach with origins in decision theory (Keeney and Raiffa, 1993) and aims to allow decision makers to consider multiple criteria beyond the scope of health by specifically avoiding the quantification of all decision criteria (Thokala et al., 2016). The multiple criteria can be combined by developing weights for certain attributes (Goldman et al., 2010, Devlin and Sussex, 2011) however previous approaches to using weights in MCDA for health economic decision making have been criticised for priority setting (Briggs, 2016).

Outcomes measures that move beyond simply capturing health

Moving away from frameworks and analytical approach, there have been a number of outcomes that have attempted to broaden the aspects of value along with health. Brazier and Tsuchiya (Brazier and Tsuchiya, 2015) suggested the use of a well-being-adjusted life-year (WELBY) except rather than using EQ-5D to measure health outcomes measures such as ICECAP (Al-Janabi et al., 2012), ONS-4 or WEMWBS (Tennant et al., 2007) could be used to measure wellbeing. Cookson and colleagues (Cookson et al., 2021c) presented an alternative composite measure of health to capture non-health benefits of a programme. They introduced a ‘wellbeing QALY’ for the purpose of evaluating a programme when cost and benefits fall on multiple sectors by deviating from capturing *years of healthy life* to *years of good life* through the combination of health and consumption. Caro et al. (Caro et al., 2019) provide a summary of alternatives to expressing outcomes in QALYs that attempt to expand aspects of value.

Non-CEA frameworks

Beyond the extra-welfarist perspective, Wildman and Wildman (Wildman and Wildman, 2019) argue that an alternative approach to combining health outcomes and non-health outcomes is to simply revert to a welfarist perspective and use CBA, which reports all outcomes in monetary units (see Chapter 1 for a discussion of CBA). This would consider all benefits, whether health or non-health, using the common numeraire of money. They argue that disaggregating and valuing attributes will make explicit how trade-offs occur, and that the CBA approach will give no priority to health outcomes. This would, however, require the monetary valuation of all health and non-health outcomes.

Choice of method for incorporating broader costs and outcomes

For the incorporation of non-health costs and outcomes, the framework proposed by Walker et al. (Walker et al., 2019) that builds on the the Second Panel on Cost-Effectiveness in Health and Medicine (Sanders et al., 2016) will be used. Rather than prescribe what non-health costs and outcomes should be included and how they should be included, the framework allows the explicit reporting of additional sectors and aspects of value while being transparent. It is also consistent with an extra-welfarist approach, which ties in with the approach adopted in the equity research. Cost-consequence analysis would also facilitate the transparent reporting of costs and outcomes under an extra-welfarist approach but as it does not allow aggregation the Walker framework (Walker et al., 2019) was preferred.

3.3 Conclusions and thesis structure

The identification of the methods available and the way in which some have been used in the literature (see Chapter 2) provides the opportunity to consider the strengths and weaknesses of those methods and to decide on which are suitable to consider adding additional aspects of value relevant to early childhood public health resource allocation in the UK.

It should be noted that the estimation of QALYs in the remaining chapters is through the approach adopted in the published E-SEE Steps economic evaluation (Cox et al., 2022). That is, the SDQ score from the E-SEE Steps trial is mapped to the generic preference-based measure of paediatric HRQL Child Health Utility (CHU9D) (Stevens, 2009, Stevens, 2011) which is used to estimate HRQL weights for the infants. This approach of mapping from a non-preference-based measure (i.e. SDQ) to a generic preference-based measure of health (i.e. CHU9D) is required as the non-preference-based measures do not permit the estimation of QALYs directly. The use of such 'mapping' approaches has highlighted multiple areas of concern (McCabe et al., 2013) including but not limited to a loss of dimensional information, i.e. loss of content that was not included in the descriptive system (Round and Hawton, 2017), and statistical issues around clustering and censoring in the datasets (McCabe et al., 2013).

Aside from general methodological and theoretical issues around mapping, the use of the Furber et al. (Furber et al., 2014) mapping algorithm which was used in the published economic evaluation of E-SEE Steps has specific limitations. First, it was developed using an Australian sample of limited sample size (n=200) from a narrow

population of children receiving mental health services. The results were also based on caregivers' responses to the SDQ and CHU9D, which may differ from responses given by children (Petrou et al., 2022). Finally, CHU9D was originally developed for use with children aged 7 to 11 years old and the sample included in E-SEE Steps trial were less than 2 years old. The remainder of the thesis will be structured as follows. Health equity is introduced and explored in Chapter 4 and Chapter 5. Distributional-cost-effectiveness analysis is used as the method of incorporating health equity into an evaluation. However, prior to conducting a DCEA, a decision needs to be made on how the population will be categorised to consider health equity. That is, across which groups in the population are we in interested in measuring and improving health inequalities? When that decision has been made the existing level of health across those groups should be estimated to get to know what the existing level of health inequalities are. Chapter 4 focuses on measuring health gradients across different measures of socioeconomic position (SEP). The results from Chapter 4 are useful to begin to think about health gradients for children and the estimated distribution of health is required as an input into DCEA. A DCEA of E-SEE Steps is then conducted in Chapter 5.

Chapter 6 then explores the extrapolation of the within-trial results of E-SEE Steps through the use of the LifeSim model. Finally, Chapter 7 brings together non-health costs and outcomes as a result of E-SEE Steps into the economic evaluation to consider a broader perspective. It is at this point that the incorporation of health equity and non-health costs and outcomes over a lifetime are all introduced into an evaluation. It is hoped the introduction of each of the three elements will serve to demonstrate an example of how they can be incorporated into an economic

evaluation and to show the impact they may have on the assessment of value for money. Chapter 8 then brings together a discussion of the results and of resource allocation regarding early childhood interventions.

Chapter 4: The Incorporation of Equity Considerations and the Role of Socioeconomic Position Part 1: Estimating distribution of lifetime health using alternative approaches to socioeconomic stratification

A condensed version of this Chapter has been published in *Value in Health*:

> **Murphy P**, Hinde S, Richardson G. Appropriate Categorization of Inequality to Inform Policy Decisions: Estimating Distribution of Lifetime Health Using Alternative Approaches to Socioeconomic Stratification. *Value in Health*. 2024 Jan 1;27(1):26-34.

This work was presented at HESG Winter 2023: University of Manchester.

4.1 Introduction

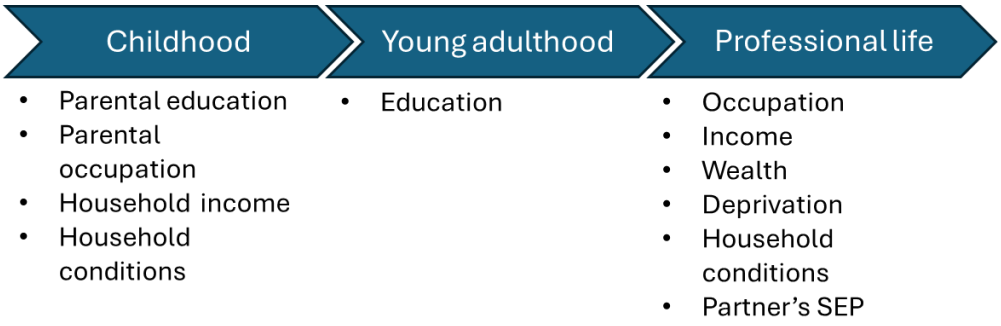
The incorporation of equity into an economic evaluation using DCEA requires measurement of the existing difference in health across groups in the population. Measuring inequalities in lifetime health forms an essential part of assessing the extent of differences and how best to alleviate them. Yet, measurement requires the consideration of a number of issues that are sometimes implicit but are fundamental to the interpretation. They have been described by Cookson (Cookson, 2016) as:

- How we define health (i.e. *Equality of what?*)
- Across which groups we are interested in measuring the health inequality (i.e. *Equality between whom?*)
- How we measure and assess the inequality (i.e. *Equality measured how?*)

When considering how to define health, approaches to summarizing experienced lifetime health have moved beyond simple measures relying solely on mortality, such as life expectancy (LE), to combine mortality and continuous measures of health-related quality of life (HRQL). An example is quality-adjusted life expectancy (QALE) (Collins, 2013, Love-Koh et al., 2015), which provides a sensitive measure of health capturing mortality and morbidity into a single health metric. Expressing lifetime health in QALE further allows the incorporation of results consistent with cost-effectiveness analysis used in the UK e.g., in which outcomes are expressed in QALYs (National Institute for Health Care Excellence, 2022). For the economic evaluation of E-SEE Steps, health outcomes were expressed in QALYs making QALE a compatible measure.

Yet to date, there has been limited exploration of how the inequalities in QALE differ when comparing different ways of defining the social groups over which the health inequality can be compared. A common way to categorise social groups is along the lines of 'socioeconomic position' (SEP), which is used to refer to socially derived structural locations within society (Bartley, 2004). Examples of SEP include area-level approaches (e.g. by postcode) and individual-level approaches to stratification (e.g. by educational attainment or income) (Lynch and Kaplan, 2000). There is ample evidence linking SEP with health; indicating lower SEP results in poorer health (Galobardes et al., 2006b, Galobardes et al., 2006a). This is particularly important in children as early childhood SEP is a strong determinant of poorer health in adulthood (Smith et al., 1997). A study by Galobardes et al. (Galobardes et al., 2006a) detailed a number of the indicators of SEP across the life course. This can be seen in Figure 3.

Figure 3 – Measures of SEP throughout the life course



Adapted from Galobardes et al. (Galobardes et al., 2006a)

Significant contributions to estimating the social distribution of QALE in England have focussed on area-level approaches to describe inequitable variation in health

(Collins, 2013, Love-Koh et al., 2015). Collins (Collins, 2013) estimated QALE for the most and least deprived areas in the Northwest of England and Love-Koh et al. (Love-Koh et al., 2015) estimated QALE across index of multiple deprivation (IMD) quintiles. The use of such area-level indices is a means of stratifying groups by deprivation and leans on the notion that place can affect health (Tunstall et al., 2004). Yet, there has been limited analyses describing similar variation in QALE across individual-level indicators of SEP such as those highlighted in Galobardes et al. (Galobardes et al., 2006a) for example parental education and income.

The aim of this study is therefore to estimate the social distribution of QALE across the population of England and explore the impact of altering the groups across which we measure inequality. This will be achieved through estimating QALE across individual-level indicators of SEP to compare the inequality within individual-level measures and also comparisons to area-level measures of SEP. It is hoped this will indicate the health someone born into different social groups is expected to experience providing information for policy-makers interested in improving childhood health equity. It is also hoped this may reveal important differences in life course measures indicating the choice of measure of SEP may be important. Finally, the estimated distribution of health will provide an important input into the DCEA in Chapter 5.

4.2 Area- versus individual-level groups

The choice of describing health inequalities by individual or area-level indicator of SEP matters as each indicator emphasizes an aspect of social stratification (Galobardes, 2012, Galobardes et al., 2006b, Galobardes et al., 2006a). Area-level

indices are useful if the delivery of services and policies are targeted at the area-level and can act as proxies for individual-level SEP indicators. Such indices are used when the geographical area is the object of the analysis not the individual (Galobardes et al., 2006b). An example includes IMD, which is a composite measure capturing seven domains and measures deprivation in small geographical areas. However, there are reasons that it may be useful to consider the impact of individual-level indicators of SEP over and above area-level indicators.

First, individual-level indicators of health may be more attuned to the intervention level. That is, if individual-level explanations of health are to be targeted by an intervention with the aim of improving health inequalities, then area-level indicators may not be appropriate to stratify delivery of the intervention. Second, evidence suggests that individual effects on health may be greater than the corresponding area effects (Pickett and Pearl, 2001) meaning important inequality information is masked. Furthermore, the variability in health across SEP groups based on an area-level indicator will always be less than an individual-level indicator (Geronimus, 2006). This means the true magnitude of the existing health inequality may be underestimated. There are many individual-level indicators of SEP and it is not theoretically compelling to define a single best indicator (Galobardes et al., 2006b, Galobardes et al., 2006a). Examples include education and income which both measure the level of a particular asset and capture social opportunities which can impact health (Galobardes et al., 2006b, Galobardes et al., 2006a). Income effects on health are believed to operate in absolute terms through access to services (Luo et al., 2009), improved nutrition (Casey et al., 2001), and the resources rooted in social networks, (Heritage et al., 2008) as well in relative terms through a feeling of

deprivation resulting in adverse mental health consequences (Eibner et al., 2004). Education effects on health have been widely studied and are generally described through a number of frameworks including fundamental cause theory (Link and Phelan, 1995); human capital theory (Becker, 2009); and the signalling perspective. (Collins, 2019).

The classification of SEP groups is a further important consideration for researchers to make and should be grounded in an *a priori* assessment of the theory of specific measures of SEP on health (Arcaya et al., 2015). With regards to education groups, the decision was made to collapse into groups that represent levels of education in England and therefore act as a proxy for the time spent in education. Education (knowledge) can be seen as key social and economic resource and one that is likely to increase with increased time spent in education (Link and Phelan, 1995, Becker, 2009). There are a number of studies presenting compelling evidence of the link between time spent in education with increased health (Clark and Royer, 2013, Silles, 2009, Raghupathi and Raghupathi, 2020). In addition, completion of the increased levels of education brings additional qualifications which also earns social and economic returns (Collins, 2019).

With regards to the income groups, collapsing was in the form of income quintiles as this ordered stratification allows the ranking of the relative position of individuals to their peers (Arcaya et al., 2015). Consideration of whether this is preferred to absolute levels of income needs is required but using relative income incorporates psychosocial pathways between income to health (Arcaya et al., 2015). Income quintile are also used to describe the income distribution across UK households (Department for Work and Pensions, 2022).

Equivalised income is an approach to adjusting household income which accounts for the difference in household size and composition. An advantage of using equivalised income is that it allows for more accurate comparisons of income levels between households of different sizes by accounting for larger households typically requiring more resources to achieve the same standard of living as smaller households. It can also be advantageous if it is the ability to spend and consume that is of interest to the impact on health as equivalised income may better reflect the consumption opportunities. Limitations of the approach are the fact that the approach assumes that all household members share resources equally and that it does not capture the individual earnings, which may be important if it is the act of earning that is considered to be pertinent to health.

4.3 Method

The estimation of the social distribution of health across educational attainment groups and income quintiles is described below and follows the approach used by Love-Koh et al. to estimate QALE by IMD quintile (Love-Koh et al., 2015). This is achieved through estimating health related quality of life (HRQL) weights by age, sex, and SEP. The HRQL weights are combined with multivariate mortality rates through the use of Sullivan life tables (Sullivan, 1971), which are adapted using the Chiang II method (Chiang, 1984). This approach converts mortality information into period life expectancy by calculating the expected years lived of a hypothetical cohort by year of age, in which a proportion of the surviving cohort die according to the age-specific mortality rate. The result is a QALE estimate, which is calculated for each SEP group.

4.3.1 Data

4.3.1.1 Mortality Rates

Mortality rates by age, sex, and SEP were obtained from the literature. Ingleby et al. (Ingleby et al., 2021) estimated the variation in LE by education, occupation and wage for the population of England and Wales. The estimates were based on 2011 census data from the Office for National Statistics (ONS). Mortality rates by each year of life from 20 years of age to 100 years of age were provided by Ingleby et al. through personal communication (Belot, 2022, personal communication, unreferenced).

The classification of education groups in the data was based on highest educational qualification according to the following categories: *no qualifications*; *1-4 GCSEs or equivalent*; *5+ GCSEs or equivalent*; *apprenticeships and vocational qualifications*; *A-levels or equivalent;* and *degree-level education and higher*. These qualifications represent the normal qualifications achieved in England and Wales. To align with the grouping of time spent in education, the *no qualifications* group was retained. The *1-4 GCSEs or equivalent* and the *5+ GCSEs or equivalent* groups were collapsed into a single *GCSEs* group as they both represented qualifications attained by individuals completing secondary education. The same approach to collapsing was adopted for the *apprenticeships and vocational qualifications* and the *A-levels or equivalent* groups, creating an '*A-levels and equivalent'* group which represents qualifications earned in further education. Finally, the *degree and higher* group was retained as this represents the completion of higher education. The mortality rates were

therefore collapsed into *No qualifications*; *GCSEs*; *A-levels or equivalent*; and *Degree and higher*.

Sensitivity analysis was conducted in which the *1-4 GCSEs or equivalent* group was included in the *No qualifications* group to make a *No qualifications or low-level qualifications* group. This was conducted as the literature highlights the poor health of adults with low educational attainment (Marmot and Bell, 2009) and the *No qualifications or low-level qualifications* group was considered a proxy for low educational attainment.

Although income groups were sought, mortality rates by income were not provided in the Ingelby data, rather wage was captured. Wage quintiles were provided and were considered a reasonable proxy for income quintiles. Mortality rates by wage quintiles were reported from lowest wage (Q1) to highest wage (Q5). The median wages across each quintile are presented in the appendix.

Mortality rates in the Ingleby data were in the form of annual mortality rates by sex and SEP from 20 to 100 years of age. However, for use in the Sullivan life tables, rates were required in 10-year age bands up to 85 years of age with a final age from 85 to 100 years of age. Corresponding age band-specific mortality rates were calculated as the mean mortality rate within the age band. The age, sex, SEP mortality rates for those under 20 years of age were not available in the Ingleby data, therefore supplementary data were sought. Relevant mortality rates for income and education subgroups for those under 20 years of age were not available in the literature. The analysis therefore used national age and sex mortality rates for those under 20 years of age, obtained from the ONS (Office for National Statistics, 2013).

All mortality rates were provided separately for males and females. Combined mortality rates were calculated as the weighted average according to the proportion of males and females in each age band in England in 2011 (Office for National Statistics, 2013).

4.3.1.2 Utility values

The estimation of the age, sex, SEP, and HRQL weights were based on pooled data from the 2010, 2011 and 2012 rounds of the Health Survey for England (HSE) (University College London Department of Epidemiology and Public Health NatCen Social Research, 2013, University College London Department of Epidemiology and Public Health NatCen Social Research, 2014, University College London Department of Epidemiology and Public Health NatCen Social Research, 2012). The HSE is an annual survey collecting data on health, health-behaviour, demographic and socioeconomic information of adults and children living in private housing in England (Mindell et al., 2012). The demographic is a nationally representative sample selected using a random sampling process (Mindell et al., 2012). There were 35,062 observations in the three rounds of the HSE.

The HRQL weights estimated from the HSE are based on the EuroQol-5D (EQ-5D) health questionnaire. EQ-5D is a self-reported, generic measure of HRQL that facilitates comparisons across different patients and disease areas by providing a single index value for health status. It is accompanied by weights to reflect the relative importance of different types of ill health. The version of the EQ-5D questionnaire used in the 2011 and 2012 HSE was the EQ-5D-3L. This comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and

anxiety/depression, with each dimension having three levels: no problems, some problems or severe problems, albeit the specific wording may differ between dimensions. Thus, resulting in 243 possible combinations plus an additional two to represent dead and unconscious. The resulting 243 health states have their own country-specific utility score based on elicited preferences of a sample of the UK population (Dolan, 1997). The HRQL weights for the various health states range from -0.594 to 1 (perfect health) using the York MVH A1 tariff (MVH Group, 1995). The EQ-5D-3L UK value set was applied to the data (Dolan et al., 1995).

The HRQL weights were estimated by age, sex and SEP, the latter representing income or education. The education variable provided within the HSE stratified individual's educational attainment into groups according to National Vocational Qualification (NVQ) levels[12] and includes the following categories*: no qualifications*; *NVQ1*; *NVQ2*; *NVQ3*; *higher education below degree*; *NVQ5/4 or degree*}; *foreign/other*; and *not applicable*.

As with the Ingleby data, collapsing of the education subgroups was required to align with the mortality rates. The *NVQ1* and the *NVQ2* groups were collapsed as these represent qualifications attained by individuals in at the level of secondary education in England and align with the *GCSEs* mortality group. The *NVQ3* and the *higher education below degree* subgroups were also collapsed into a single group as they are both attained at the level of further education and align with the *A-levels* group. The *NVQ4, NVQ5 and Degree* was retained as these are higher education

[12] NVQ levels range from 1-8 and are stratified according to the following qualification/grades: 1, GCSE grades D, E, F, G; 2, GCSE grades A*, A, B, C; 3, A-levels, higher education diploma; 4: certificate of higher education; 5, diploma of higher education; 6, degree with honours; 7, master's degree, PGCE; 8, PhD.

qualifications. The resulting base case education groups for estimating the HRQL weights were as follows: *no qualifications*; *NVQ1 and NVQ2*; *NVQ3 and higher education below degree*; *NVQ4, NVQ5 and Degree.* The impact of the grouping assumptions on the age, sex and SEP utility values was estimated in the form of scenario analysis. The *no qualifications* and *NVQ1* were combined into a single group to align with the formation of the *No qualifications or low-level qualifications* included in the mortality rate sensitivity analysis.

Those categorised as *Foreign/other* were handled in a number of ways. First, they were assumed to be missing completely at random (MCAR), which implicitly assumes they are a random subset of the wider data. Sensitivity analysis was also conducted in which the *Foreign/other* individuals were assumed to be in the *No qualifications* group and separately the *Degree and higher* group.

The income variable provided in the HSE was equivalised income. The equivalised income captured in the HSE adjusts the exact net household income [13] by the number of people living in the household.[14] Equivalisation has become standard methodology to allow the comparison of the standard of living across households with different household sizes and different resource needs. The population were

[13] The method adopted for estimating equivalised income captured the exact income of the household, rather than selected from banded incomes which is used in to estimate gross income variables

[14] This process is done by assigning every member of the household a score based on the McClemens scoring system. The individual scores are: First adult or household reference person (HRP), 0.61; Spouse or partner of HRP, 0.39; Other second adult, 0.46; Third adult, 0.42; Subsequent adults, 0.36; Dependent aged 0-1, 0.09; Dependent aged 2-4, 0.18; Dependent aged 5-7, 0.21; Dependent aged 8-10, 0.23; Dependent aged 11-12, 0.25; Dependent aged 13-15, 0.27; Dependent aged 16+, 0.36. The total net income is divided by the household McClemens score.

grouped into equivalised income quintiles, with Q1 representing those with the lowest income and Q5 representing those with the highest income.

4.3.1.3 Missing data

There was a considerable degree of missing data across EQ-5D (n = 2,415, 9.5%), education (n = 501, 2.0%) and income in the HSE (n = 5,182, 20.5%). Logistic regression modelling, in which the probability of the variables was observed, revealed statistically significant evidence (P < .01) against EQ-5D values and income being MCAR as age, income, and EQ-5D (but not sex) were predictive of missingness. The missingness analyses can be found in the appendix. To address this, multiple imputation (MI) by chained equations with predictive mean matching was conducted to impute the missing values. (Little and Rubin, 2019, White et al., 2011) The number of imputations was set at 7 to align with recommendations (von Hippel, 2020). To aid MI, auxiliary variables were sought from the HSE data by identifying variables correlated with the missing variables (r > 0.4) to improve imputation. (White et al., 2011) The HRQL weights estimated using the imputed results were generated by regressing EQ-5D values on age, sex, and SEP. The results of the MI regression model are compared with the results of the model assuming MCAR, referred to as the “complete case” results. Given that the logistic model revealed data were not MCAR, the MI results form the base case.

4.3.2 Regression analyses

Linear regression modelling was used to model the values using the HSE data. Ordinary least squares (OLS) was used as it was consistent with the approach

adopted by Love-Koh et al. (Love-Koh et al., 2015). The sensitivity of the results to an alternative Tobit estimator were assessed. The results of the combined 2010, 2011 and 2012 rounds of HSE did show skewness in the EQ-5D results with approximately 4% of the population reporting a utility of less than 0.516; 68% reporting a utility of greater than 0.883 with 41% reporting a utility of 1. Despite the potential for skewed data, this approach was deemed appropriate due to previous studies showing OLS performed well when modelling HRQL in large sample sizes (Petrou and Kupek, 2008). To estimate the utility values, the following regression model was implemented for education and income (denoted in equation 1 below as the generic variable 'SEP'):

$$HRQL = \beta_0 + \sum_{i=1}^{8} \beta_1 \, age_i + \sum_{j=1}^{n} \beta_2 \, SEP_j + \beta_3 \, sex + \varepsilon \qquad (1)$$

Where HRQL are the estimators of the HRQL weights for age, SEP group and sex; β_0 is the constant term; β_1, β_2, and β_3 are the coefficients for a series of age, SEP and sex dummy variables that take on either a value of 0 or 1 depending on subgroup membership; n is the number of categories of SEP for the variable of interest, which is four for education and five for income; and ε is the error term. When all the variables are set to zero, the predicted weight is the constant term only and represents the 'reference' group: individuals aged 16 to 24, in the highest education or income SEP group and male. All statistical analyses were carried out in STATA version 17.0 (Stata Corporation, College Station, TX, USA).

4.3.3 Life Tables

Assumptions are made about the proportion of the interval survived by those dying, assumed to be 0.5. Life expectancy at birth is calculated as the sum of the number of years lived in the interval and all other subsequent intervals divided by the number of individuals alive at the beginning of the interval using the following equation:

$$\mathrm{LE}_{i,j,k} = \frac{\sum_z^i L_i^j}{I_{i,j}} \qquad (2)$$

where $LE_{i,j,k}$ is the LE at the start of the age interval, i, for each SEP group, j, and sex, k, with z being the last age interval. L_i^j is the person years lived in age interval or the combined number of years lived in the age interval by the surviving cohort; $I_{i,j}$ is the number of the cohort surviving to age i. Hence, LE at birth is calculated using the above calculation and setting i as the first age interval (i.e., 0-4 years of age). Estimated life expectancy at birth reflects the life expectancy of a baby born if they are to experience the age-related mortality rates that exist at their birth. Life expectancy is then adjusted using morbidity weights and summing the total number of health-adjusted person years lived from age i. For calculating QALE at birth, this is the total number of quality-adjusted person years from birth divided by the proportion of the cohort surviving:

$$QALE_{i,j,k} = \frac{\sum L_{i,j,k} U_{i,j,k}}{I_i} \qquad (3)$$

Where $U_{i,j,k}$ represents the HRQL weights. Details of a example of the estimation of QALE including estimating life expectancy via the life table and the incorporation of

the utility values can be found in the appendix. The resulting QALE estimates for each of the SEP groups forms the social distribution of health. The LE less the QALE reveals the quality-adjusted years of life lost (QAYLL) for each group, that is, the amount of life people live in less than perfect health adjusted for quality.

4.3.2 Inequality analysis

The inequality in the resulting social distribution of QALE can be summarised using a number of indices. The first of these indices is a simple measure of inequality in which the health of those in the highest and lowest SEP groups are compared. The absolute gap, G_A, displays the absolute difference in QALE between those at the top and bottom of the distribution and is estimated using Equation (4). The relative gap, G_R, shows the difference in relative terms, Equation (5). A G_A and a G_R of 0 represents no inequality and the higher the value the greater the inequality.

$$G_A = QALE_T - QALE_B \tag{4}$$

$$G_R = \frac{QALE_T - QALE_B}{QALE_T} \tag{5}$$

4.4 Results

4.4.1 Mortality rates

Across all groups, mortality rates increased with age with the exception of the 5-9 age group which was lower than the 0-4 age group. Mortality rates were higher the

lower the educational attainment. This holds true for all of the educational subgroups with the exception of those over 85 years of age, which show no general trends. Across all educational subgroups, the mortality rates were lower in females than males. The results of the scenario analysis showed the mortality rates are insensitive to changes in the education groupings.

Across wage quintiles, rates are higher the lower the wage, albeit this trend does not hold for all groups. For example, the mortality rates were lower for males in the lowest wage quintile (Q1) compared to those in the second lowest (Q2) for all ages from 16 to 84 years of age. Yet for the other male subgroups, the mortality rates decrease from Q3 to Q5 (i.e. as we move up the income gradient). In all female income subgroups, mortality rates increased the lower the income. The mortality rates by age, education and income group can be found in the appendix.

4.4.2 Regression Results

The descriptive statistics of the EQ-5D data from the HSE are provided in Table 8. The results show utility values generally decrease with age. Utility can also be seen to be marginally lower in females than in males. Utility values also decrease as SEP decreases, i.e. lower educational attainment and decreased income.

Table 8 - HRQL values from the Health Survey for England and sample statistics

Variable	EQ-5D value	Observations	Sample, %
Age group (years)			
16-24	0.9275	2,555	10.1
25-34	0.9145	3,642	14.4
35-44	0.8781	4,340	17.1
45-54	0.8461	4,423	17.5

55-64	0.8029	4,077	16.1
65-74	0.7986	3,434	13.6
75-84	0.7433	2,170	8.6
85+	0.703	679	2.7
Total	0.8449	25,320	100
Sex			
Male	0.8579	11,204	44.2
Female	0.8347	14,116	55.8
Total	0.8449	25,320	100
Education			
Degree or higher	0.9022	5,847	23.1
A-levels	0.8791	6,498	25.7
GCSEs	0.8435	6,515	25.7
No qualifications	0.7464	5,959	23.5
Foreign/other	0.7758	402	1.6
Not applicable	0.8374	99	0.4
Total	0.8449	25,320	100
Income			
Q5 (highest)	0.9052	4,170	16.5
Q4	0.8948	4,320	17.1
Q3	0.8494	4,064	16.1
Q2	0.8077	3,965	15.7
Q1 (lowest)	0.764	3,619	14.3
Not applicable	0.8297	5,173	20.4
Total	0.8485	25,320	100

Note. Percentages may not add up to 100% due to rounding.

Abbreviations: GCSE indicates General Certificate of Secondary Education; HRQL, health-related quality of life.

Plots showing the overlap of individual's Education, income and IMD are presented in the appendix. The plots show no apparent visual trend in the overlap between measures of SEP. For example, individuals in IMD Q2 are split proportionately between Income quintiles Q1 to Q5. The results from the regression models estimating utility values by age, sex and SEP can be seen in . shows the HRQL weights by age, sex and education both for the complete case and the MI data. For the complete case and the MI results (the base case), almost all covariates were statistically significant ($P < .01$). The signs and magnitude of the regression coefficients reflect the general directions observed in the descriptive statistics. That

is, HRQL weights decrease with increased age, lower educational qualification and lower income. In the *education model* (the regression model with education used to represent SEP) based on the MI model, the HRQL weights range from 0.979 for a male, aged between 16-24 and with a degree or higher; to 0.6672 for a female, aged 85+ with no educational qualifications. In the *income model* (the regression model with income used to represent SEP) showed similar trends.

The results for the scenario analysis showed marginal variation in the magnitude of the HRQL weights but on the whole the results were relatively insensitive to the formation of a *No qualifications and low-level qualifications*; the inclusion of the individuals in the *Foreign* education group in the *No qualifications* group; and the inclusion of *Foreign* in the *Degree or higher* group. The results of the regression models for the scenario analyses can be found in the appendix. The results of the regression model were not drastically different when comparing the OLS and Tobit models, as was found in the Love-Koh et al. results (Love-Koh et al., 2015). The signs on the coefficients are consistent with the relationship observed in the OLS model: lower education and income was associated with lower HRQL, while ageing and being female are associated with lower HRQL.

Table 9 Results from the OLS regression model of utility values on age, sex and SEP defined by education and income

	Education - MI		Education - CC		Income - MI		Income - CC	
	Utility	**(SE)**	**Utility**	**(SE)**	**Utility**	**(SE)**	**Utility**	**(SE)**
Age group								
16-24	0	(.)	0	(.)	0	(.)	0	(.)
25-34	−0.0228***	-0.006	−0.0229***	-0.006	−0.0323***	-0.006	−0.0344***	-0.007
35-44	−0.0576***	-0.006	−0.0563***	-0.006	−0.0715***	-0.006	−0.0706***	-0.006
45-54	−0.0840***	-0.006	−0.0806***	-0.006	−0.1051***	-0.006	−0.103***	-0.006
55-64	−0.1159***	-0.006	−0.114***	-0.006	−0.1479***	-0.006	−0.143***	-0.006
65-74	−0.1041***	-0.006	−0.103***	-0.006	−0.1375***	-0.006	−0.136***	-0.007
75-84	−0.1454***	-0.007	−0.145***	-0.007	−0.1811***	-0.007	−0.184***	-0.008
85+	−0.1756***	-0.011	−0.175***	-0.011	−0.2193***	-0.011	−0.220***	-0.013
Sex								
Male	0	(.)	0	(.)	0	(.)	0	(.)
Female	−0.0203***	-0.003	−0.0208***	-0.003	−0.0190***	-0.003	−0.0187***	-0.003
Education								
Degree or higher	0	(.)	0	(.)	-	-	-	-
A-levels	−0.0249***	-0.004	−0.0249***	-0.004	-	-	-	-
GCSE	−0.0537***	-0.004	−0.0530***	-0.004	-	-	-	-
No Qualifications	−0.1156***	-0.005	−0.116***	-0.005	-	-	-	-
Income								
Q1	-	-	-	-	0	(.)	0	(.)
Q2	-	-	-	-	−0.0092*	-0.005	−0.00865	-0.004
Q3	-	-	-	-	−0.0450***	-0.005	−0.0431***	-0.005
Q4	-	-	-	-	−0.0835***	-0.005	−0.0834***	-0.005
Q5	-	-	-	-	−0.1340***	-0.006	−0.138***	-0.005
Constant	0.9793***	-0.006	0.979***	-0.006	1.000***	-0.006	1.000***	-0.006
Observations	25 320	-	22 498	-	25 320	-	18 582	-

R^2	-	-	0.095	-	-	-	0.109	-

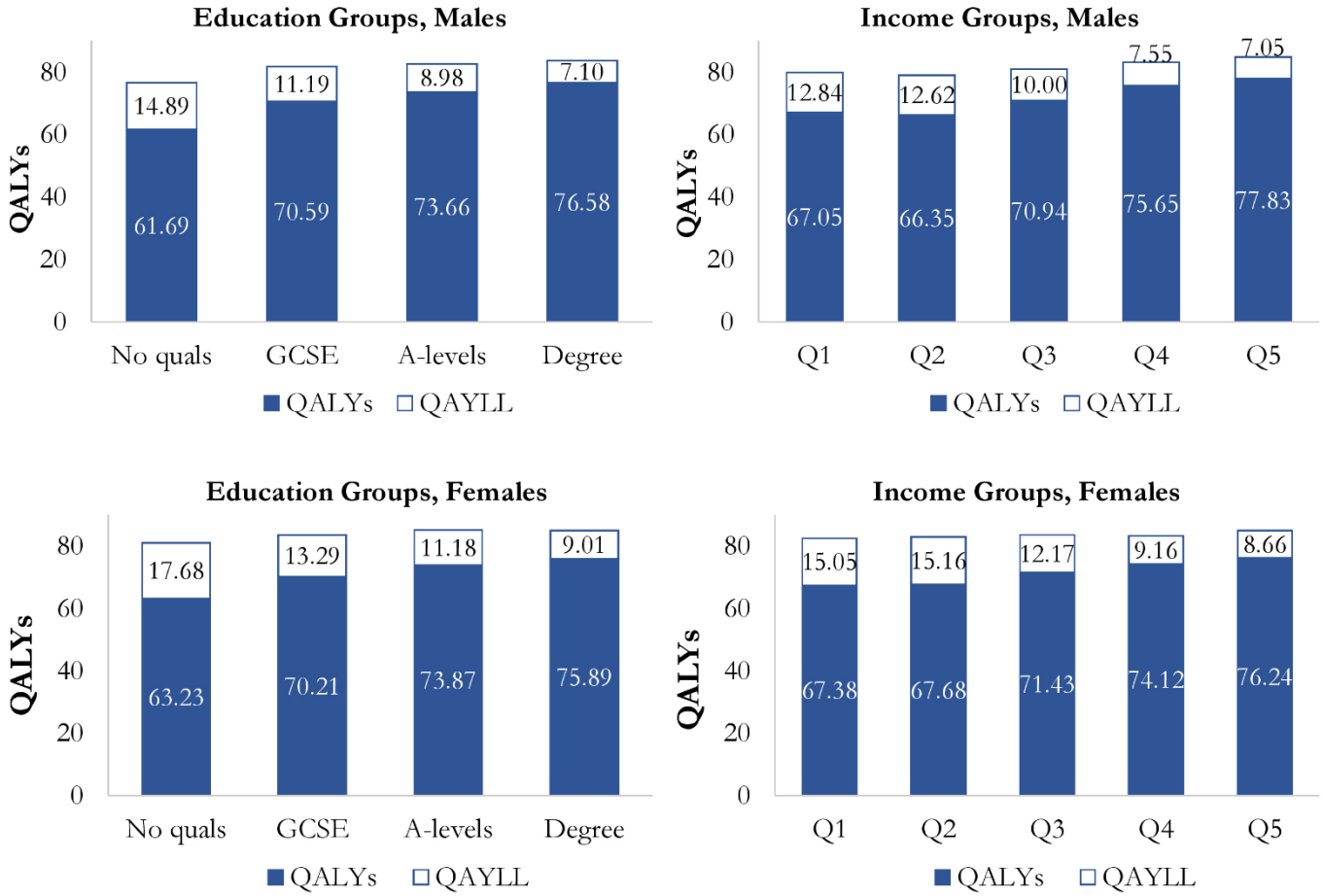
Note: *** p<0.01, ** p<0.05, * p<0.10. Model A depicts the results of regressing EQ-5D on age, sex and education. Model B depicts the results of regressing EQ-5D on age, sex and income. Education is defined by the highest educational qualification attained. Income is defined by equivalised weekly income quintiles. Abbreviations: CC, complete case; MI, multiple imputation; OLS, ordinary least squares; SEP, socioeconomic position.

4.4.3 Social Distribution of Health

The extent of the existing inequalities in estimated QALE, LE and QAYLL across education and income groups can be seen by sex in Figure 4 and for the combined population in Figure 5. For example, the estimated QALE for males in the no qualifications group is 61.69 quality-adjusted life-years (QALYs), with 14.89 QAYLL. This is in contrast to the QALE for males in the degree or higher group, which is 76.58 QALYs and 7.10 QAYLL. As can be seen in the male, female, and combined populations, there is a steeper gradient in QALE across education groups than income groups. The results of the complete case analysis and the SAs show the base-case results are insensitive to the method of HRQL weight estimation and the groupings of education and income.

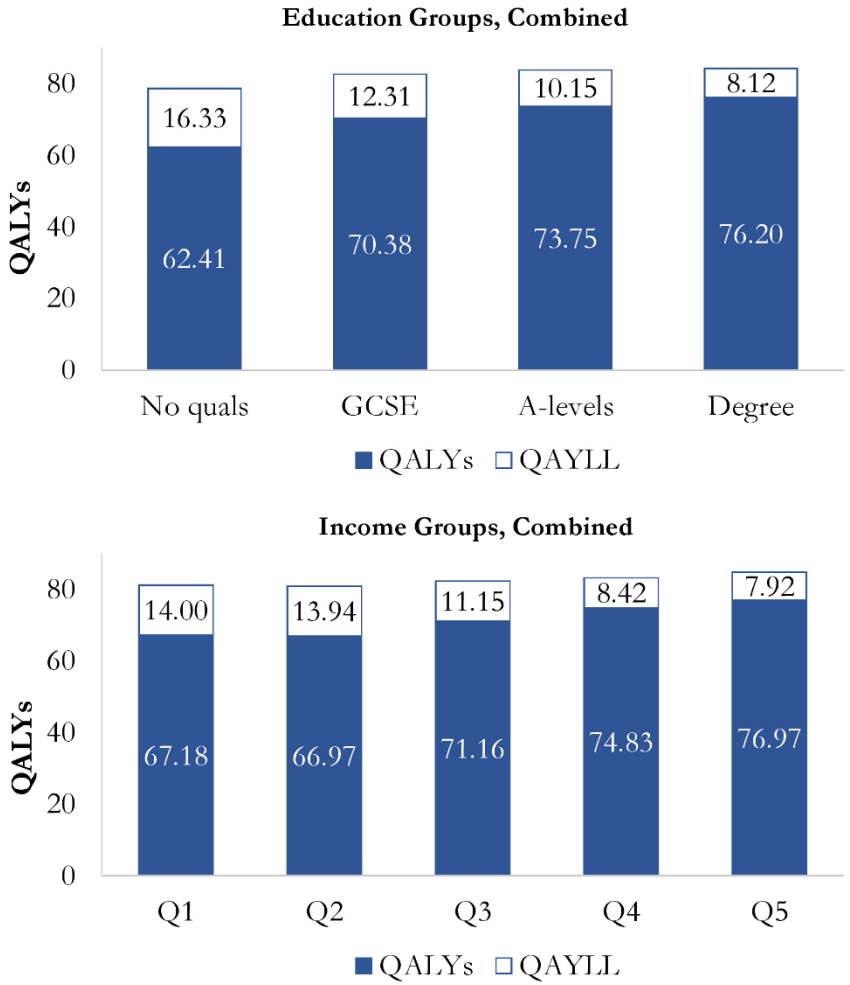
The inequality analysis estimates an absolute gap of 13.79 QALYs across education groups. This is considerable larger than the absolute gap across income quintiles which was estimated to be 9.79 QALYs. Contrast this with the absolute gap across IMD quintiles as estimated by Love-Koh et al. (Love-Koh et al., 2015) which was estimated to be 10.97 QALYs (Figure 6).

Figure 4 - QALE by sex and socioeconomic position



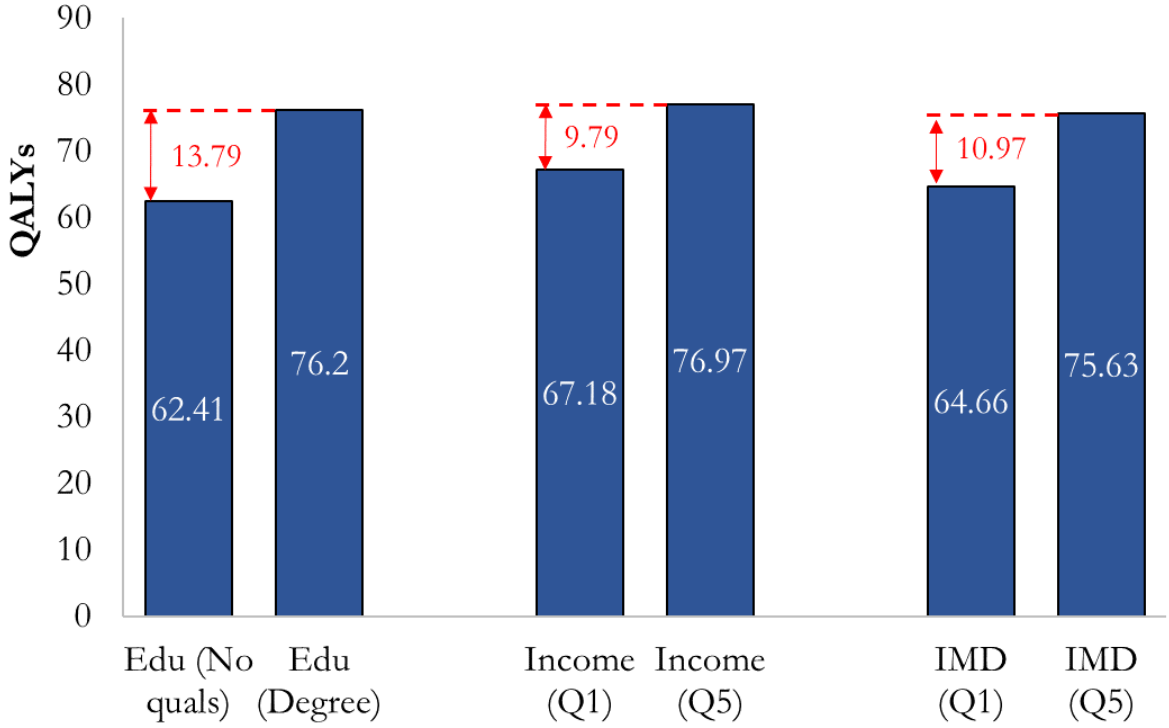
Education is defined by the highest educational qualification attained. Income is defined by equivalised weekly income quintiles: Q1, £239 and under; Q2, £239-£370; Q3, £370-£574; Q4, £574-£950; Q5, £950 and over. Abbreviations: No quals, no qualifications; QALE; quality-adjusted life expectancy; QALYs, quality-adjusted life years; QAYLL, quality-adjusted years of life lost

Figure 5 - QALE by socioeconomic position for the combined population



Education is defined by the highest educational qualification attained. Income is defined by equivalised weekly income quintiles: Q1, £239 and under; Q2, £239-£370; Q3, £370-£574; Q4, £574-£950; Q5, £950 and over. Abbreviations: No quals, no qualifications; QALE; quality-adjusted life expectancy; QALYs, quality-adjusted life years; QAYLL, quality-adjusted years of life lost

Figure 6 - Absolute gap in QALYs across education groups, income quintiles and comparison to IMD quintiles



The results across IMD quintiles are taken from the literature: Love-Koh J, Asaria M, Cookson R, Griffin S. The social distribution of health: estimating quality-adjusted life expectancy in England. Value in health. 2015 Jul 1;18(5):655-62.

Abbreviations: IMD, index of multiple deprivation; QALYs, quality-adjusted life years.

Table 10 Absolute measures of inequality across the estimated baseline distributions of QALE

	Absolute gap in LE (years)	Relative gap in LE (years)	Absolute gap in QALE (QALYs)	Relative gap in QALE (QALYs)
Education				
Male (MI)	7.1	0.09	14.9	0.24
Female (MI)	4	0.05	12.66	0.2
Combined (MI)	5.59	0.07	13.79	0.22
Income				
Male (MI)	5.91	0.07	10.78	0.17
Female (MI)	2.47	0.03	8.86	0.13
Combined (MI)	3.98	0.05	9.79	0.15
IMD*				
Love-Koh et al. distribution - combined	7.27	0.09	10.97	13.5

*The inequality across IMD was estimated from the literature: Love-Koh J, Asaria M, Cookson R, Griffin S. The social distribution of health: estimating quality-adjusted life expectancy in England. Value in health. 2015 Jul 1;18(5):655-62. Abbreviations: IMD, index of multiple deprivation; MI, multiple imputation, QALYs, quality-adjusted life years

4.5 Discussion

4.5.1 Main Findings

This study highlights the existence of substantial health gradients across individual-level SEP indicators. Building on the work by Ingleby (Ingleby et al., 2021), this study shows the impact on the magnitude of existing health inequalities when adjusting mortality to account for morbidity using self-reported HRQL, and allows the comparison of the health gradients both within differing individual-level indicators of SEP as well as across area-level indicators. The results show the direction of the inequality in QALE is consistent across income and education, and also across published estimated of the QALE across IMD groups (Love-Koh et al., 2015). This is unsurprising given they all measure aspects of the same underlying social stratification which may be linked and impact health through similar mechanisms (Galobardes et al., 2006a). For example, lower educational attainment may mean lower wages meaning individuals have less time and resources to seek out healthcare. IMD is also a composite measure of SEP based on aggregates of a number of individual-level indicators such as income and employment albeit estimated at the area level. There is often a complex and bidirectional relationship between deprivation and health but the mechanisms through which they operate may be common to the alternative approaches to SEP categorisation such as those at the bottom of the social stratification have increased stress, a lack of feeling in control, inadequate access to healthcare and inadequate opportunities to adopt and maintain healthy behaviours (Joseph Rowntree Foundation, 2014).

The difference in the magnitude of the existing inequalities based on alternative SEP indicators is highlighted in this study. The absolute gap across education and income was estimated to be 13.79 QALYs and 9.79 QALYs, respectively. This difference appears to be driven by the group at the bottom of the social stratification: Individuals with no qualifications have a QALE of 62.41, approximately 4.8 QALYs lower than the lowest income group, which has a QALE of 67.18. This is explained in part by higher mortality rates in the lowest educational attainment group informing the QALE calculations. It is also driven by the differential HRQL weights used to adjust health for quality of life, which are estimated, from the regression model. The HRQL decrements are larger for the least educated compared with the lowest income. This holds for the no qualifications group as well as the no qualifications and low-level qualifications group, indicating a strong association between low education and ill health. There are numerous mechanisms described through which income (Luo et al., 2009, Casey et al., 2001, Heritage et al., 2008, Eibner et al., 2004) and education (Link and Phelan, 1995, Becker, 2009, Collins, 2019) impact health. To compare causal mechanisms of education and income on health is beyond the scope of this work. However, what is apparent from this study is the clear difference in the existing magnitude of the health gradients whether we stratify the population by education or income. Such comparison does require the consideration of the lack of standardization of the groups. For example, the no qualifications group is 23.5% of the population and Q1 is 14.3%

The results of this study also highlight the difference in the health gradients when comparing individual-level to area-level SEP indicators. The absolute gap across IMD described by Love-Koh et al.(Love-Koh et al., 2015) was shown to be 10.97

QALYs (Love-Koh et al., 2015), which is lower than the 13.79 QALYs estimated across education groups, yet higher than the 9.24 estimated across income groups. The calculation of IMD includes income and education at the area level as two of the seven domains meaning there may be an averaging effect when estimating the health of IMD groups. There may also be the possibility that the area is affecting health over an above the individual characteristics which could be explaining the difference in QALE across education, income and IMD. Further work may consider the impact each domain of IMD has on health, albeit the domains of IMD are not individual characteristics but area characteristics. The magnitude of the inequality based on IMD may be sufficient if the evaluation of health policies and provision of services is to be based on area. However, if the area-level SEP indices are used as proxies for individual-level SEP, then this study confirms there can be an underestimation of the extent of inequalities across individuals. Measurement error arising from scoring all individuals in an area the same score is believed to be the cause (Smith et al., 1998), although the potential for bidirectional bias has also been highlighted (Geronimus, 2006).

It is important to note the results of the regression model and the resulting social distribution of health across education and income are not designed to be a causal interpretation of the health-SEP association. Rather the results describe the existing variation in lifetime health by age, sex and SEP. This negates the need for the regression model to consider issues such as confounding in the estimation.

4.5.2 Strengths and limitations

This study used mortality data based on a very large sample size of approximately 340,000 individuals. The HRQL decrements estimated from the HSE were based on approximately 25,300 observations and were robust to alternative approaches to categorising the subgroups and multiple imputation. The study used a previously accepted method to estimating QALE (Love-Koh et al., 2015) which was shown to be robust to alternative regression estimators and alternative approaches to handling the missing data. The use of the previously accepted method allows comparisons of the results across education, income and IMD. Contemporary QALE estimates have updated the results by Love-Koh et al. (McNamara et al., 2023, Love-Koh et al., 2023) and have used the same method and use of IMD to stratify the population. In this article, we have shown how care is needed in conflating IMD with SEP in all cases.

The estimated distribution of QALE not only helps identify inequalities, it can also help provide essential inputs to assess the health equity impacts of policies. The estimated gradient in this Chapter will be used as the input to the DCEA in Chapter 5. This has policy implications as it now facilitates researchers and decision makers to decide on the measure of SEP to be used in their DCEA rather than explicitly or implicitly using IMD to show inequitable variation in health.

Distributional cost-effectiveness analysis (DCEA) is a recently described framework for priority setting which incorporates equity considerations (Asaria et al., 2016). However, one of the potential limitations of DCEA resides in the requirement for a health expectancy distribution describing the existing variation in lifetime health

across social groups throughout the entire population. Previous DCEAs in the UK to date have described the health equity impacts across IMD (Ward et al., 2022). The estimated social distribution of QALE across education and income can provide an input to DCEAs in which education and income are the SEP indices describing inequitable variation in health.

A number of potential limitations in the study reside in the differing definitions used to construct the groups. For instance, the income distribution of QALE assumed that wage quintiles aligned with income quintiles and an individual in wage quintile Q1 was in income quintile Q1. Further, for the sensitivity analysis it was assumed the NVQ levels such as Level 1 which is based on GCSE grades D-G aligns and Level 2 which is based on GCSE grades C and above, aligns with 1-4 GCSEs and 5+ GCSEs, respectively. The strength of these assumptions will need to be considered. But this does highlight an issue with individual-level indices such as education and income. Although they are all measuring an individual asset, there may be many different ways of measuring and categorising. For example, education may be defined by educational attainment which may be measured by qualifications gained or years of schooling. Income may be defined as gross income, net income, individual income, household income or it may rely on proxies such as wage. Further, wealth may provide more information than income alone and so on. This study highlights a strength of using IMD as there are limited assumptions in categorisation.

In addition, researchers need to carefully consider how the social groups are constructed (Arcaya et al., 2015). When group membership is based on a continuous variable and group membership is not clearly defined (e.g. education or income

groups), the definition should be based on an *a priori* knowledge of how to collapse or expand groups (Arcaya et al., 2015). This study defined groups *a priori* but was also limited by the way in which mortality data was provided. For example, exploration of the wage groupings was limited.

The approach adopted in this study assumed the HRQL weights for those younger than 16 years of age were equivalent to the HRQL weights for the 16- to 24-year age group. This was due to limitations in the use of EQ-5D-3L as an instrument for children and the lack of observations in the data (Kwon et al., 2019). The assumption in this study does, however, base childhood HRQL weights on those estimated for 16- to 24-year-olds, meaning the study implicitly captures differential weights for children across SEP groups. It is unclear whether EQ-5D differs for children in different SEP groups but this assumption may be considered appropriate given the association between childhood SEP and adverse childhood experiences reported in the literature (Walsh et al., 2019).

Acknowledgment is also given to the nature of the income data that are captured at the household level. The decision to opt for individual or household income may be a pragmatic one based on data limitations, but it should also reflect whether it is the act of earning or the ability to consume that matters. If it is the latter, then household income may better inform categorization of SEP (Galobardes et al., 2006a).

Conclusion

In conclusion, this study highlights the magnitude of the differences in lifetime experienced health inequalities when using education, income and IMD to stratify the

population by SEP. The reliance on IMD may be masking important information on the magnitude of the existing health inequalities. Further work in Chapter 5 will build on this work and consider the impact different measures of SEP may have on the equity assessments of an intervention.

Chapter 5: The Incorporation of Equity Considerations and the Role of Socioeconomic Position Part 2: A Case Study of a Distributional Cost-Effectiveness Analysis of the E-SEE Steps Trials

This work was presented at iHEA Cape Town 2023.

5.1 Introduction

Despite the importance of tackling health inequities along the lines of SEP, the health equity impacts of investments in PHIs in early childhood are rarely incorporated in economic evaluations in the UK (see Chapter 2). This may be explained, in part, by the nature of 'traditional' methods of economic evaluation in which the objective function is based on the maximisation of population health (i.e., efficiency objectives). Implicitly this considers the costs and benefits of the intervention for the 'average' individual in the population and fails to provide information on the social distribution of costs and benefits, thus neglecting potentially important equity objectives. Cost-effectiveness analysis (CEA) is an example of such a framework that is based solely on efficiency objectives. Its use in the UK dominates the early childhood public health economic evaluation literature (see Chapter 2), likely resulting from NICE guidance (National Institute for Health Care Excellence, 2022).

As described in Chapter 1 and Chapter 3, there are now a number of methodological advances that allow the formal incorporation of equity into the economic evaluation framework (Cookson et al., 2017a, Ward et al., 2022, Avanceña and Prosser, 2021). The method selected for this thesis is distributional cost-effectiveness analysis (DCEA) (Asaria et al., 2016). It provides an explicit framework to evaluate both efficiency and equity objectives and allows the consideration of the impact of social value judgments on trade-offs between maximising health and improving health equity (see Chapter 3 for a description of DCEA).

Yet, despite DCEA providing the framework, any equity-informative analysis still requires the explicit specification of the equity objective function. One of the key questions of the equity objective function is: *Equality between whom?* (Cookson, 2017) Chapter 4 discussed the differences in individual- and area-level measures of SEP and demonstrates the importance of the choice of measure of SEP when doing any equity-informative analysis.

To date, DCEAs conducted in a UK context have focussed on the use of Index of Multiple Deprivation (IMD) to categorise the population by SEP and therefore to describe inequitable variation in health (Ward et al., 2022). It stands that the precedent of using the area-level indicator IMD over which to evaluate equity objectives in a DCEA may be masking important equity information (see Chapter 4).

The aims of this chapter are therefore two-fold. The first aim covers the more general aim of incorporating equity considerations into the economic evaluation of an early childhood public health intervention by conducting a DCEA. The second aim is to explore the impact of altering the assumptions in the equity objective regarding the question of: *equality between whom?* This will be achieved through comparing an area-level indicator of SEP (IMD) to individual-level indicators (education and income) for the purpose of describing inequitable variation in health. This is all demonstrated through the use of the E-SEE Steps trial (Bywater et al., 2022), which is used as an exemplar of a real-world early childhood public health intervention (see Chapter 3 for a full description of the ESEE Steps trial).

5.2 Method

The methods are presented as follows. First the ESEE Steps intervention and the parameters used in the case study are described in Section 5.2.1. This is followed by the DCEA parameters in Section 5.2.2 and the methodological approach used to conduct the DCEA in Section 5.2.3 and Section 5.2.4.

5.2.1 Analysis of the E-SEE Steps Trial

The evaluation of the E-SEE Steps trial to provide equity informative evidence for use in the DCEA was conducted using the same approach used in the published economic evaluation of E-SEE Steps (Cox et al., 2022). This allowed consistency in the estimation of costs and QALYs when compared to those in the published literature. The costs and QALYs for the IY and SAU groups were estimated over the 18-month time horizon of the trial. Costs and QALYs were estimated for the adult and the child. In the published economic evaluation of E-SEE Steps (Cox et al., 2022), the authors also estimated overall cost-effectiveness by combining the adult and child costs and outcomes. For the purpose of the DCEA being conducted in this chapter, the overall (combined) results were not considered in a DCEA. This was due to the unintuitive nature of what an average equity impact would mean across generations. For example, whether it would be useful to average an equity improvement in a parent with an equity harm in their child. In the estimation of the QALY analyses, linear regression models were used for covariate control in the form of ordinary least squares models. For the cost analyses, generalised linear models (glm) were used as costs do not distribute normally. A gamma distribution was used in the glm as it generates non-negative, positively skewed data. The gamma

distribution was adopted with a log-link function. [xv] The analyses controlled for: treatment allocation, baseline HRQL scores, child age, parent age, gender, ethnicity and relationship status of the parents. The results of the diagnostic tests (i.e. Akaike information criterion (AIC) and Bayesian information criterion (BIC)) used to select the preferred distributional form and link function for the GLM models is presented in the appendix.

The results of the costs and QALY regression models using multiple imputation provided the results across the entire E-SEE Steps trial population. The coefficients for the individual SEP sub groups were also estimated and used to estimate subgroup costs and QALYs. To align with the SEP stratification in the baseline distributions estimated in Chapter 4, the approaches to stratification of the E-SEE Steps Trial participants was as follows: 1) IMD quintiles; 2) income quintiles (based on income quintile of the primary caregiver, non-equivalised); and 3) education attainment categorised using the following categories: *no qualifications*; *1-4 GCSEs or equivalent*; *5+ GCSEs or equivalent*; *apprenticeships and vocational qualifications*; *A-levels or equivalent;* and *degree-level education and higher*. Educational attainment was also categorised as *No qualifications or low-level qualifications*; *GCSEs, 5 or more*; *A-levels or equivalent*; and *Degree and higher* to align with the sensitivity analysis.

Uncertainty in the costs and QALYs estimated from the regression models were captured using Monte Carlo simulation in which samples were taken from all uncertain distributions associated with each parameter. The Cholesky decomposition

[xv] The link function in a glm links the expected value of the response to the linear predictors in the model. The log link function can be used when the log of the expected value is related to the linear predictor variable.

method was used as this explicitly takes into account the correlation between variables (Briggs, 1999) and is commonly used in economic models (Stevenson et al., 2014).

5.2.2 Economic evaluation

The analyses described in Section 5.2.1 detailed the approach to estimating the costs and QALYs for each SEP subgroup based on the analysis of the E-SEE Steps Trial. The economic evaluation proposed is a DCEA, which requires a number of parameters, which are described below.

The DCEA is reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement (Husereau et al., 2022). The perspective of the DCEA was that of the National Health Service and Personal Social Services (NHS & PSS). The time horizon over which the costs and outcomes were assessed was 18 months as this was the length of the follow-up in the trial. In line with UK guidelines, costs and outcomes were discounted at a rate of 3.5% per annum (National Institute for Health Care Excellence, 2022). The location of the evaluation is based on that of the original E-SEE Steps trial (Bywater et al., 2022) (see Chapter 3). That is, four trial sites across the North of England, Midlands and South of England. The setting for intervention delivery was local community venues.

The assessment of the cost-effectiveness of the ESEE-Steps trial was made by comparing the results to two cost-effectiveness thresholds: £15,000 per QALY to align with the Department of Health in England; (Department of Health and Social

Care Office for Life Sciences, 2017) and £30,000 per QALY to align with the upper bound of the threshold used by the National Institute for Health and Care Excellence (NICE) (National Institute for Health Care Excellence, 2022). The threshold can be used to represent the health opportunity cost, which is the consideration of the displaced resources as a result of the decision to fund a programme or intervention (see Chapter 1 for an overview of the health opportunity cost and its role in economic evaluation). In a DCEA, consideration must be given to distribution of the health opportunity cost across the population. The base case for this economic evaluation assumes the health opportunity cost is equally distributed across all IMD, income or education groups. However, there may be reasons to assume that the health opportunity costs are borne proportionately more by the most deprived groups, i.e. the lowest IMD, lowest income or those with the lowest educational attainment as these groups may rely more on public services. Indeed, Love-Koh et al. (Love-Koh et al., 2020) estimated the social variation in the health opportunity cost across IMD quintiles and found greater health opportunity costs were imposed on the most socioeconomically deprived. To account for this, sensitivity analysis is conducted in which the Love-Koh et al. estimated distribution of the health opportunity cost is used across IMD quintiles. The estimated social distribution is then translated to income quintiles and educational attainment groups by maintaining the estimated gradient in health opportunity cost and assuming the gradient measured across IMD quintile equates to the gradient across income quintiles and educational attainment groups. The parameters used in the DCEA can be seen in Table 11.

Table 11: Parameters used in the base case and in scenario analysis

Parameter	Value	Source
Costs by subgroups	Estimated from regression model	See Section 2.2.2
QALYs by subgroup	Estimated from regression model	See Section 2.2.2
Discount rate	3.5%	NICE (2022) (National Institute for Health Care Excellence, 2022)
Time horizon	18 months	E-SEE Steps trial
Perspective	NHS & PSS	NICE (2022) (National Institute for Health Care Excellence, 2022)
Cost effectiveness threshold	£15,000 per QALY	DHSC (Department of Health and Social Care Office for Life Sciences, 2017)
Alternative cost effectiveness threshold	£30,000 per QALY	NICE (2022) (National Institute for Health Care Excellence, 2022)
Distribution of the health opportunity cost (proportion of cost borne by the most to least deprived subgroup) – base case		
IMD quintiles	0.2, 0.2, 0.2, 0.2, 0.2	Assumed
Income quintile	0.2, 0.2, 0.2, 0.2, 0.2	Assumed
Educational attainment group	0.25, 0.25, 0.25, 0.25	Assumed
Distribution of the health opportunity cost (proportion of cost borne by the most to least deprived subgroup) – scenario analysis		
IMD quintiles	0.264, 0.219, 0.218, 0.161, 0.138	Love-Koh (2020) (Love-Koh et al., 2020)

Income quintile	0.264, 0.219, 0.218, 0.161, 0.138	Assumed
Educational attainment group	0.297, 0.266, 0.234, 0.203	Assumed

Abbreviations: DHSC, Department of Health and Social care; IMD, index of multiple deprivation; QALY, quality-adjusted life year.

5.2.3 Equity Impact Analysis

Using the parameters outlined in Section 5.2.3, the net health benefit approach can be used. Incremental net health benefit (iNHB) is calculated using the following equation:

$$iNHB = \Delta\, health - \frac{\Delta\, costs}{\lambda} \qquad (6)$$

Where ∆health represents the incremental health generated by the intervention; ∆costs represent the incremental costs; and λ represents the health opportunity cost. The term ∆costs divided by λ converts the costs into foregone health to provide the net health benefit of the E-SEE Steps programme less the health opportunity cost of E-SEE Steps. The resulting units of iNHB are in QALYs. The iNHB will be positive if the intervention is cost-effective as iNHB is simply a linear transformation of the incremental cost-effectiveness ratio (ICER) [xvi] (Craig and Black, 2001) (see Chapter 1 for a discussion of ICERs).

[xvi] An ICER is calculated using the following formula: $ICER = \frac{incremental\ costs}{incremental\ effects}$

The DCEA requires the results from an efficiency perspective (i.e. the cost-effectiveness of the whole programme based on total costs of the programme and the total QALYs generated from the programme) as well as the equity-informative one (i.e. the QALYs generated for each SEP subgroup and the costs falling on each subgroup). The efficiency results of the E-SEE Steps Trial are simply estimated as the iNHB of the entire trial. However, the generation of the equity results requires a number of additional steps.

First, the calculation of the iNHB for the purpose of equity impact analysis requires that the iNHB is estimated for each of the individual subgroup populations. This is done by using the incremental health effects for each subgroup which are estimated directly from the trial results (see Section 5.2.1). Then the subgroups costs are based on the total incremental cost of the entire E-SEE Steps programme converted to health opportunity costs using λ and then apportioned to each subgroup using the social distribution of the health opportunity cost (see Section 5.2.2 and Table 1). This step occurs as the health opportunity cost of funding E-SEE Steps is borne by the entire population, not simply the subgroup in which the direct trial costs fall.

The resulting social distribution of iNHB for each SEP subgroups can then be combined with the baseline distribution of health across SEP subgroups (estimated in Chapter 4) to assess whether the resulting QALE has increased or decreased for each subgroup. The assessment of the resulting health equity impact is based on changes in a measure of health referred to as the slope index of inequality (SII) or relative index of inequality (RII).

Both SII and RII form a group of indices referred to as regression-based indices. These reflect the gradient observed across all of the groups while taking into account the proportion of the population within each group (Wagstaff et al., 1991).

The SII is the coefficient of a simple one variable regression of QALE (Q) on the fractional rank (r).[xvii] The incorporation of fractional rank allows for the differences in the size of SEP subgroups to be accounted for. The RII is simply a transformation of the SII to a relative scale. The SII and RII are estimated using Equation (7) and Equation (8), respectively.

$$SII = \frac{Covariance(Q,r)}{Variance(r)} \tag{7}$$

$$RII = \frac{SII}{Q} \tag{8}$$

The SII and RII can be interpreted as the absolute difference in health when moving up the social gradient from the lowest to highest SEP groups. A value of 0 represents no inequality with higher values indicating greater inequality. Positive values signify the outcomes are concentrated in the groups at the top of the social gradient with the converse for negative values. In both SII and RII, a linear relationship between health and SEP is assumed. These indices are considered

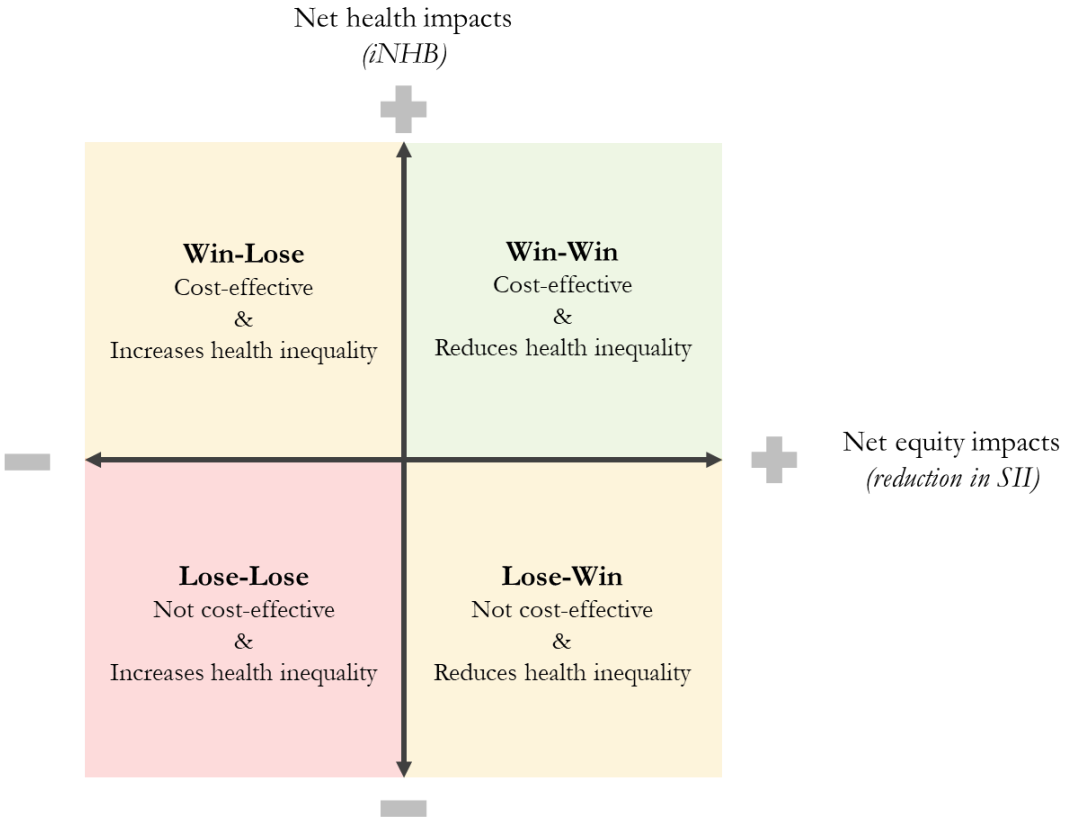
[xvii] To calculate the fractional rank, the states are ranked in terms of QALE from highest to lowest. The subgroups are then weighted according to the proportional distribution of the population within the subgroup. The subgroup is then represented in terms of the cumulative midpoint of the population range of each subgroup.

suitable when rank ordering of the SEP groups is meaningful, as in the case of education, income and IMD.

Absolute and relative inequality are both presented in this study. The choice between using absolute and relative measures of inequality rely on value judgements when considering what distribution of health change would preserve or improve population inequality (Kjellsson et al., 2015, Asada, 2007).

The results are reported as the reduction in the SII compared to the SII of the baseline distribution: a positive value (i.e. a reduction) means health inequality has been reduced. The results of the health equity impact analysis are presented on a health equity impact plane (Cookson et al., 2017a). This plots the efficiency/cost-effectiveness of the E-SEE Steps trial, presented as the iNHB of the entire trial population, against the equity impacts of the E-SEE Steps trial as measured by the reduction in SII. Figure 7 shows an illustration of the equity-impact plane.

Figure 7 Health equity impact plane



As can be seen in Figure 7, the results can yield programmes that have a positive incremental net health benefit (i.e. they are cost-effective) and reduce health inequalities (north-east quadrant); those that are not cost-effective and increase health inequalities (south-east quadrant) and those that require trade-offs between the two criteria in the north-west and south-east quadrants.

5.2.4 Equity Trade-Off Analysis

To allow for the potential trade-off between improvements in population health and improvements in health equity, health-related social welfare functions (HRSWF) are required. Examples include the Atkinson (Atkinson, 1970) and Kolm (Kolm, 1976) social welfare functions, which measure the change in social welfare as a function of health efficiency (through mean health) and health inequality.

The social preference for reductions in health inequalities can be captured using an "inequality aversion" parameter. As the inequality aversion parameter increases, improvements in social welfare are valued more highly as a result of health benefits being accrued by the most deprived in society. An inequality aversion parameter of 0 indicates no aversion to health inequalities.

Inequality can be incorporated on a relative scale using the Atkinson index (ε) or on an absolute scale using the Kolm index (α), which use the inequality aversion parameters ε and α, respectively. In lieu of a clear choice of preference for absolute or relative inequality (Asada, 2010) it may be preferable to report in multiple measures (Asaria et al., 2016). The parameters are expressed through a single number and indicate how maximising population health and improvements in population health inequalities should be traded-off. A health inequality aversion value with ε = 10.95 and α = 0.15 has previously been derived for England (Robson et al., 2017). This value was elicited by asking a sample of participants in England (n = 244) about health trade-offs between the 'richest fifth' and 'poorest fifth' of the population. Individuals were asked to choose between programmes that maximise total health for the population and those that trade off some of the health to improve health inequalities. The point of indifference, i.e. the point at which respondents were indifferent between the programmes allowed the EDE equations to be solved for ε and α. The results showed that the majority (81.51%), were willing to trade-off some total health to reduce health inequality.

The aversion to inequality may differ according to the nature of the inequality. For example, the population's aversion to health inequality across income groups may differ from that of education groups. It is assumed the aversion to inequality is

independent of the nature of the inequality (i.e., α is consistent across education, income and IMD). This is an assumption, as there is no evidence of the populations' health inequality aversion across education or income. The elicited values of ε and α are therefore used as tentative starting points for the equity trade-off analysis and the sensitivity of the results are assessed by altering the values of ε and α.

The resulting social distribution of health (based on QALE following the E-SEE Steps trial) is compared to the pre-intervention distribution using standard economic dominance rules. If one does not dominate the other then a HRSWF, such as the Atkinson index or the Kolm index, is used to represent how a decision-maker trades off improving total health and improving health equity. This trade off represents the amount of total population health a decision maker is willing to sacrifice to achieve a more equitable health distribution and is usually reported in terms of the equally distributed equivalent (EDE)[xviii] level of health to aid interpretation. Using this scale, the mean health less the EDE level of health is the amount of health per person a decision maker would be willing to sacrifice to achieve full health equity. The EDE based on the Atkinson social welfare index is calculated as follows:

$$h_{EDE} = \left[\frac{1}{n}\sum_{i=1}^{n}[h_i]^{1-\epsilon}\right]^{\frac{1}{1-\epsilon}} \qquad (9)$$

The EDE based on the Kolm social welfare index is calculated as follows:

[xviii] Equally distributed equivalent health is the common level of health in a hypothetical equal distribution of health that has the same level of social welfare as the actual unequal distribution of health

$$h_{EDE} = -\left(\frac{1}{\alpha}\right)\log\left(\frac{1}{n}\sum_{i=1}^{n} e^{-\alpha h_i}\right) \quad (10)$$

Where n is the size of the population and h_i is the level of health for the subgroup. The incremental QALYs for the entire population are compared to the incremental EDE. The result shows the value of the improvements in health inequality in units of QALYs. For example, if the EDE is calculated to be 15 QALYs and the mean health generated from the programme is 12 QALYs, then the reduction in health inequality as a result of the programme is valued at 3 QALYs.

To estimate the EDE, estimates of the size of the population are required. As data are not available on the size of the SEP subgroup populations in England, it was assumed the eligible population was 1,000 parent and children dyads.

5.3 Results

5.3.1 E-SEE Steps Trial SEP Characteristics

The E-SEE Steps Trial participant characteristics have been reported in detail elsewhere (Bywater et al., 2022) (see Chapter 3 for an overview of the E-SEE Steps Trial participants characteristics). Briefly, the trial enrolled 341 children and parents: 285 in the IY arm and 56 in the SAU arm. The parents enrolled in the trial and informing the economic evaluation were female (100%) and had a mean age of 30.9 years at baseline. The sample of children enrolled in E-SEE Steps was gender balanced (51% male) and the children had a mean age of 6 weeks at baseline.

The categorisation of the SEP of the E-SEE Steps trial participant's is, however, described in this study for the first time. Table 12 shows the SEP of the trial participants in terms of IMD quintile, educational attainment and income quintiles across trial arms. The results show the E-SEE Steps trial enrolled a disproportionately higher number of those in the most deprived IMD quintile (121 out of 336) and income quintile (104 out of 336) yet the reverse can be seen for the educational attainment groups with a disproportionately higher number of those in the least deprived education group (146 out of 329). Missing IMD, educational attainment and income data were low (<10%) for each.

Table 12: Baseline socioeconomic position of the E-SEE Steps trial participants

Categorical variable	**SAU**	**IY**	**All**
IMD			
IMDQ1	21 (37.5%)	100 (35.7%)	121 (36%)
IMDQ2	11 (19.6%)	42 (15%)	53 (15.8%)
IMDQ3	7 (12.5%)	46 (16.4%)	53 (15.8%)
IMDQ4	13 (23.2%)	54 (19.3%)	67 (19.9%)
IMDQ5	4 (7.1%)	38 (13.6%)	42 (12.5%)
Total	56 (100%)	280 (100%)	336 (100%)
Education			
No qualifications and low-level qualifications	6 (11.1%)	31 (11.3%)	37 (11.2%)
GCSEs: 5 or more	6 (11.1%)	15 (5.5%)	21 (6.4%)
A-levels or equivalent	20 (37%)	105 (38.2%)	125 (38%)
Degree or higher	22 (40.7%)	124 (45.1%)	146 (44.4%)
Total	54 (100%)	275 (100%)	329 (100%)
Income			
Q1	17 (30.4%)	87 (31.1%)	104 (31%)
Q2	12 (21.4%)	44 (15.7%)	56 (16.7%)
Q3	11 (19.6%)	42 (15%)	53 (15.8%)
Q4	10 (17.9%)	56 (20%)	66 (19.6%)
Q5	6 (10.7%)	51 (18.2%)	57 (17%)
Total	56 (100%)	280 (100%)	336 (100%)

Abbreviations: IMD, index of multiple deprivation; inc, income; IY, incredible years; SAU, service as usual.

For comparison across measures of SEP, Sankey plots in Figure 8, Figure 9 and Figure 10 illustrate which SEP subgroups the E-SEE Steps trial participants fall in. In Figure 8, the plot indicates a high degree of overlap between the trial participants that fall into IMD quintile Q1 and income quintile Q1. This appears to hold for IMDQ4 and income Q4, and IMDQ5 and income Q5. However, Figure 9 and Figure 10 show that when compared to the educational attainment groups, there appears to be little overlap between the IMD quintile or income quintile and the educational attainment groups.

Figure 8 Sankey diagram showing the IMD quintile and income quintile of the participants enrolled in the E-SEE Steps Trial

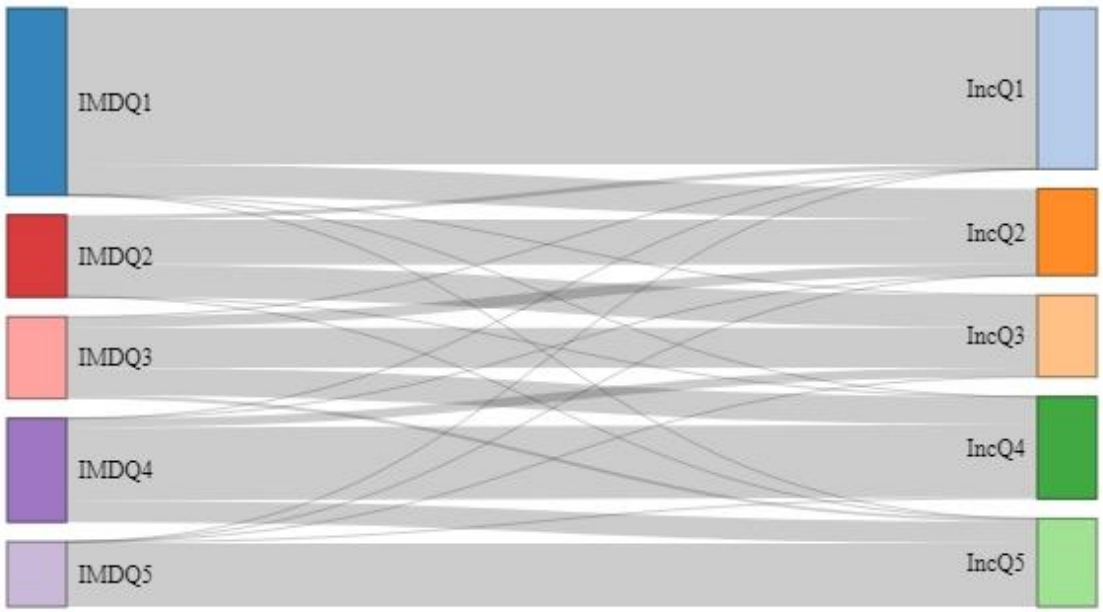


Figure 9 Sankey diagram showing the IMD quintile and educational attainment group of the participants enrolled in the E-SEE Steps Trial

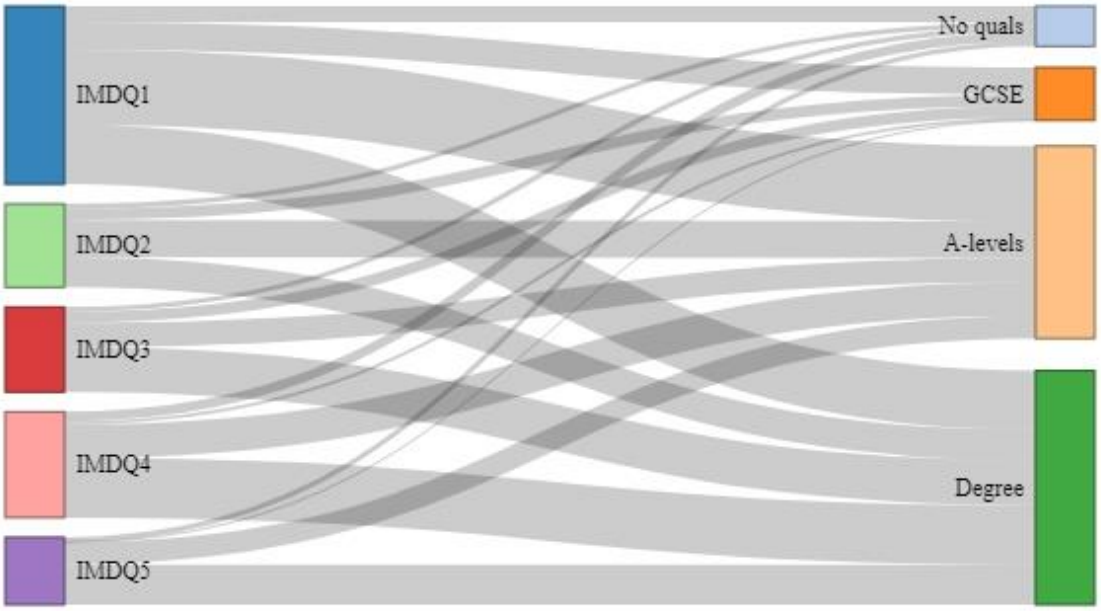
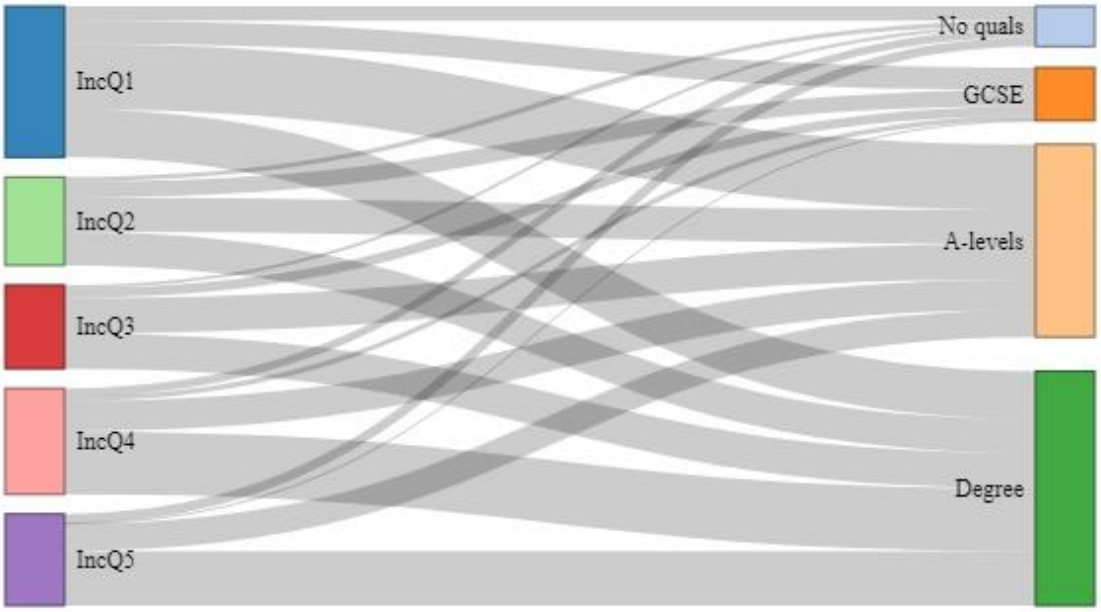


Figure 10 Sankey diagram showing the income quintile educational attainment group of the participants enrolled in the E-SEE Steps Trial



5.3.2 E-SEE Steps Trial Results

The results of the regression models estimating costs and QALYs in the E-SEE Steps trial showed non-significant EQ-5D coefficients across the SEP subgroups for IMD, education and income. No clear trends were observed for the EQ-5D values and costs across SEP groups. Regression results used to inform the cost-effectiveness analysis can be found in the appendix.

The estimated costs and QALYs for each SEP subgroup can be seen for the adults and children in Table 13 and 14 respectively. The average total costs from an NHS and PSS perspective were higher in the E-SEE Steps arm compared to SAU across all IMD quintiles, educational attainment groups and income quintiles. The same was observed for the estimated QALYs across all IMD quintiles, educational attainment groups and income quintiles. No real trend was observed in the QALYs or costs by SEP gradient. The overlap of the 95% confidence intervals between E-SEE Steps and SAU across almost all SEP subgroups highlighting the uncertainty in the results.

Table 13: Adult costs and QALYs by E-SEE Steps Trial arm and SEP subgroup

	Costs (95% CI)		QALYs (95% CI)	
SEP subgroup	**E-SEE Steps**	**SAU**	**E-SEE Steps**	**SAU**
IMD				
IMDQ1	£1444 (£974, £1914)	£811 (£178, £1445)	1.34 (1.29, 1.38)	1.32 (1.20, 1.44)
IMDQ2	£2110 (£1309, £2911)	£832 (£180, £1843)	1.33 (1.28, 1.37)	1.32 (1.16, 1.47)
IMDQ3	£1274 (£663, £1885)	£461 (£129, £792)	1.38 (1.34, 1.42)	1.26 (1.11, 1.41)
IMDQ4	£984 (£641, £1327)	£835 (£68, £1601)	1.37 (1.34, 1.40)	1.34 (1.23, 1.44)
IMDQ5	£1346 (£881, £1810)	£220 (£92, £532)	1.36 (1.32, 1.39)	1.30 (1.02, 1.57)
Total	£1,388 (£1142, £1639)	£942 (£604, £1461)	1.35 (1.33, 1.36)	1.31 (1.27, 1.35)
Education				
No qualifications and low-level qualifications	£1912 (£956, £2868)	£1102 (£20, £2425)	1.29 (1.18, 1.40)	1.40 (1.24, 1.55)
GCSEs: 5 or more	£689 (£113, £1492)	£417 (£78, £1211)	1.44 (1.37,1.50)	1.19 (0.65, 1.72)
A-levels or equivalent	£1928 (£1418, £2438)	£684 (£190, £1178)	1.34 (1.31,1.37)	1.28 (1.18, 1.39)
Degree or higher	£1056 (£817, £1294)	£799 (£144, £1455)	1.36 (1.33, 1.38)	1.33 (1.26, 1.41)

Total	£1,388 (£1142, £1639)	£942 (£604, £1461)	1.35 (1.33, 1.36)	1.31 (1.27, 1.35)
Income				
IncQ1	£1587 (£1038, £2137)	£655 (£176, £1134)	1.34 (1.29, 1.38)	1.32 (1.17, 1.46)
IncQ2	£1456 (£780, £2133)	£1145 (£127, £2417)	1.36 (1.31, 1.40)	1.29 (1.14, 1.45)
IncQ3	£1592 (£929, £2255)	£679 (£269, £1089)	1.37 (1.32, 1.41)	1.31 (1.19, 1.42)
IncQ4	£1057 (£642, £1473)	£653 (£62, £1569)	1.37 (1.34, 1.40)	1.34 (1.21, 1.46)
IncQ5	£1328 (£925, £1732)	£329 (£91, £568)	1.35 (1.31, 1.38)	1.32 (1.17, 1.47)
Total	£1,388 (£1142, £1639)	£942 (£604, £1461)	1.35 (1.33, 1.36)	1.31 (1.27, 1.35)

Abbreviations: CI, confidence interval; IMD, index of multiple deprivation; QALYs, quality-adjusted life years; SAU, service as usual.

Table 14: Child costs and QALYs by E-SEE Steps Trial arm and SEP subgroup

	Costs (95% CI)		QALYs (95% CI)	
SEP subgroup	**E-SEE Steps**	**SAU**	**E-SEE Steps**	**SAU**
IMD				
IMDQ1	£1072 (£787, £1356)	£1320 (£624, £2016)	1.26 (1.26, 1.27)	1.279 (1.265, 1.292
IMDQ2	£1179 (£729, £1630)	£733 (£448, £1017)	1.27 (1.26, 1.28)	1.275 (1.253, 1.296
IMDQ3	£1079 (£709, £1449)	£919 (£340, £1498)	1.28 (1.27, 1.29)	1.268 (1.241, 1.294
IMDQ4	£1251 (£905, £1597)	£1104 (£640, £1568)	1.27 (1.26, 1.28)	1.269 (1.253, 1.286
IMDQ5	£1390 (£1109, £1670)	£481 (£284, £677)	1.27 (1.27, 1.28)	1.286 (1.232, 1.34
Total	£1,177 (£1035, £1340)	£1,000 (£746, £1322)	1.27 (1.27, 1.27)	1.27 (1.27, 1.27)
Education				
No qualifications and low-level qualifications	£1493 (£788, £2197)	£1451 (£-165, £3068)	1.27 (1.26, 1.28)	1.25 (1.22, 1.28)
GCSEs: 5 or more	£947 (£197, £1697)	£765 (£-156, £1687)	1.27 (1.26, 1.29)	1.29 (1.27, 1.31)
A-levels or equivalent	£1256 (£975, £1538)	£881 (£592, £1169)	1.27 (1.26, 1.27)	1.27 (1.25, 1.28)
Degree or higher	£1109 (£922, £1296)	£1192 (£660, £1723)	1.27 (1.27, 1.28)	1.29 (1.28, 1.30)

Total	£1,177 (£1035, £1340)	£1,000 (£746, £1322)	1.27 (1.27, 1.27)	1.27 (1.27, 1.27)
Income				
IncQ1	£1095 (£795, £1395)	£954 (£414, £1494)	1.26 (1.26, 1.27)	1.28 (1.27, 1.30)
IncQ2	£962 (£541, £1382)	£1319 (£363, £2274)	1.27 (1.26, 1.28)	1.26 (1.24, 1.29)
IncQ3	£1273 (£850, £1696)	£1080 (£500, £1659)	1.28 (1.27, 1.28)	1.27 (1.25, 1.29)
IncQ4	£1130 (£833, £1427)	£896 (£561, £1231)	1.27 (1.26, 1.28)	1.28 (1.25, 1.30)
IncQ5	£1414 (£1085, £1744)	£746 (£88, £1404)	1.28 (1.27, 1.28)	1.28 (1.25, 1.31)
Total	£1,177 (£1035, £1340)	£1,000 (£746, £1322)	1.27 (1.27, 1.27)	1.27 (1.27, 1.27)

Abbreviations: CI, confidence interval; IMD, index of multiple deprivation; QALYs, quality-adjusted life years; SAU, service as usual.

5.3.3 Equity Impact Analysis

Step by step calculations shown in Table 15 demonstrate the approach to calculating the iNHB for each subgroup. The example shown in Table 15 is the iNHB and the post-intervention distribution of health for the child outcomes across IMD quintiles. The results for the adult and child outcomes across all SEP subgroups can be seen in Figure 11 and Figure 12. The results shown in Figure 11 and Figure 12 are based on a health opportunity cost of £15,000/QALY and £30,000/QALY, respectively.

The results indicate the impact the choice of threshold (i.e. £15,000/QALY or £30,000/QALY) has on the results. Taking IMD quintile as an example, 3 of 5 quintile groups have a positive iNHB when using £15,000/QALY. This rises to 4 out of 5 when using £30,000/QALY. The choice of cost-effectiveness threshold has no impact on the health gradient, as it impacts the magnitude of the iNHB in each group proportionately.

The results across groups appear to be unstable with no trend by SEP group and the magnitude of the iNHB gain/loss. In the example of the adults according to educational attainment group, there is an iNHB of 0.0260 QALYs for the A-level group and -0.0056 QALYs for the degree-level group.

When estimated across the children, the E-SEE Steps programme results in negative iNHB across all of the subgroups across IMD quintile groups, income quintile groups and all but one of the education groups. This is as expected as the intervention was deemed not cost effective in the original E-SEE Steps analysis (Cox et al., 2022). Note, for the income quintile iNHB graphs shown in Figure 11 and Figure 12, Q2 is the left most subgroup. This occurs as the baseline distribution of

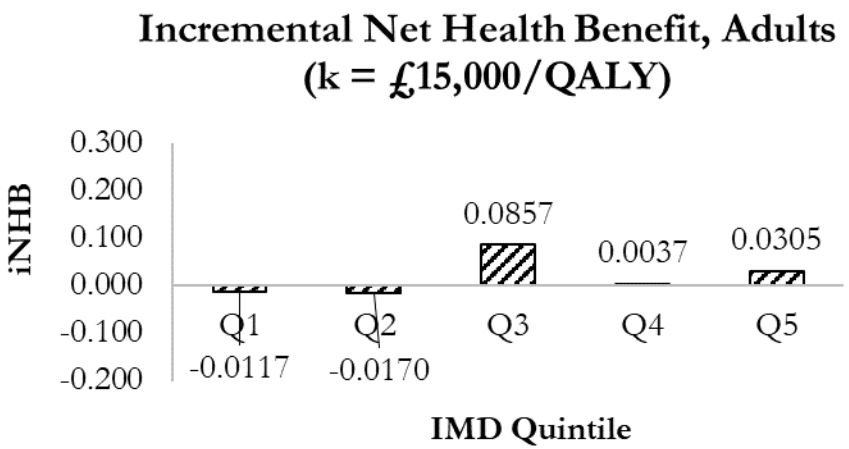
QALE across income quintiles was higher in Q1 than in Q2 and the DCEA requires rank ordering of the subgroup from lowest to highest health at baseline.

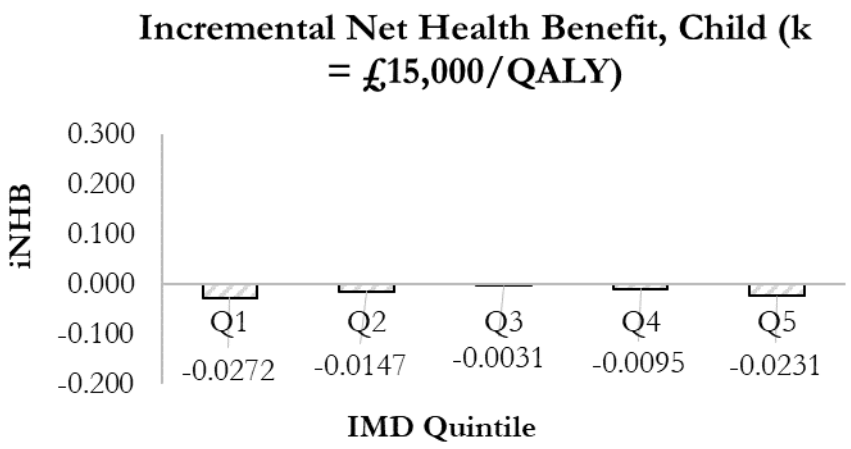
The resulting iNHB when using the distribution of the health opportunity cost estimated by Love-Koh et al. (Love-Koh et al., 2020) rather than assuming an equal distribution which is represented in the base case is shown in the appendix. The results are insensitive to the alternative estimation of the distribution of the health opportunity cost.

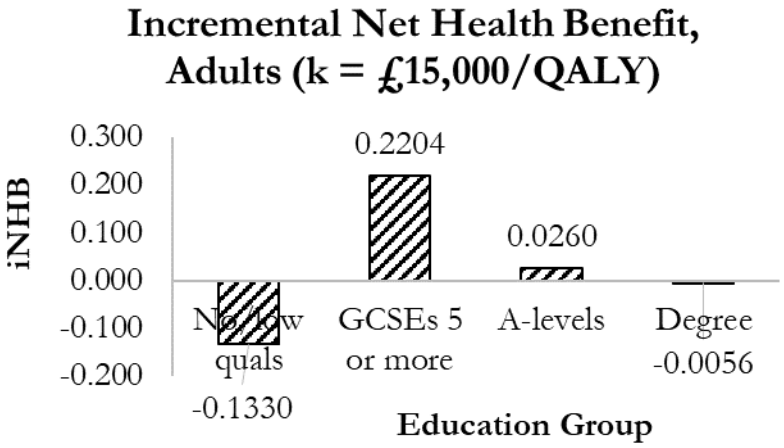
Table 15: Worked example of the incremental net health benefit calculation and the estimation of the post-intervention distribution of health

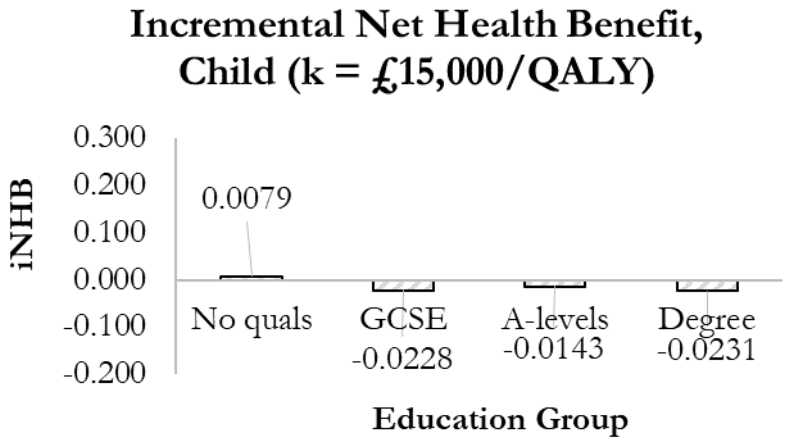
		Calculation	IMDQ1	IMDQ2	IMDQ3	IMDQ4	IMDQ5	Total
a)	Incremental Direct Health Effects	-	-0.015	-0.003	0.009	0.002	-0.011	-
b)	Total Costs	-		-	-	-	-	£885
c)	Total health opportunity cost	b) / £30,000		-	-	-	-	0.03
d)	Proportion of the health opportunity cost	-	20%	20%	20%	20%	20%	-
e)	Distribution of the health opportunity cost	c) x d)	0.006	0.006	0.006	0.006	0.006	-
f)	Incremental net health benefit	a) - e)	-0.021	-0.009	0.003	-0.004	-0.017	-
g)	Baseline distribution of health	-	64.66	68.55	70.58	73.57	75.63	-
h)	Post-intervention distribution of health	f) + g)	64.64	68.54	70.58	73.57	75.61	-

Abbreviations: IMD, index of multiple deprivation.


Incremental Net Health Benefit, Adults (k = £15,000/QALY)
iNHB
0.300
0.200
0.100
0.000
-0.100
-0.200
0.0857
0.0037
0.0305
Q1
Q2
Q3
Q4
Q5
-0.0117
-0.0170
IMD Quintile


Incremental Net Health Benefit, Child (k = £15,000/QALY)
iNHB
0.300
0.200
0.100
0.000
-0.100
-0.200
Q1
Q2
Q3
Q4
Q5
-0.0272
-0.0147
-0.0031
-0.0095
-0.0231
IMD Quintile


Incremental Net Health Benefit, Adults (k = £15,000/QALY)
iNHB
0.300
0.200
0.100
0.000
-0.100
-0.200
0.2204
0.0260
No low quals
GCSEs 5 or more
A-levels
Degree
-0.1330
-0.0056
Education Group


Incremental Net Health Benefit, Child (k = £15,000/QALY)
iNHB
0.300
0.200
0.100
0.000
-0.100
-0.200
0.0079
No quals
GCSE
A-levels
Degree
-0.0228
-0.0143
-0.0231
Education Group

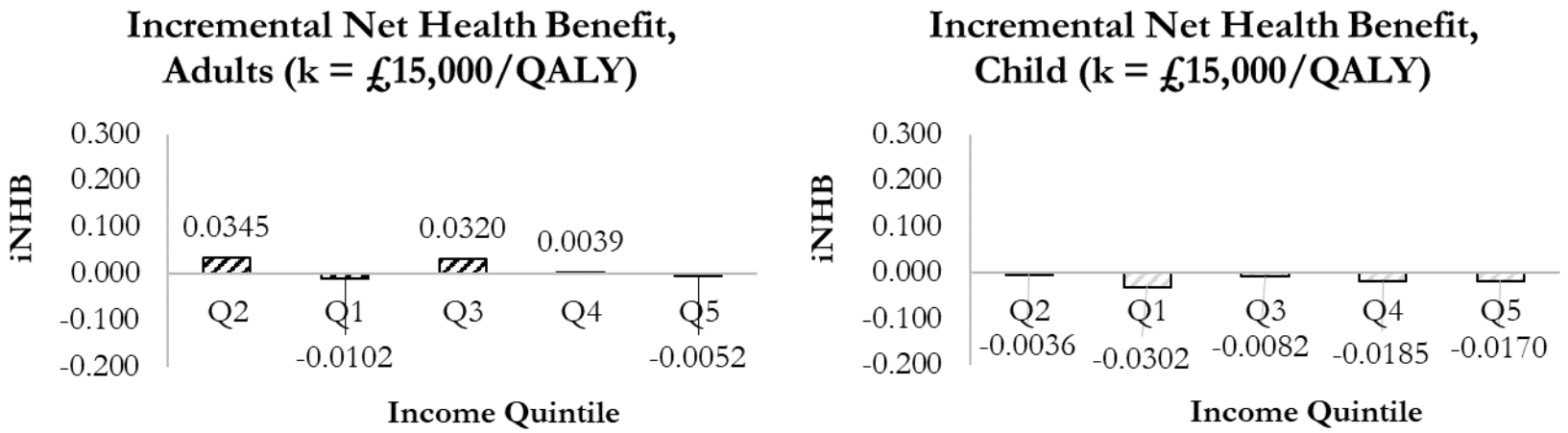
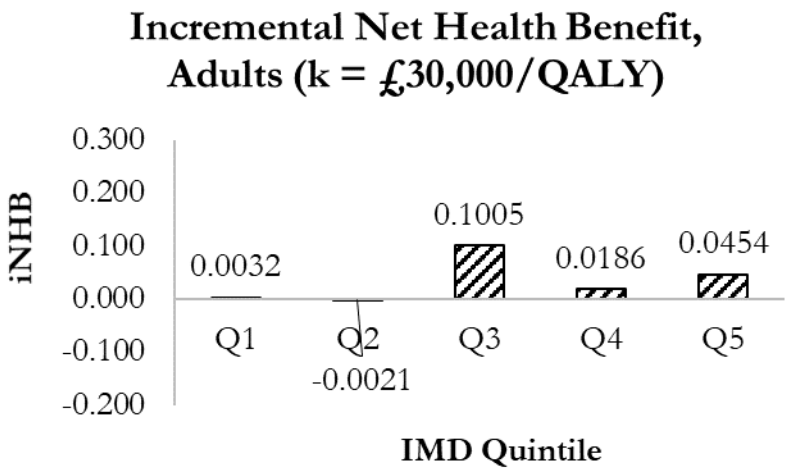
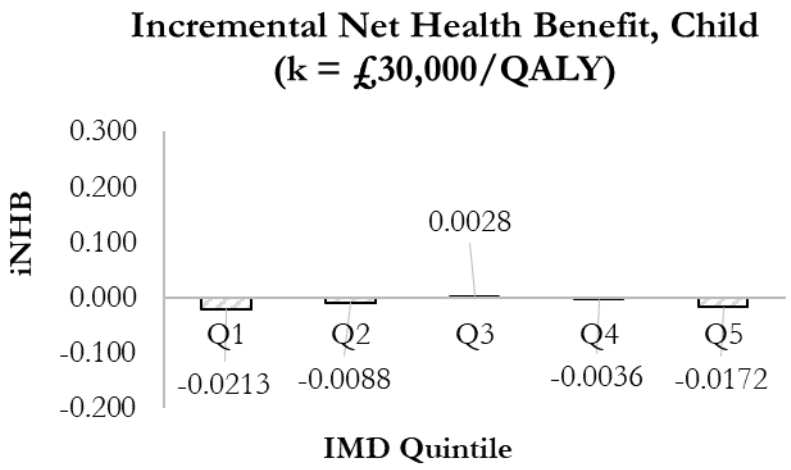
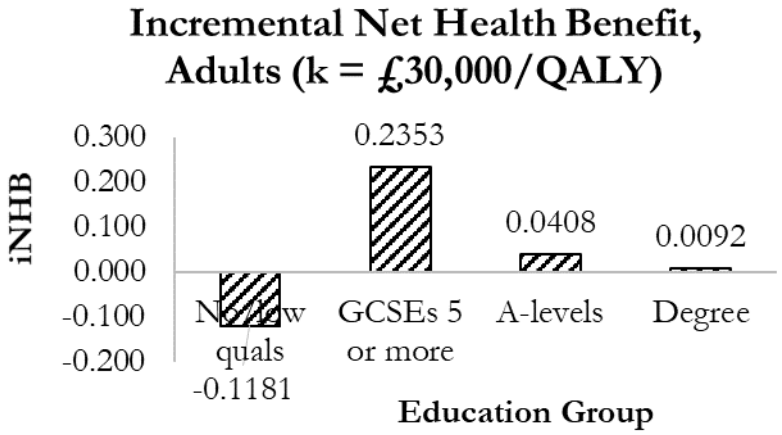
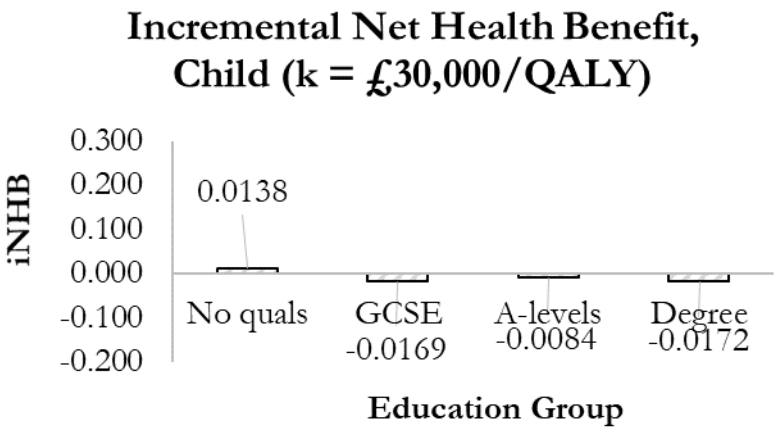


Figure 11 - Incremental net health benefit of the E-SEE Steps programme falling on each SEP subgroup assuming a threshold of £15,000/QALY.


Incremental Net Health Benefit, Adults (k = £30,000/QALY)
iNHB
0.300
0.200
0.100
0.000
-0.100
-0.200
0.0032
-0.0021
0.1005
0.0186
0.0454
Q1
Q2
Q3
Q4
Q5
IMD Quintile


Incremental Net Health Benefit, Child (k = £30,000/QALY)
iNHB
0.300
0.200
0.100
0.000
-0.100
-0.200
-0.0213
-0.0088
0.0028
-0.0036
-0.0172
Q1
Q2
Q3
Q4
Q5
IMD Quintile


Incremental Net Health Benefit, Adults (k = £30,000/QALY)
iNHB
0.300
0.200
0.100
0.000
-0.100
-0.200
-0.1181
0.2353
0.0408
0.0092
No/low quals
GCSEs 5 or more
A-levels
Degree
Education Group


Incremental Net Health Benefit, Child (k = £30,000/QALY)
iNHB
0.300
0.200
0.100
0.000
-0.100
-0.200
0.0138
-0.0169
-0.0084
-0.0172
No quals
GCSE
A-levels
Degree
Education Group

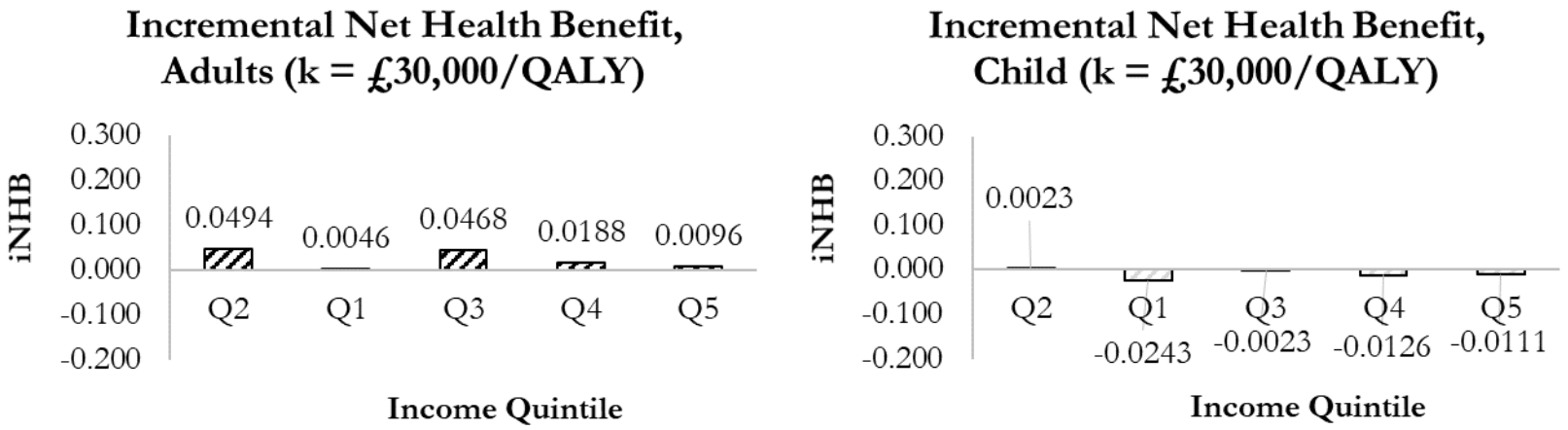


Figure 12 Incremental net health benefit of the E-SEE Steps programme falling on each SEP subgroup assuming a threshold of £30,000/QALY.

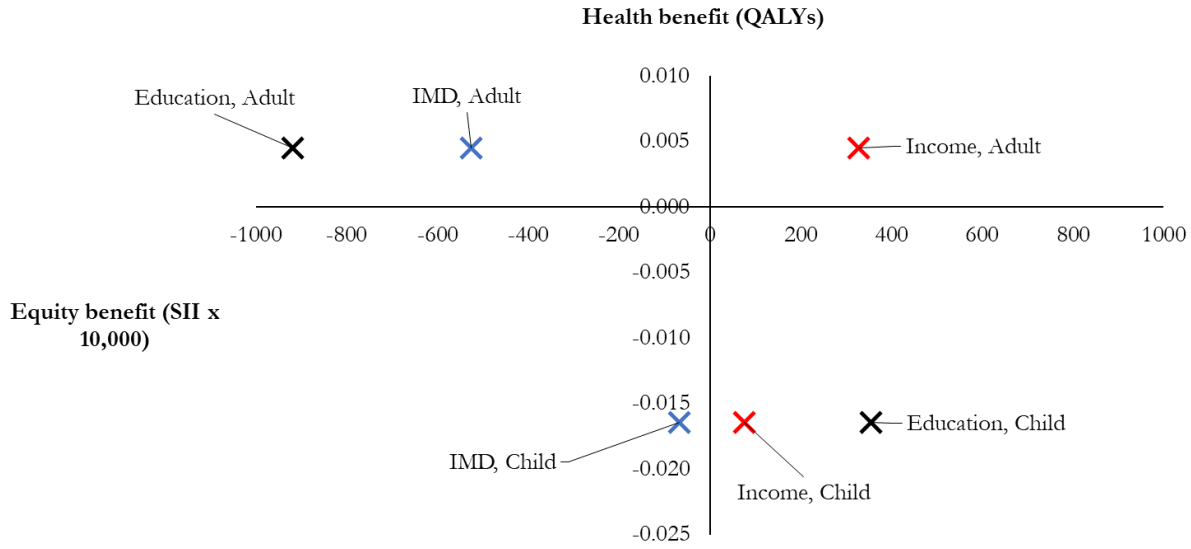
Abbreviations: HOC, health opportunity cost; IMD, index of multiple deprivation; iNHB, incremental net health benefit.

Figure 13 and Figure 15 show the results of E-SEE Steps plotted on the health-equity impact plane which compares the E-SEE Steps programme to SAU in equity-cost-effectiveness space. Note, in these figures, proportionate distribution of the health opportunity cost is included. The results demonstrate that when evaluated across IMD quintile groups, E-SEE Steps results for the adults are cost effective and equity-harming (i.e. the Win-Lose quadrant in Figure 7, Section 5.2.3). This holds when evaluated across educational attainment groups, yet the result indicates across education, E-SEE Steps is more equity-harming. Across income quintile groups, the results for the adult participants is cost-effective and equity improving (Win-Win).

The evaluation of the child results demonstrate again a mixed picture in terms of the equity impact based on the measure of SEP. It is only when evaluated across IMD and income that the results are consistent in terms of the direction of the equity impact compared to the adult results. Across IMD quintile groups, the results are not-cost effective and equity-harming (Lose-Lose); across income quintile groups the results are not-cost-effective and equity improving (Lose-Win). Compared to the adult results, the magnitude of the equity harm/benefit is reduced. The results across the educational attainment groups are not-cost-effective and equity improving (Lose-Win), with a greater equity benefit compared to the results across income quintile groups. The results of the scenario analysis in which the distribution of the health opportunity cost is based on estimates by Love-Koh et al. (Love-Koh et al., 2020) can be seen in **Threshold** = £15,000/QALY. Abbreviations: HOC, health opportunity cost; IMD, index of multiple deprivation; QALYs, quality-adjusted life year; SII, slope index of inequality.

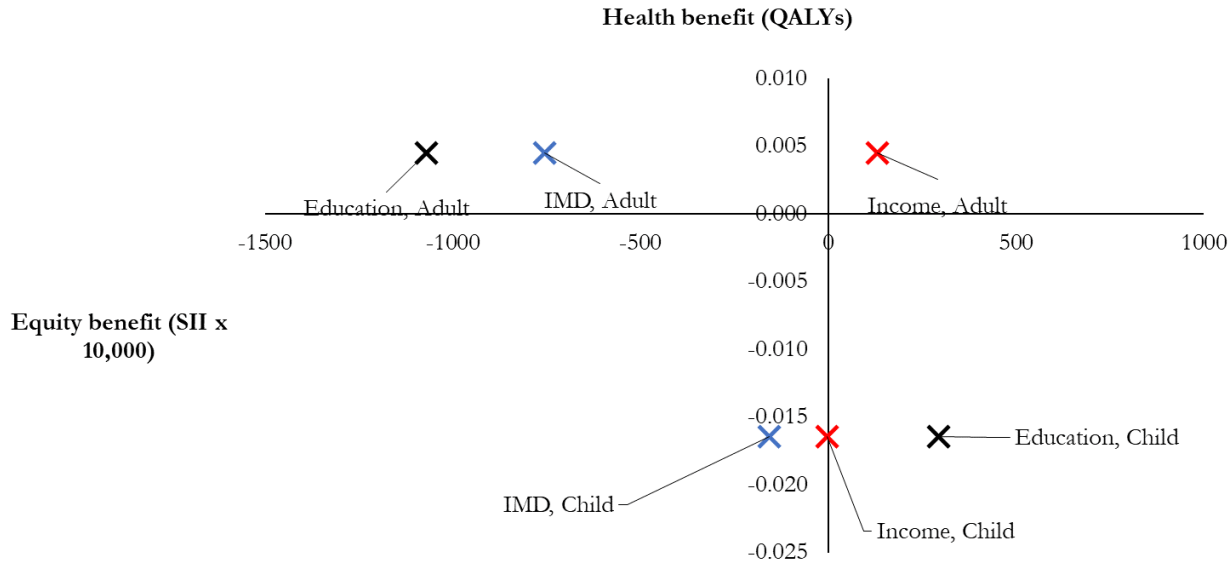
Figure 14 and Figure 16. The results are insensitive to the distribution of the health opportunity cost.

Figure 13 - Equity impact plane of the E-SEE Steps Trial, base case analyses.



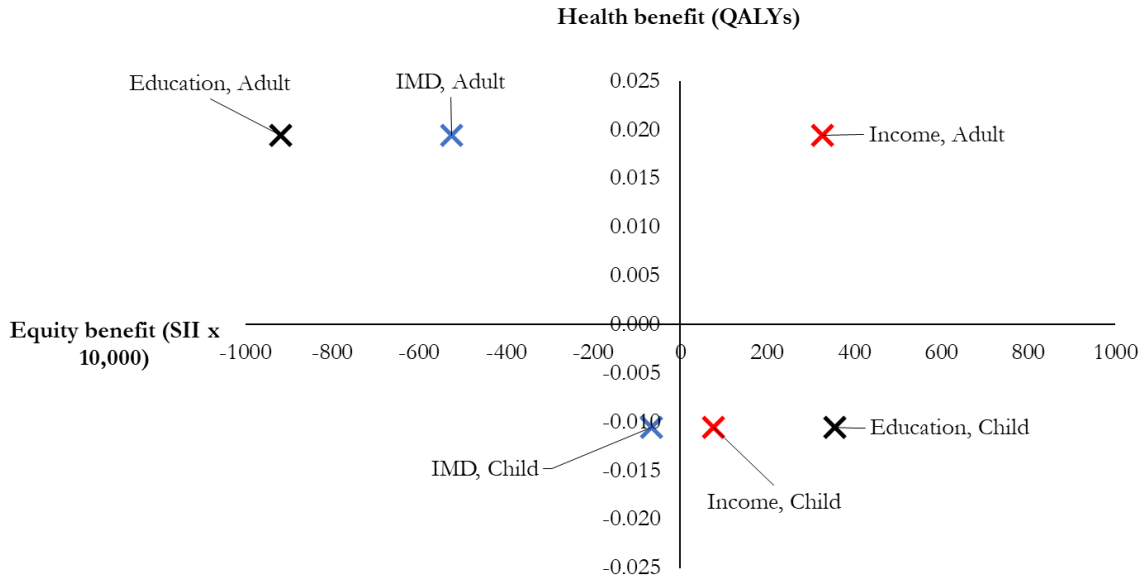
Threshold = £15,000/QALY. Abbreviations: HOC, health opportunity cost; IMD, index of multiple deprivation; QALYs, quality-adjusted life year; SII, slope index of inequality.

Figure 14 - Equity impact plane of the E-SEE Steps Trial, scenario analysis assuming the Love-Koh et al. distribution of the HOC.



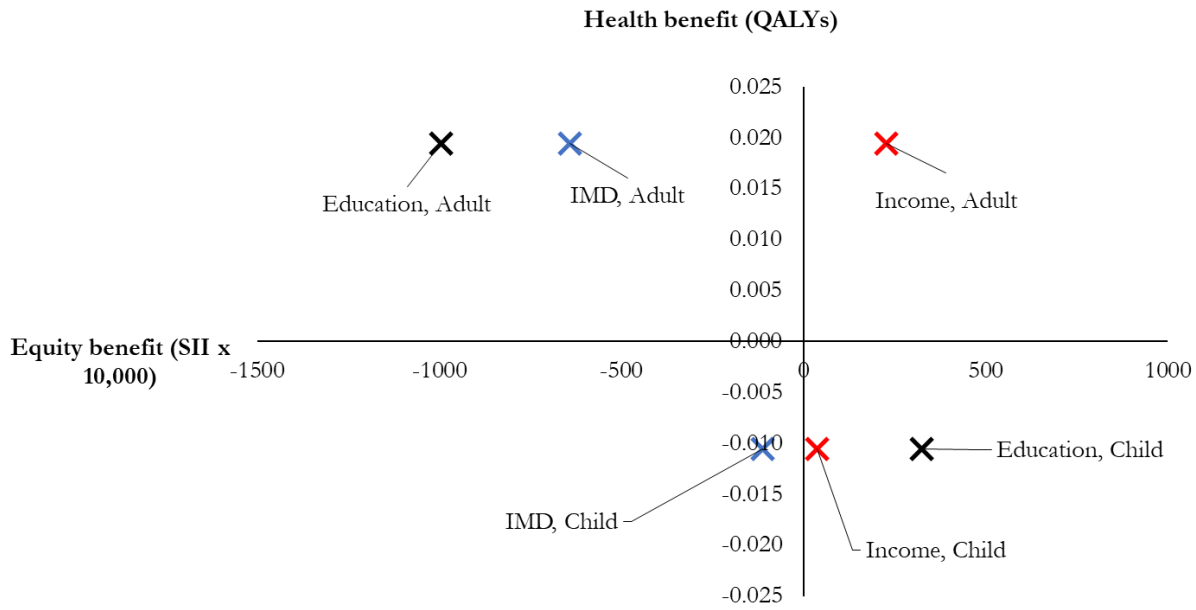
Threshold = £15,000/QALY Abbreviations: HOC, health opportunity cost; IMD, index of multiple deprivation; QALYs, quality-adjusted life years.

Figure 15 Equity impact plane of the E-SEE Steps Trial, base case analyses.



Threshold = £30,000/QALY. Abbreviations: HOC, health opportunity cost; IMD, index of multiple deprivation; QALYs, quality-adjusted life year; SII, slope index of inequality.

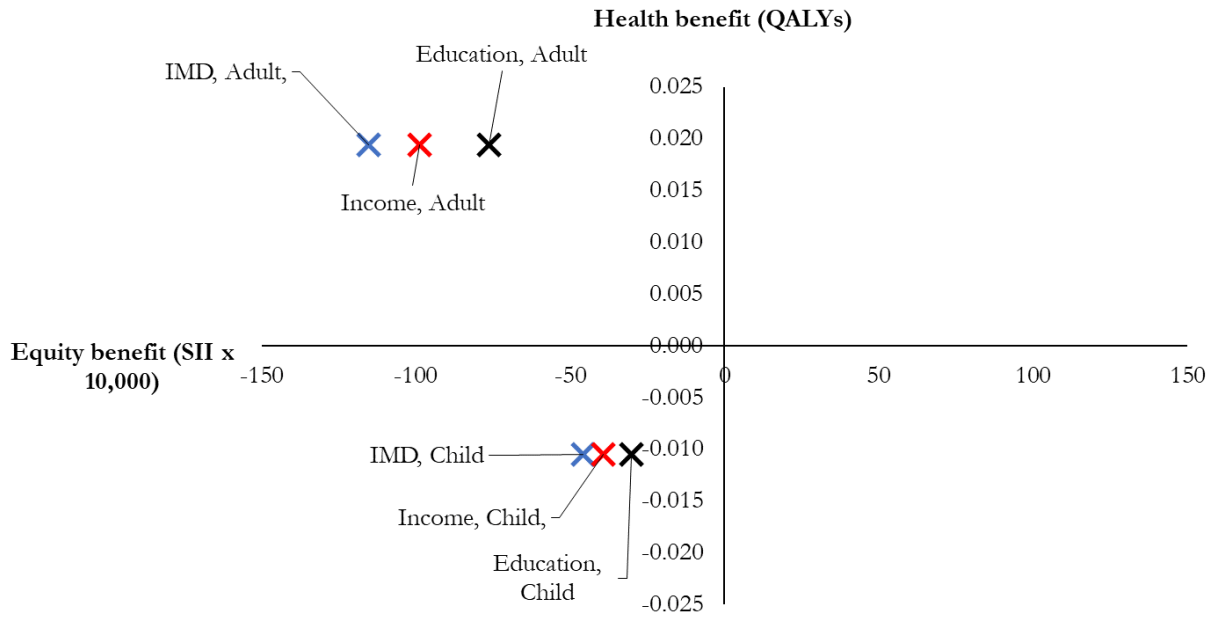
Figure 16 Equity impact plane of the E-SEE Steps Trial, scenario analysis assuming the Love-Koh et al. distribution of the HOC.



Threshold = £30,000/QALY Abbreviations: HOC, health opportunity cost; IMD, index of multiple deprivation; QALYs, quality-adjusted life year; SII, slope index of inequality.

As described in Section 5.3.2, the coefficients for the costs and QALYs for each of the SEP subgroups estimated from the regression models were inconclusive whether there was a significant difference. Scenario analysis is therefore presented in which the QALY outcomes are assumed to be equal across all subgroups. The results of the scenario are presented Figure 17. They show when assuming equal incremental health outcome as the outcome across SEP subgroups (i.e. the mean health outcomes across the whole trial) but using the estimated distribution of the health opportunity cost (Love-Koh et al., 2020) the E-SEE Steps programme is equity harming for all measures of SEP.

Figure 17 Equity impact plane of the scenario analyses of the E-SEE Steps Trial



Although there is uncertainty in the direction and magnitude of the difference in both QALYs *and* costs across SEP subgroups, scenario analysis in which equal costs are assumed is not considered due to the nature of the costs in the iNHB calculation. The iNHB is based on the cumulative incremental cost of the E-SEE Steps programme, which is then distributed according to the distribution of the health opportunity cost (see Table 15 for the step-by-step calculation). The cumulative incremental costs across all subgroups will be the same irrespective of whether the individual subgroup costs are assumed to be equal or estimated.

Note, Figure 13 to Figure 17 present change in equity as SII x 10,000. This was done to present the results on a scale that is easier to read off the plots as the change in SII in this DCEA was small. As the aim of the research was to show the impact the measure of SEP has relative to other measures of SEP, the scale of the reported SII in the equity-impact planes is not considered to be important. A decision-maker may be interested in the magnitude of the change in SII however as

yet there does not appear to be a benchmark of what constitutes as meaningful change in SII therefore it is up to decision makers to interpret the relative and absolute change in health when moving up or down the health gradient.

5.3.4 Equity Trade-Off Analysis

Figure 18 and Figure 19 display the difference in social welfare for adults and children at a range of levels of absolute inequality aversion, α, when scaled up to the population level. The graphs showing relative inequality aversion, ε, can be found in the appendix.

At zero inequality aversion, the EDE is equal to the mean level of health generated by E-SEE Steps for the population. As inequality aversion increases, the social welfare of E-SEE Steps increases. For the adult population, when ESEE Steps is evaluated across income quintile groups, the E-SEE Steps programme is always the preferred strategy as it yields the highest social welfare at all levels of inequality aversion. Figure 18 demonstrates this by revealing the E-SEE Steps curve for income never crosses the x-axis. The interpretation is that the E-SEE Steps programme has higher social welfare irrespective of the aversion to inequality. This makes intuitive sense for the results across income groups as the results across income quintile groups are in the Win-Win quadrant of the equity-impact plane. However, for the results across IMD quintile groups and education groups, the results fall in the Win-Lose quadrant. This explains why these curves in Figure 18 approach the x-axis as aversion to inequality increases. Eventually, at greater values of α the curves cross the x-axis. E-SEE Steps is shown to have a greater magnitude of equity-harm across education groups (see Figure 13) hence the curve in Figure 18

crosses the x-axis at low levels of inequality aversion. The gains in net health benefit (as a result of E-SEE Steps being cost-effective) are valued more highly than the losses in equity. As the aversion to inequality increases, the baseline EDE becomes the preferred strategy as it results in higher social welfare meaning the equity losses outweigh the gains in net health benefit. This can be seen in Figure 18 as the point at which the education line crosses the x-axis, which is at approximately $\alpha = 0.09$. A similar picture can be seen for the results across IMD expect the curve crosses the x-axis at approximately $\alpha = 0.35$.

The results for the children show a different picture. At zero inequality-aversion social welfare is higher at baseline, as demonstrated by the curves lying above the y-axis in Figure 19. This means no weight is given to inequality impacts therefore the only thing that provides social welfare is the net health benefit, i.e. whether it is cost-effective. As E-SEE Steps is not cost-effective from an efficiency perspective the social welfare is greater at baseline. When evaluated across IMD, social welfare is always higher at baseline compared to E-SEE Steps and increases as inequality aversion increases. This makes intuitive sense as the child results evaluated across IMD quintile groups falls in the Lose-Lose quadrant of the equity impact plane, i.e. as aversion to inequality increases, we see higher social welfare for interventions that improve inequality. The results when estimated across education groups show the social welfare curve crossing the x-axis at $\alpha = 0.125$. This makes intuitive sense as E-SEE is equity-improving when measured across education groups (Figure 13).

Figure 18 Sensitivity analysis of the absolute inequality aversion results for adults across different measures of SEP

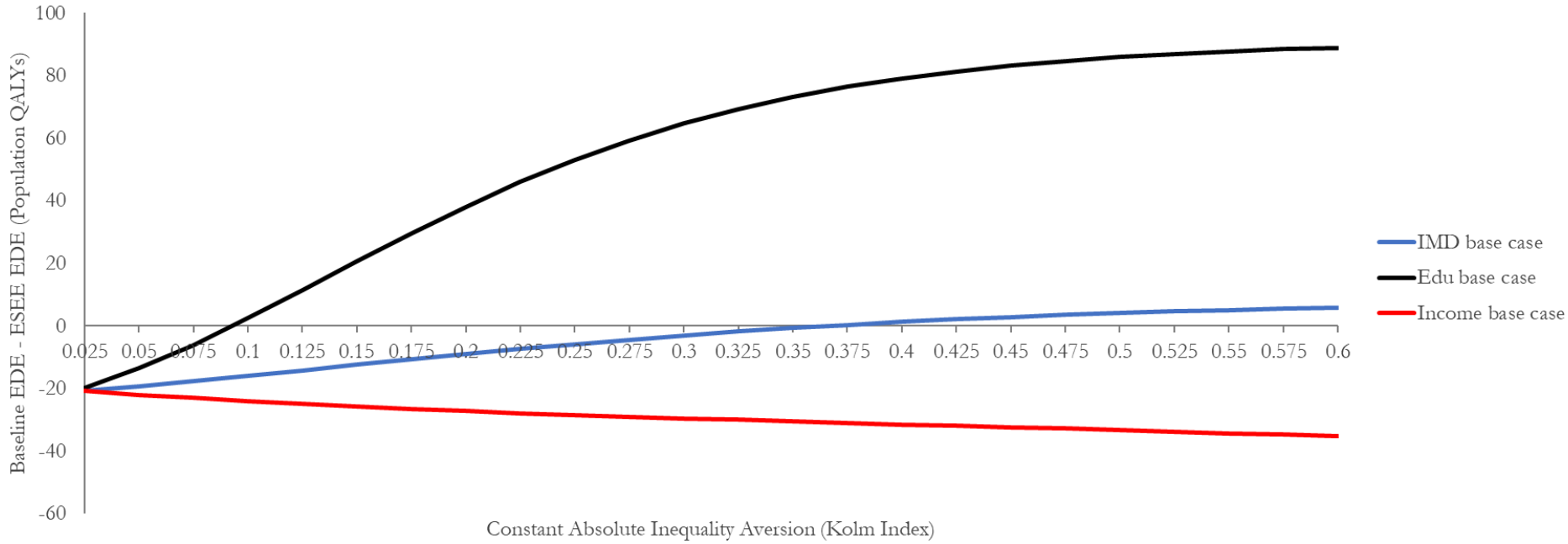
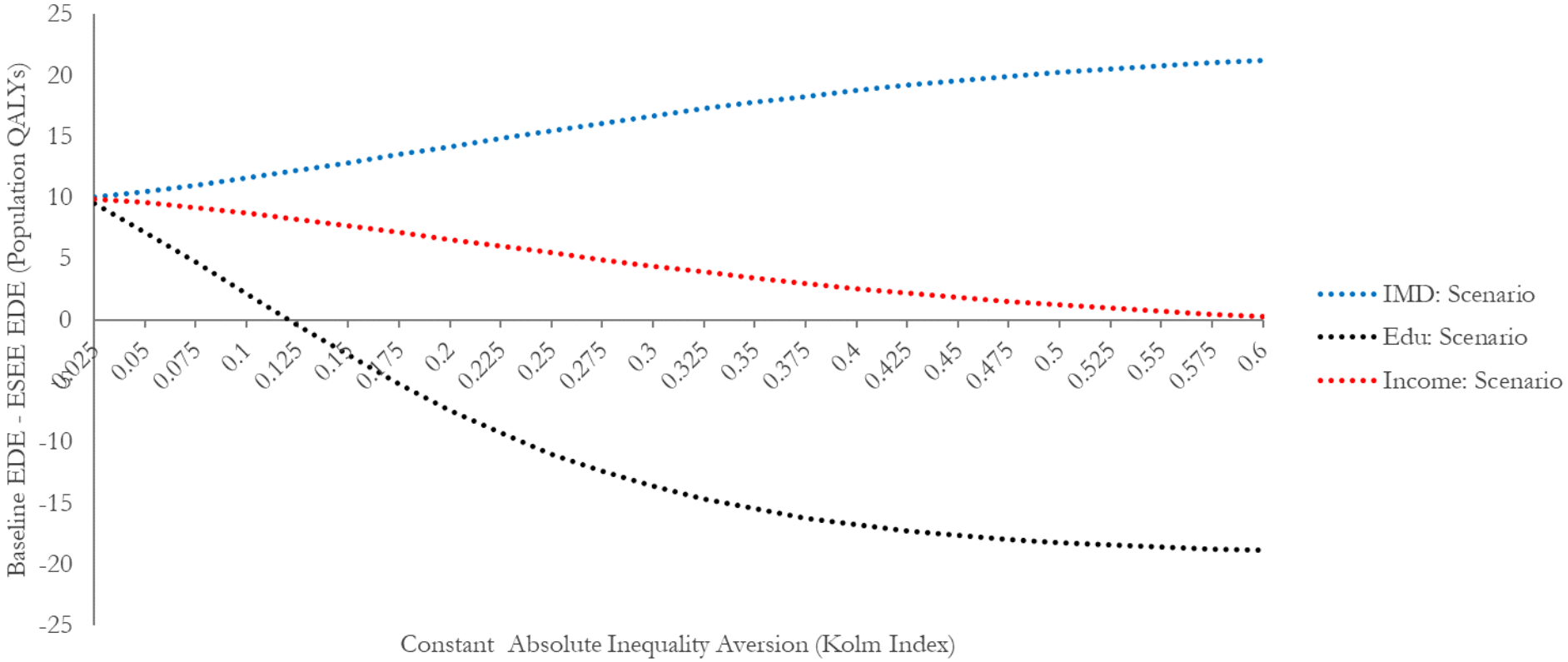


Figure 19 Sensitivity analysis of the absolute inequality aversion results for children across different measures of SEP



Based on the elicited level of inequality aversion in England (Robson et al., 2017), which revealed a Kolm parameter α = 0.15, the determination of whether the E-SEE Steps programme generated higher social welfare than baseline (i.e. no E-SEE Steps programme) is reported in Table 16. The results reveal the maximisation of social welfare when using the elicited values of inequality aversion parameters differs across measure of SEP.

Table 16 – Approach (i.e., E-SEE Steps or baseline) that maximises social welfare at the elicited value of the general population

	IMD	Education	Income
Adult	E-SEE Steps	Baseline	E-SEE Steps
Child	Baseline	E-SEE Steps	Baseline

Abbreviations: IMD, index of multiple deprivation

5.4 Discussion

5.4.1 Principal findings

This chapter illustrates the impact of incorporating health equity into the economic evaluation of a childhood intervention. This is done through conducting a DCEA of the E-SEE Steps programme. This evaluation went beyond the published DCEAs to date and considered the impact of altering the measure of SEP. The results revealed the E-SEE Steps programme was cost-effective for the adults in the trial but the determination of whether it resulted in net health equity harm or benefit was sensitive to the measure of SEP used. The results for the children indicated E-SEE Steps was

not cost-effective and the net health equity results were similarly sensitive to the measure of SEP.

The incorporation of health equity appears to have a considerable impact on the potential value of a child health programme. ‘Traditional’ methods of economic evaluation fail to consider those individuals or groups that gain the health (or other benefits) and those that bear the costs; in other words, the social distribution of the impacts of the health intervention. This may be an important omission when evaluating the social value of child health interventions as reducing inequitable health inequalities may be a primary objective of the programme (Powell, 2019). Further, these interventions can have inequality impacts throughout the life course (Marmot, 2015) and interventions can, and typically do, (White et al., 2009) increase health inequalities as socially advantaged individuals are better able to seek, co-invest and benefit from them (Cookson et al., 2021a).

Despite uncertainty in the trial results the DCEA of E-SEE Steps did reveal interesting findings. E-SEE Steps could be considered a pro-poor intervention when evaluated across income quintile groups for both the child and the parent. It could also be considered equity-harming across IMD groups across both child and parent. Using the inequality aversion parameter elicited for the general population in England (Robson et al., 2017), E-SEE Steps resulted in contrasting social welfare when considering both child and parent across all measures of SEP. It should be noted that the inequality-aversion parameter was elicited by asking individuals about inequality between rich and poor groups so the results may not be applicable to education groups (Robson et al., 2017). In addition, the study asked survey respondents about trade-offs in life expectancy at birth. Inequality aversion may

differ depending on the age of the individuals experiencing the inequality given the importance placed on tackling health inequalities in the early years (Pearce et al., 2019). Although this has not been elicited, this could be the basis of future work.

Recent methods to incorporate equity considerations into economic evaluation have stressed the importance of the ignored distributional consequences as a result of focussing economic evaluation on efficiency (Love-Koh et al., 2019a, Cookson et al., 2017b). This study builds on this concept by revealing the ignored distributional consequences of focussing on only one approach to categorising SEP, which has predominantly been IMD to date (Ward et al., 2022). This study does not advocate for the use of a single best SEP indicator over another, as this approach is not considered useful or theoretically compelling (Galobardes et al., 2006b, Galobardes et al., 2006a). Rather these indicators provide complementary evidence on the equity impacts and social welfare of an intervention for the purpose of decision making with an equity objective. It may be important to be aware of competing equity objectives if making adoption decisions based on one measure of SEP is then followed by making a different decision on a separate policy or intervention based on an alternative measure of SEP.

The E-SEE Steps trial was not powered for *ex poste* exploration of subgroup effect sizes and as a result the results appear to be very sensitive to the small numbers of individuals. For example, there are small numbers in the No Qualifications and GCSE education subgroups (i.e., n = 6 in the SAU arms for both of these subgroups) and we have a large swing in the iNHB across these subgroups (i.e., -0.1181 QALYs for the No Qualification groups and +0.2353 for the GCSE group). The results are evidently uncertain as can be seen in the cost and outcome differences between the

arms of the study (see Table 13 and Table 14). Examining treatment differences across multiple subgroups does increase the chance of false positives and is therefore not recommended (Burke et al., 2015). Questions should be asked as to whether there is compelling evidence of a difference in effectiveness across subgroups. In this case study the answer would probably be ‘no’, there is no compelling evidence. However, if a decision maker is interested in an equity-informative evaluation the analyst requires effectiveness (in this case costs and QALYs) across each of the subgroups. In the absence of compelling evidence of a difference in effectiveness, the average result from the trial could be used, which then begs the question of whether a DCEA is required. I would argue that there *is* compelling evidence of a difference in the health opportunity cost across SEP subgroups in this case (Love-Koh et al., 2020) albeit limited to IMD. It was for this reason that a scenario analysis was conducted to show the health equity impact when we assume the average effect size for all subgroups. Figure 17 shows the results and they can be seen to be in the equity-harming side of the equity-impact plane. This is based on empirical evidence of the distribution of the health opportunity cost across IMD only and therefore assumptions were made about how it falls across education and income groups. Future research may consider the distribution of the health opportunity costs across education and income groups to provide more compelling evidence for or against exploring equity-informative subgroups.

The baseline characteristics of the E-SEE Steps trial revealed interesting results when compared across SEP indicators. Of those recruited to the trial, the most populous IMD quintile was Q1 indicating recruitment was successfully targeted at the

most deprived based on IMD. The same story can be seen with income. Yet the most populous educational attainment group was *Degree level or higher*. This could be interpreted in a number of ways. First, this could be explained through the "inverse equity hypothesis" (Victora et al., 2018) which leans on Tudor Hart's inverse care law (Hart, 1971) and states "new health interventions are adopted earlier by advantaged populations thereby initially increasing inequalities" (Cookson et al., 2021a). It is the most "advantaged" educational groups within the lowest IMD groups that are seeking out E-SEE Steps. Second, the proportion of the population with a university degree may now be higher than the proportion with no qualifications, GCSEs or A-levels meaning E-SEE Steps is representative of the population. Results from the ONS revealed in 2011 that approximately 40% of 24-35-year-olds had a university degree (Office for National Statistics, 2016). Despite the increase in university educated individuals, there are clearly individuals in the population with no qualifications or low-level qualifications who have lower health expectancies at birth and may suffer adversely due to the resulting equity impacts of choosing to adopt interventions.

5.4.2 Strengths and limitations

This chapter presents a DCEA of a real-world childhood intervention. The analysis presented is a novel addition to the literature as it is the first DCEA to explore the impacts of alternative measures of SEP.

As with all economic evaluations the handling and reporting of uncertainty is fundamental if decision makers are to be fully informed (Briggs, 1999, Drummond et al., 2015). The DCEA presented in this chapter uses point estimates of the costs and

QALYs for each subgroup meaning the results are deterministic and may confer a false sense of accuracy. A decision was made to limit the analysis to point estimates for two reasons. First, limitations in the evaluation of child outcomes in original E-SEE Steps evaluation meant there was considerable uncertainty in the results of which could not be parameterised (see Chapter 3). Second, as the purpose of the evaluation was to explore the impacts of ignoring equity and the SEP categories it was considered the deterministic results could illustrate this point. Given the lack of parameterised uncertainty in the results and the uncertainty in the E-SEE Steps costs and outcomes I would not recommend a decision-maker using this evidence for decisions on E-SEE Steps. But it can certainly be used to illustrate the implications of ignoring equity and failing to ask the question of '*equality between whom?'*

This study recognises the time varying nature of IMD, education and income. Such indicators are not fixed and may change over the life course. Indeed, such indicators may exhibit reverse causality on health for example, poor health could reduce income. This study provides a snapshot of the QALE at birth at a point in time, hence mortality and the morbidity being based on data from 2011-2012. Those using this evidence should consider whether the results reflect the likely health of individuals at the time of decision making. In addition, the use of the results to represent childhood inequalities should be considered. The E-SEE Steps trial considered both parent and child costs and outcomes and although the DCEA only considered the adults, the same baseline distribution estimated in this study would have been used to represent child health inequalities. Income and education were selected as the SEP indicators as parental education and income are considered good indicators for

childhood SEP (Galobardes et al., 2006b, Galobardes et al., 2006a). This implicitly assumes a child's SEP is their parent's SEP and the suitability of this assumption must be considered. Evidence does suggests the UK has low social mobility and lower than the majority of OECD countries (OECD, 2018), indicating the assumption of using parental SEP indicators may be a reasonable assumption for children.

The original economic evaluation results of the E-SEE Steps trial reported outcomes for the child, adult and dyad (Cox et al., 2022) whereas this Chapter does not consider the dyad results in equity-efficiency space. DCEA provides a method of trading-off equity and efficiency and can in theory incorporate multiple interventions or arms (Asaria et al., 2016) but as yet there are no means of trading-off results across child and adult. For example, if an intervention was cost-effective and equity improving for the adults (Win-Win) and cost-effective but equity harming for the children (Win-Lose). A social welfare function could apply weights to the results and combine them in a specified social welfare function but the weights may be difficult to conceptualise. It could be assumed that the primary outcome is the child and that the adult outcomes are considered spillovers, methods of which has been described to allow the incorporation of spillovers and their distribution (Henry and Cullinan, 2024). There is as yet limited methodological guidance on addressing such equity concerns.

5.5 Conclusion

To our knowledge this is the first study to explore the measure of SEP. The importance of incorporating equity into economic evaluations has recently been underlined in the health economics literature, this study hopes to help underline the importance of asking the question of *Equality between whom?*

Chapter 6: Extending the time horizon

The thesis has considered the impact of incorporating equity into the evaluative space of an early childhood PHI. The next aspect to introduce to the case study of E-SEE Steps is the impact of extending the time horizon of the evaluation.

6.1 Introduction

The time horizon of any economic evaluation should be sufficiently long to capture the differences in costs and outcomes of alternative programmes (Drummond et al., 2015). We saw in Chapter 3 that the economic evaluation of E-SEE Steps considered an 18-month time horizon meaning this may not be sufficiently long to capture the impacts of the intervention across the child's life. Further, the literature is rich with evidence of the importance of impacts in early childhood being felt throughout the child's life (Cunha and Heckman, 2007, Guyer et al., 2009). This includes health but also wellbeing and the 'human capital' skills required to prosper and be productive in society (Goodman et al., 2015, Almond et al., 2018b). As such, evaluation based on short term outcomes may not reflect the full value for money of a childhood intervention.

Long-term clinical trials in which the outcomes and costs of an intervention are measured well into adulthood may not be feasible owing to costs associated with running such a trial or they may not even be desirable as the results of the trial may be outdated by the time they are realised. Extrapolation of the short-term effectiveness of an early childhood intervention is required but presents difficulties. The approach of fitting parametric models to extrapolate patient level data from clinical trials for HTA decision making is well established (Latimer, 2011). But given the long-time horizons and the potential impact of behaviour on the future, it cannot

be assumed that extrapolation would follow a parametric distribution. The potential for feedback loops based on changes in behaviour not just in the individual but in their social environment could impact long-term outcomes. This creates challenges in the decision modelling (see Chapter 1 for an introduction to decision modelling) approach used for generating economic evidence.

Decision modelling provides the means to extrapolate but given the complex correlation of health and human capital (see Chapter 3) a decision model that captures the costs and outcomes for the purpose of economic evaluation should allow for the interaction of such elements. For example, the causal impact of income and education on health (Cutler and Lleras-Muney, 2006, Mirowsky, 2017, Kirkpatrick Johnson et al., 2016, Gunasekara et al., 2011, Raghupathi and Raghupathi, 2020) and the reverse causality (Deaton, 2003). The impact of SEP also impacts health (Marmot, 2020, Galobardes et al., 2004, Darin-Mattsson et al., 2017) and human capital (Currie and Goodman, 2020, Currie, 2009) and can result in compounding of advantages and disadvantages. There are a handful of examples of published models that account for some of this complexity (Van de Ven, 2016, Wolfson and Rowe, 2014, Hennessy et al., 2015, Skarda et al., 2021). These have been detailed in Chapter 3. LifeSim (Skarda et al., 2021) is one example that models the life course of individuals, accounting for the dynamic interaction of health, wellbeing, human capital and SEP.

This chapter aims to use LifeSim to extend the time horizon of the evaluation of E-SEE Steps, which is used as a case study throughout the thesis (see Chapter 3 for a description of E-SEE Steps). To my knowledge, this would make it the first example of a real-world application of the LifeSim model. It is hoped this will also demonstrate

the impact on the assessment of value for money of extending the time horizon from a within-trial evaluation to consider the life course.

6.2 Methods

The method section is described in a number of distinct stages. First, LifeSim, the model used to extrapolate the outcomes, will be briefly described. Second, the approach and challenges in linking the E-SEE Steps trial data to the LifeSim model will be detailed. Third, the impact of incorporating a longer time horizon on our assessment of value for money is evaluated.

6.2.1 Introduction to LifeSim

LifeSim is a discrete event simulation that models the lifetime health and wellbeing of individuals. Discrete event simulation is a modelling technique that captures the individual patient experience through the likelihood of a list of discrete events occurring over time and summing the costs and health impacts of the events (Karnon et al., 2012). The LifeSim model has been described in detail elsewhere (Skarda et al., 2021) but a brief overview is presented here.

The model is based on data from six sweeps [19] of the Millennium Cohort Study (MCS) and progresses individuals through their life from birth to death, capturing health, economic and social outcomes. It takes a human capital [20] approach to child development (see Chapter 1 for an overview of human capital) and extrapolates these aspects beyond childhood. Each individual that progresses through the model starts with initial characteristics. These are based on MCS data and include the child's sex, household income (used as a measure of socioeconomic position), parental education and parental mental health status at the time of birth. The model then captures longitudinal data on an individual's social skills and cognitive skills. Social skills are estimated in the form of the SDQ conduct problem score (Goodman, 1997, Goodman, 1999). The SDQ conduct problem score is one of five domains of which comprise the overall SDQ score. The cognitive skills are based on various measures of cognition provided in the MCS data. The measure is different in each MCS sweep and includes the following: British Ability Scales II, the Bracken School Readiness Assessment, the National Foundation for Educational Research Progress in Maths and Cambridge Neuropsychological Test Automated Battery tests and Applied Psychology Unit. Principal component analysis was conducted on the cognitive skills assessment scores to allow standardisation with a mean of 1 and standard deviation of 0.15 (Jones and Schoon, 2008). A number of additional data points from the MCS sweeps then feed into the model at various

[19] At the time of development of LifeSim there had been 6 sweeps of the MCS: Sweep 1 (9 months old); Sweep 2 (3 years old); Sweep 3 (5 years old); Sweep 4 (7 years old); Sweep 5 (11 years old); and Sweep 6 (14 years old).

[20] Human capital represents a measure of the health, skills and knowledge and individual will invest in and accumulate throughout the life course.

points in the child's life, such as: the presence of parental depression at aged 5 years; parental wealth at age 11 years; whether the child smokes at aged 14 years.

The data are then extrapolated using equations in the model. The equations estimate a number of outcomes listed below:

- Social
    - Probability of developing conduct disorder
    - Probability of obtaining a university degree at aged 19 years
    - Probability of being employed in the working years of life
    - Probability of being in poverty
    - Probability of being in prison
    - Probability of living in a care home
- Health
    - Probability of smoking
    - Probability of developing depression
    - Probability of having coronary heart disease
    - Probability of dying
- Economic
    - Earnings from employment, interest, pension
    - Savings
    - Inherited family wealth
    - Taxes paid
    - Benefits received
- Wellbeing
    - Consumption
    - Health related quality of life

The full specification of the modelling equations is described in Skarda et al. (Skarda et al., 2021).

6.2.2 Linking E-SEE Steps and LifeSim

The E-SEE Steps results were linked to LifeSim through the use of the SDQ score estimated in the E-SEE Steps trial. This was chosen for two reasons. First, as detailed above, the SDQ score provided a key input to the LifeSim model. Second, the SDQ score was selected as the outcome measure of interest used to evaluate the cost-effectiveness of E-SEE Steps for the children enrolled in the trial (Cox et al., 2022). For a description of the economic evaluation results of E-SEE Steps, see Chapter 3.

There were, however, challenges in linking the E-SEE Steps results to LifeSim. These were: the form of the SDQ score; the lack of baseline data; and the SDQ instruments used in E-SEE Steps and LifeSim. These challenges are described below.

SDQ Score vs SDQ Conduct Score

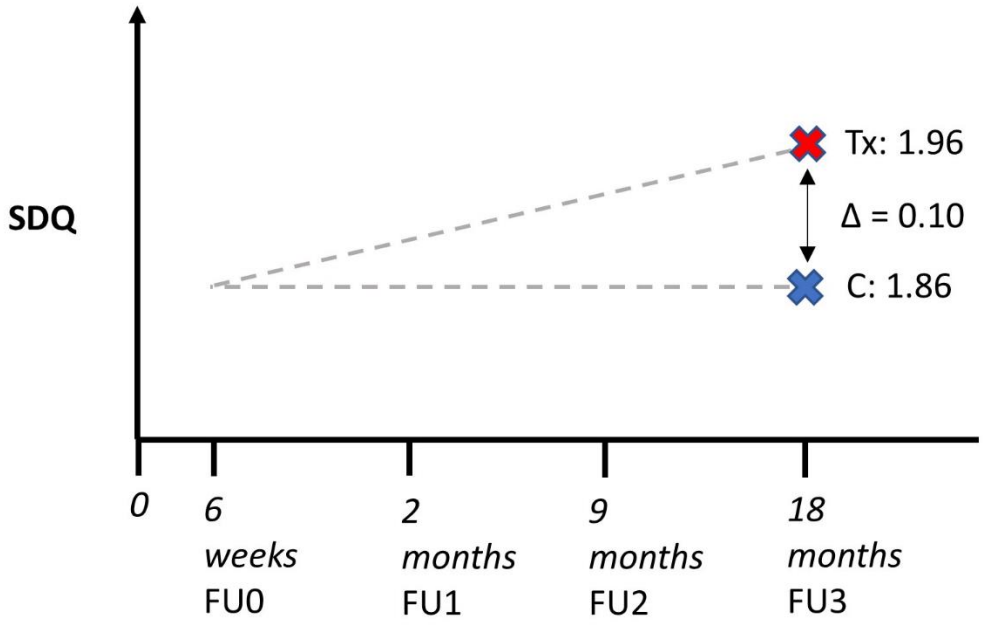
The SDQ results from the E-SEE Steps trial were reported in the form of the overall SDQ Score, whereas LifeSim utilises one domain of the SDQ Score known as the SDQ Conduct Score. As a result, estimation of the SDQ Conduct score for each arm of the trial data was required to input into LifeSim. This involved conducting an analysis of variance (ANOVA) of the patient-level SDQ conduct score for the E-SEE Steps arm and the SAU arm of the trial. ANOVA can be used to compare the means of different groups and indicate if there is a statistical difference between them. An assumption of the ANOVA is that the independent groups have equal variance. Histograms were plotted to compare the distribution of the data in each trial arm. The

SDQ Conduct score for each arm was then compared to the overall SDQ Score to sense check the results and see if there was a directional change when comparing the mean difference of the SDQ Conduct score compared to the reported overall SDQ score.

Lack of baseline data of SDQ scores

Despite the SDQ score in the E-SEE Steps trial being used to inform the economic evaluation there was a considerable limitation in the SDQ trial data. The SDQ score in the E-SEE Steps trial was estimated at single time point (18 months, third follow-up time point (FU3)) and no baseline SDQ data were collected. The published economic evaluation (Cox et al., 2022) therefore assumed that the SDQ Score at 18 months had not changed from baseline for the individuals in the SAU arm. It was also assumed that individuals in the E-SEE Steps arm had changed over time from baseline and the baseline SDQ Score in the E-SEE arm was assumed to be equivalent to those at baseline in the SAU arm. The mean difference in SDQ Score was 0.10 and was assumed to be attributable to the E-SEE Steps programme. This assumption is illustrated in Figure 20.

Figure 20 – Illustration of the SDQ score assumption in the S-SEE Steps trial



The impact of this assumption is that the causal link between E-SEE Steps and a change in SDQ score is not established and potential baseline differences across arms of the trial are not accounted for. The sensitivity of the results to the assumption of a 0.10 change in SDQ conduct score being attributable to the E-SEE Steps programme has been assessed through assuming the change in SDQ conduct score attributable to E-SEE Steps is 0.05.

SDQ Instruments applied in LifeSim

The SDQ conduct scores obtained from the MCS and therefore providing the input to LifeSim are measured at ages 4, 5-6, 7-10, 11-13 and 14+. The instrument used to measure these SDQ conduct scores was an instrument designed for 4-17 year olds. However, within the E-SEE Steps trial individuals had a mean age of approximately 20 months at the point at which SDQ score was measured (i.e., 18 months, FU3)

and as such, SDQ conduct score was measured using an instrument designed for 2-4 year olds and had not been validated in 20 month old children (Cox et al., 2022).

Ignoring the uncertainty in the results due to the instrument not being validated in 20-month-old children, the question becomes whether it can be assumed that an SDQ conduct score measured using one instrument equates to the equivalent score in the other instrument. There are similarities between the questions being asked in both instruments but they are not identical. For example, there are differences in the wording of questions and unlike the 4-17 year old instrument, there is a lack of national data to inform the banding of scores in the 2-4 year instrument (Early Intervention Foundation, 2023). To date there is currently no published mapping of the 2-4 year instrument to the 4-17 year instrument. The results is that the linking of E-SEE Steps to LifeSim requires the assumption that any change in SDQ score measured using the 2-4 year instrument results in an equivalent change in SDQ score measured using the 4-17 year instrument.

Note, SDQ conduct score feeds into the model through the observed MCS data but the outcome of the LifeSim model is reported in QALYs. SDQ conduct score impacts QALYs through a number of pathways. At baseline, each individual is born into a SEP group, which is based on household income quintile, and a corresponding QALE is assigned based on QALE estimated by Love-Koh et al., (Love-Koh et al., 2015). Decrease in QALE is linked to negative health experiences, which are limited to depression and coronary heart disease (CHD). The probability of negative health experiences is dependent on many variables in the model including the probability of developing childhood conduct disorder, unemployment, smoking and going to prison. An increased SDQ score (modelled through a policy impact in the model) can impact the aforementioned variables in LifeSim and therefore increase the probability of depression and CHD. Depression and CHD have HRQL weights which are obtained from Sullivan et al., (Sullivan et al., 2011). The HRQL weights used in LifeSim are 0.603 for the presence of depression and 0.629 for the presence of CHD.

Conclusions on linking E-SEE Steps and LifeSim

The challenges described above result in considerable uncertainty in the attributable impact E-SEE Steps has on the SDQ score and the uncertainty in mapping across SDQ instruments. Therefore, the analysis presented throughout the remainder of this chapter will primarily serve as an illustrative example of the impact of extending the time horizon, introducing non-health costs and outcomes and incorporating equity into the framework. E-SEE Steps is still linked to LifeSim to generate the output required but should not be considered a definite evaluation of E-SEE Steps.

The linking of E-SEE Steps to LifeSim is achieved by setting LifeSim to run a ‘policy’ arm and a ‘no policy’ arm. The no policy arm is set to have a baseline SDQ Conduct

score that is equal to the SAU trial arm SDQ Conduct score estimated from the ANOVA. The policy arm is similarly achieved by setting the baseline SDQ Conduct score to that of the E-SEE Steps trial arm. The model is set to run for 1,000 individuals and is implemented in R (R Core Team, 2021).

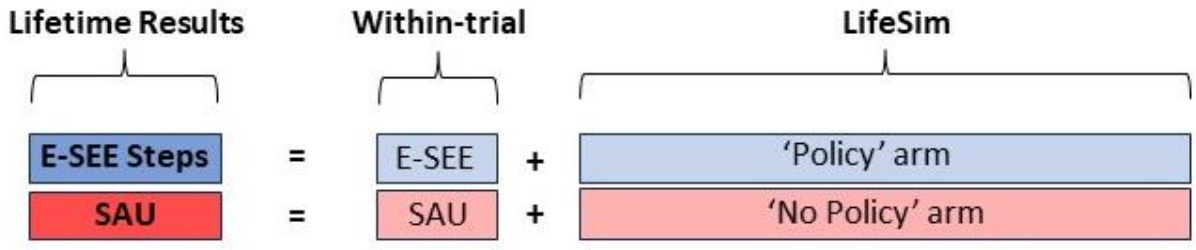
Presentation of extrapolated E-SEE Steps results

The economic evaluation of the extrapolated E-SEE Steps results (through the use of LifeSim) are presented. For this evaluation, cost-effectiveness analysis (CEA) is used. It is the preferred evaluative framework for the economic evaluation of health interventions in the UK (National Institute for Health Care Excellence, 2022) and was used for the published within-trial evaluation of E-SEE Steps (Cox et al., 2022).

The perspective of the evaluation is that of the National Health Service and Personal Social Services (NHS & PSS). The time horizon over which the costs and outcomes were assessed is the individual's lifetime. In line with UK guidelines, costs and outcomes are discounted at a rate of 3.5% per annum (National Institute for Health Care Excellence, 2022). The location of the CEA is assumed to be England which aligns with that of the original E-SEE Steps trial (Bywater et al., 2021), see Chapter 3 for further details.

The interventions being considered are the E-SEE Steps programme compared to SAU. The lifetime costs and health outcomes (QALYs) for E-SEE Steps and SAU are estimated by summing the within-trial results estimated from the literature (Cox et al., 2022) to the 'policy' and 'no policy' arms from LifeSim, respectively. Figure 21 illustrates the approach to calculating the lifetime results.

Figure 21 – Illustration of the estimation of the lifetime results



An illustration of how the lifetime costs and QALYs for the E-SEE Steps arm and the SAU arm are estimated through the use of the E-SEE Steps within-trial results and the LifeSim results.

Abbreviation: SAU, service as usual.

Two cost-effectiveness thresholds are used to estimate net health benefit (see Chapter 5). The baseline threshold is assumed to be £15,000 per QALY to align with the Department of Health in England (Department of Health Office for Life Sciences, 2017). A second threshold of £30,000 per QALY is used in scenario analysis to align with the upper bound of the threshold used by NICE (National Institute for Health and Care Excellence, 2022).

6.3 Results

6.3.1 SDQ Conduct Score

The ANOVA results of the E-SEE Steps trial can be seen in Table 17. The results show a non-significant increase in the mean SDQ conduct score of 0.10 (-0.34, 0.53) for children in the E-SEE Steps arm compared to SAU. For comparison, the E-SEE Steps results for the mean overall SDQ score are also provided in Table 17 and show similarities in the direction and magnitude of the results given the SDQ conduct score is one of four domains which are summed to generate an overall SDQ score.

Note, both an increased SDQ score and an increased SDQ Conduct score are indicators of higher risk of mental health issues and conduct disorder (Goodman, 1997, Goodman, 2001).

Table 17 – SDQ conduct score results from the E-SEE Steps trial

	E-SEE			SAU			
	n	**Mean**	**SD**	**n**	**Mean**	**SD**	**Mean diff (95% CI)**
SDQ Conduct Score	266	1.96	1.51	53	1.86	1.77	0.10 (-0.34, 0.53)
SDQ	266	9.67	4.27	53	9.15	4.53	0.64 (-0.75, 1.79)

Abbreviations: SAU, service as usual; SDQ, strengths and difficulties questionnaire.

The histograms of the SDQ conduct scores for each arm of the trial show similarity in the distribution of SDQ conduct scores. The histograms are shown in the appendix.

6.3.2 LifeSim results

Healthcare outcomes

The LifeSim model results are presented as a ‘policy’ arm which is used to represent the E-SEE Steps arm of the trial and a ‘no policy’ arm which represents the SAU arm of the trial. Both model arms were set to simulate the life course of the population assuming the baseline SDQ conduct was equal to the ANOVA results from Section 6.3.1. That is, the E-SEE Steps arm and the SAU arm of the model were set to have

baseline SDQ conduct scores of 1.96 and 1.86, respectively. The healthcare results of the LifeSim model for each arm are presented in Table 18. The results show very little difference in the discounted lifetime QALYs (0.001 QALYs) and small difference in the lifetime healthcare costs (£16). The results of the sensitivity analysis in which a 0.05 change in SDQ conduct score was implemented through inputting an E-SEE Steps arm SDQ conduct score of 1.91 and maintaining the SDQ conduct score of 1.86 in the SAU arm revealed the results were insensitive to this change. They showed no change in the lifetime discounted QALYs (i.e., 41.224 in both arms) and very little change in the difference in health care costs between the arms: E-SEE Steps had lifetime health care costs (i.e., a difference of £10 between the arms rather than £16 as in the base case).

Table 18 – Lifetime healthcare results

	E-SEE Steps	SAU
SDQ conduct score	1.96	1.86
QALYs, £ (disc)	41.223	41.224
Health costs, £ (disc)	£71,499	£71,483

Abbreviations: QALYs, quality-adjusted life years; SAU, service as usual; SDQ, strengths and difficulties questionnaire.

As described in Section 6.2.2, there is considerable uncertainty regarding the extrapolation of the E-SEE Steps results through the use of LifeSim however LifeSim does not currently incorporate such uncertainty. Relying solely on the results in

Table 18 may offer a false sense of accuracy in the lifetime QALYs and costs of the E-SEE Steps programme. To address this, we present the lifetime QALYs and healthcare costs as a function of SDQ conduct score to allow decision makers to choose their baseline level of SDQ conduct score and the mean difference in SDQ conduct score. Figure 22 and Figure 23 show the plotted results of the lifetime QALYs and healthcare costs with differing SDQ conduct scores.

Plots of the undiscounted lifetime QALYs and healthcare costs by SDQ conduct score are presented in the appendix. The results show steeper curves when moving to higher SDQ scores thus indicating the QALYs lost and healthcare costs are occurring earlier in the child's life course. Note, if there was little difference in the discounted and undiscounted results it would imply these are occurring towards the end of life.

Figure 22 – Lifetime QALYs as a function of SDQ conduct score

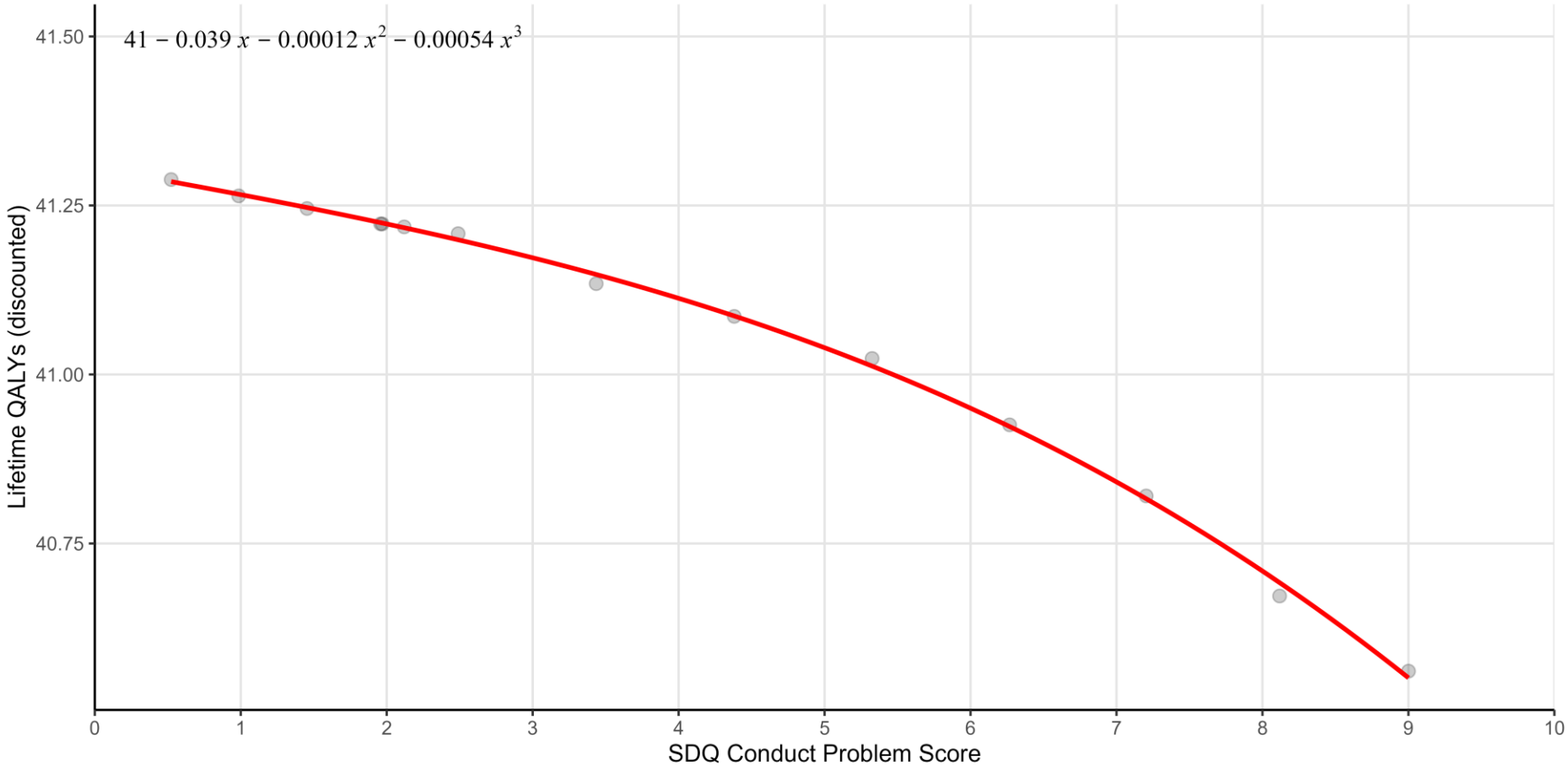
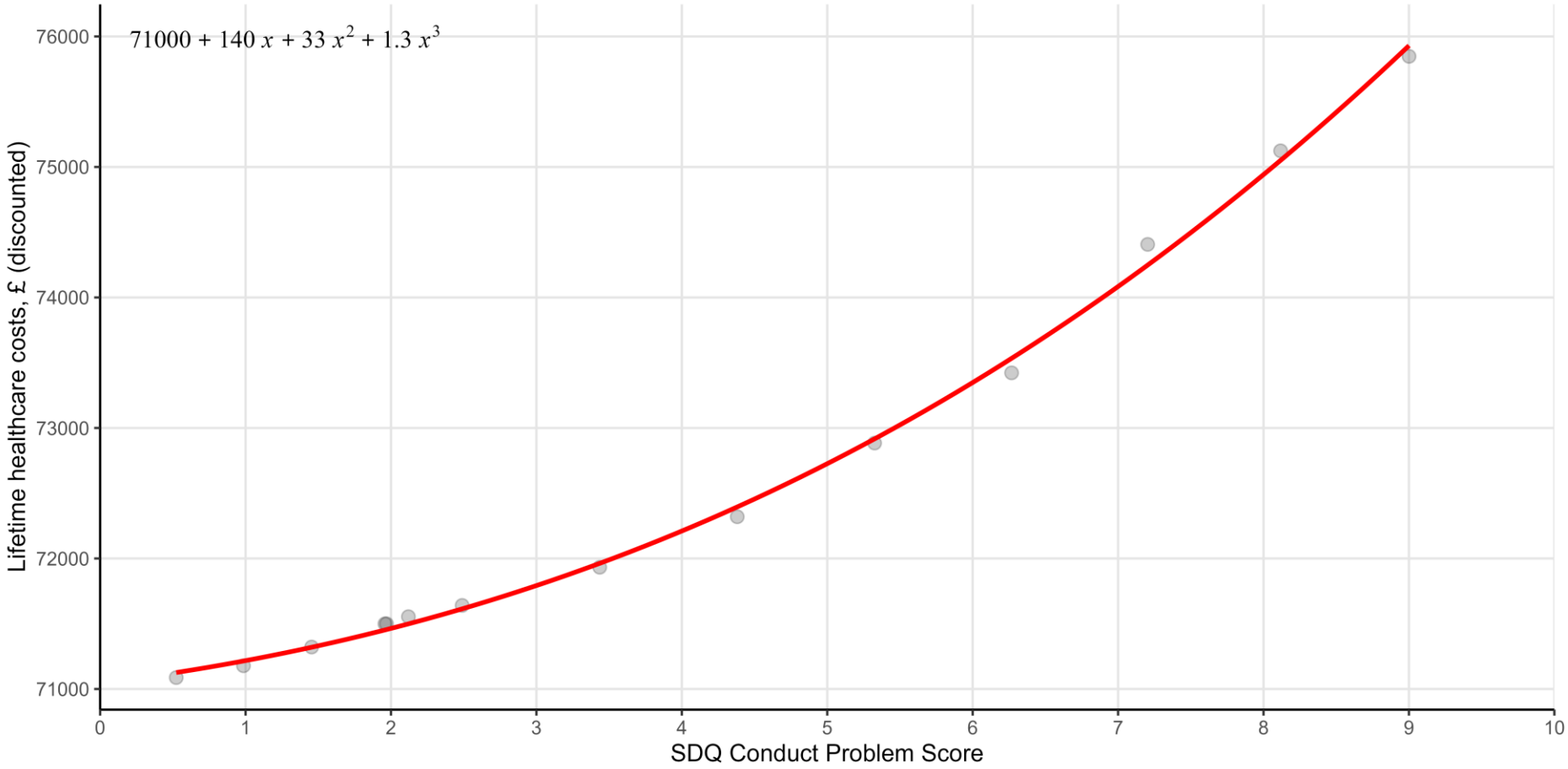


Figure 23 - Lifetime healthcare costs as a function of SDQ conduct score



Non-healthcare outcomes

The healthcare and the non-health costs and outcomes for each arm resulting from the LifeSim model are presented in Table 19. The results show no difference in the conduct disorder costs, probability of prison, prison costs and residential care costs. A very small reduction in the probability of obtaining a university degree (0.001) and a reduction in lifetime consumption (£1,040) was observed for the E-SEE Steps arm compared to SAU. Graphs displaying the results of the lifetime outcomes generated by LifeSim as a function of SDQ score are presented in the appendix.

Table 19 - Lifetime results

	E-SEE Steps	SAU
SDQ conduct score	1.96	1.86
QALYs (disc)	41.22	41.22
Health costs, £ (disc)	£71,499	£71,483
Conduct disorder costs, £	£1,638	£1,638
Probability of prison	0.0146	0.0146
Prison costs, £	£27,707	£27,707
Probability of obtaining a university degree	0.388	0.389
Consumption, £	£1,943,994	£1,945,034
Residential care costs, £	£3,585	£3,585

Abbreviations: QALYs, quality-adjusted life years; SAU, service as usual; SDQ, strengths and difficulties questionnaire.

6.3.3 Impact on the within-trial results

Healthcare perspective

As described in Section 6.2.3, one of the aims of this chapter is to consider the impact of extending the time horizon has on the economic evaluation results. This is achieved by first presenting the results of the within-trial evaluation of E-SEE Steps and then comparing to the results extrapolated using LifeSim.

The results of the within-trial economic evaluation have been reported in detail elsewhere (Cox et al., 2022) but are summarised in Table 20. We can see a small increase in the incremental costs of the E-SEE Steps arm compared to SAU and a small reduction in the QALYs. The resulting incremental net health benefit (iNHB) of the E-SEE Steps programme compared to SAU is negative (-0.0164 QALYs) assuming the health opportunity cost is £15,000.

Table 20 – E-SEE Steps, within-trial time horizon, healthcare perspective

	SAU (SE)	E-SEE (SE)	Incremental (95% CI)
Costs	£1,000 (£164)	£1,177 (£83)	£177 (-£175, £484)
QALYs	1.27420 (0.00393)	1.26957 (0.00155)	-0.0046 (-0.01333, 0.00331)
ICER	-	-	**Dom**

iNHB	-	-	**-0.0164 (**-0.03847, 0.0087)

Assuming κ = £15,000

Abbreviations: CI, confidence interval, ICER, incremental cost-effectiveness ration; iNHB, incremental net health benefit; QALYs, quality-adjusted life years; SAU, service as usual, SE, standard error.

Extending the time horizon of the evaluation to a lifetime horizon by incorporating the findings from the LifeSim extrapolation but limiting the evaluation to a healthcare perspective results in a small increase in the magnitude of the iNHB (Table 21). Thus, E-SEE Steps remains not cost-effective with a negative iNHB of grater magnitude (-0.021 QALYs) compared to the within-trial results.

Table 21 – E-SEE Steps, lifetime time horizon, healthcare perspective

	SAU	E-SEE	Incremental
Costs	£72,483 (£2,198)	£72,677 (£1,708)	£193 (-£1,786.29, £1,178.7)
QALYs	42.4986 (0.4099)	42.4922 (0.1296)	-0.0064 (-0.163, 0.149)
ICER	-	-	**Dom**
iNHB	-	-	**-0.0193 (-0.126, 0.253)**

Assuming κ = £15,000

Abbreviations: ICER, incremental cost-effectiveness ration; iNHB, incremental net health benefit; QALYs, quality-adjusted life years; SAU, service as usual.

6.4 Discussion

6.4.1 Principal findings

This chapter has demonstrated the small impact on SDQ conduct score estimated in E-SEE Steps has very modest impacts on the health care costs and QALYs throughout the life course. In LifeSim SDQ conduct score is correlated with QALYs through the development of depression, which is a function of conduct disorder. The probability of developing conduct disorder is linked to the childhood SDQ Conduct score. The change in SDQ score as a result of E-SEE Steps (increase of 0.1) is too small to cause an impact on lifetime QALYs. Within LifeSim, the model reveals that there is a trend of a natural return to the mean of high SDQ scores after early childhood meaning small changes in SDQ score have a small effect on the probability of developing conduct disorder (Skarda et al., 2021).

The limited impact of extending the time horizon on the NHB in this case study may raise questions of whether such complex modelling is necessary for small changes in effects at such early ages. The literature is rich with descriptions of the importance of childhood policies throughout the life course (Cunha and Heckman, 2007, Guyer et al., 2009) yet the results of LifeSim demonstrate mechanisms whereby children with high SDQ conduct scores drop to the normal range by 7 years (Skarda et al.,

2021). Careful consideration should be given to the trade-off of the resources and complexity in modelling the long-term outcomes with the expectation of the results.

The SDQ conduct score and the lifetime healthcare costs and QALYs resulting from the LifeSim output demonstrate the trend one would expect. A higher SDQ conduct score results in a higher risk of individual's developing conduct disorder and mental health problems. This explains the reduced expected lifetime QALYs and healthcare costs estimated for the E-SEE Steps arm. There is a small difference in the lifetime incremental NHB across trial arms but the results reveal this is perhaps due to the SDQ conduct score of the individuals in E-SEE Steps. The non-linear curves of the lifetime costs and QALYs as a function of SDQ conduct score in Figure 22 and Figure 23 indicates a trend of diminishing marginal returns as we move to lower SDQ conduct scores. Thus, we observe larger reductions in lifetime QALYs and increased healthcare costs for those at higher risk of developing conduct disorder. The interpretation of this may be that it may be a better use of resources for decision makers to try and reduce the SDQ conduct scores of those with much higher baseline scores than 1.86 as in the case of E-SEE Steps.

The results presented in Figure 22 and Figure 23 have implications for policy makers. There is the potential that due to the technical skill requirements and the computational burden of LifeSim that researchers and policy makers may not be able to run LifeSim to generate specific lifetime healthcare costs and QALYs based on inputted SDQ scores. The figures generated in Figure 22 and Figure 23 negate the necessity to run a complex model such as LifeSim by providing the lifetime healthcare costs and health outcomes as a function of SDQ. For example, if a new clinical trial revealed an intervention resulted in an SDQ conduct score of 2 and the

control arms score of 3, then rather than input this into LifeSim, policy makers could simply read off the figure. In this example, a score of 2 results in lifetime healthcare costs of £71,294 and lifetime QALYs of 40.959; a score of 3 results in lifetime healthcare costs of £71,603 and lifetime QALYs of 40.913. Furthermore, the results could be used to conduct a threshold analysis in which policy-makers could say that based on Figure 22 and Figure 23, a new intervention that improves SDQ score will need to reduce the score by 2 units to be cost-effective. Future analyses may consider generating similar plots for additional aspects of human capital that may be of interest to public health decision-makers. For example, generating lifetime earnings, criminal justice sector costs and outcomes, and educational outcomes as a function of SDQ conduct score.

The curves shown in Figure 22 and Figure 23 show a smooth trend in the relationship between SDQ conduct score and costs and outcomes. This indicates a degree of face validity in the results as there are unlikely to be step changes in the lifetime healthcare costs and outcomes at certain SDQ scores. The results show smooth curves due to health costs and outcomes being mediated through a human capital framework within the model (Goodman et al., 2015, Almond et al., 2018b). That is, within LifeSim there are many causal pathways with which SDQ conduct score impacts lifetime health and healthcare costs. For example, it affects health through probability of smoking, developing depression, earnings, education etc. For outcomes such as imprisonment, LifeSim considers only one causal pathway meaning there may be step changes in the probability of imprisonment at certain SDQ conduct score. Future research may consider generating such results to confirm.

The areas of concern in linking E-SEE Steps to LifeSim, namely the absence of baseline SDQ data, resulted in the evaluation taking an 'illustrative' approach. The SDQ Score results measured in E-SEE Steps were considered secondary outcomes. Ages and Stages Questionnaire: Social-Emotional, Second Edition (ASQ:SE-2) formed the primary outcome and baseline data were collected for this measure of childhood development. An alternative modelling approach could consider mapping ASQ:SE-2 to QALYs however, as yet there is no algorithm to map the two. Further, the ASQ:SE-2 was higher in the E-SEE Steps arm compared to SAU in all time points expect FU3 meaning ASQ:SE-2 also showed the same direction of effect of the intervention compared to control (Bywater et al., 2018).

6.4.2 Strengths and limitations

A strength of this research is that it demonstrates the first application of LifeSim for the purpose of extrapolating real-world trial data. Although the results were considered illustrative, this chapter has demonstrated the limitations in using LifeSim to evaluate E-SEE Steps, both in terms of linking the data and the limited impact on the within-trial results.

The analysis presents only the deterministic results of the evaluation and does not incorporate uncertainty. This is a limitation of the LifeSim model (Skarda et al., 2021) as it only reports point estimates. This may give a misleading impression of precision and accuracy in the lifetime results of the analysis when in reality they are very uncertain. Health economic evaluations are inherently uncertain (Briggs, 1999) and best practice dictates uncertainty is characterized and reflected in the results (Husereau et al., 2022). We have detailed the uncertainty in linking E-SEE Steps to

LifeSim and therefore stressed the illustrative nature of this but there is considerable uncertainty in the results that cannot be characterised.

Although illustrative, the results of the analysis rely entirely on the LifeSim model's ability to accurately model the life course. LifeSim is a published model and results reported in the LifeSim paper show comparability to published datasets (Skarda et al., 2021). However, the modelling equations in the paper appear to rely on associations rather than causality. As this study is not a definitive evaluation of E-SEE Steps owing to the uncertainty in linking to LifeSim rather a demonstration of the approach of combining multiple aspects of social value, the impact of the limitations of LifeSim is limited.

6.5 Conclusion

The incorporation of the lifetime health costs and outcomes introduced in this Chapter has had a small impact on the assessment of value for money of an early childhood public health intervention. Decision-makers tasked with resource allocation decisions of interventions targeting SDQ conduct score may consider this case study and the potential data and resource requirements to extrapolate the lifetime health and costs of individuals given such modest changes in SDQ conduct score.

Chapter 7: Broadening the perspective

The thesis has considered the impact of incorporating equity into the evaluative space of an early childhood PHI and separately the impact of extending the time horizon. The following chapter introduces potentially relevant non-health costs and outcomes into the evaluation.

7.1 Introduction

As has been described in Chapter 1, early childhood PHIs may have impacts felt beyond simply the health sector (Petrou and Gray, 2005). For example, improvements in child wellbeing or benefits in the 'human capital' skills required to prosper and be productive in society (Goodman et al., 2015, Almond et al., 2018a) may result from a new intervention. Public health decision-makers seeking to improve these aspects of value when allocating resources are tasked with broadening the perspective of the evaluation beyond a narrow health care perspective (Frew and Breheny, 2019, Frew and Breheny, 2020). Yet, such an endeavour presents challenges. Namely how these additional aspects can or should be incorporated into a decision rule focussing on the primary system perspective taken, e.g., healthcare. It has been argued that limiting an evaluation to a narrow healthcare perspective may lead to sub-optimal resource allocation (McDaid et al., 2003) and as evaluations for children cover multiple domains it may be optimal for such evaluations to cover multiple sectors (Petrou and Gray, 2005).

Traditional methods of CEA widely used in health resource allocation decisions in the UK (National Institute for Health Care Excellence, 2022) fail to incorporate such wider aspects of social value that may be important to decision makers (see Chapter

1 for a description of CEA). It considers one decision maker (i.e., the healthcare sector) and requires the outcomes in units of health (e.g., quality-adjusted life years (QALYs)). Cost benefit analysis is an alternative evaluative framework that allows all outcomes to be expressed in monetary units facilitating the aggregation of different outcomes falling across multiple sectors but it is commonly predicated on a different normative framework (see Chapter 1 for a description of the strengths and limitations of CEA, CBA and the normative frameworks underpinning them). Although NICE's methods guidelines do allow for the use of CBA in evaluating PHIs, it is not the preferred analysis and use is currently limited in decision-making.

There are alternative evaluative frameworks that allow the introduction of wider costs and outcomes but they have methodological areas of concern for decision-making. Return on investment and SROI express all outcomes in monetary terms allowing aggregation but there is no consistent normative underpinning in valuing the outcomes. In practice ROI and SROI do no account for the health opportunity cost (see Chapter 2). Cost-consequence analysis can provide decision makers with a summary of all of the disaggregated effects and costs across multiple sectors but it fails to aggregate the costs and outcomes making decision making difficult as the 'value' of the potential disparate outcomes may not be known.

A framework proposed by Walker et al. (Walker et al., 2019) presents a practical approach to considering multiple outcomes falling on different sectors, multiple sector budgets and opportunity costs. However, to date there is no literature on its use in the evaluation of a childhood intervention. The framework also describes the feasibility of incorporating equity concerns but again to date there has been no practical application of how this could be achieved. As equity is considered an

aspect of social value that is important in public health decision-making and of value for child interventions (Frew and Breheny, 2020, Frew and Breheny, 2019) (see Chapter 4 and Chapter 5), it is considered important to demonstrate its incorporation in the framework.

This chapter therefore aims to achieve two things. First, to introduce non-health costs and benefits into an evaluation of a childhood public health intervention. Second, this chapter aims to introduce health equity into the framework. The source of the results for the purpose of populating the evaluation are the lifetime results of E-SEE Steps, which were extrapolated through LifeSim (i.e., the results from Chapter 6). The LifeSim model generates lifetime health and human capital outcomes (Skarda et al., 2021, Skarda et al., 2022) (see Chapter 6 for a brief description of LifeSim) meaning it provides a rich resource with which to introduce non-health costs and outcomes into an expanded wider economic evaluation. Chapter 6 described in detail the limitations in linking E-SEE Steps to LifeSim and the resulting uncertainty in the results, therefore the evaluation described is considered illustrative. It is, however, hoped this Chapter demonstrates the challenges and the impact of incorporating additional aspects decision-makers may consider to be of value when to comes to early childhood PHIs.

7.2 Methods

The methods section will describe in detail the step-wise incorporation of non-health costs and outcomes into the evaluation through the use of the Walker framework (Walker et al., 2019). The steps build upon on the lifetime health results (i.e., those presented in Chapter 6) by first introducing consumption followed by the educational

outcomes as a result of E-SEE Steps. The method aims to demonstrate how the results of the evaluation change relative to the narrow, healthcare results. The final step involves introducing health equity into the evaluation.

7.2.1 Evaluative frameworks and the impact inventory

7.2.1.1 Step 1- Healthcare perspective

The first step limits the perspective of the evaluation to that of the healthcare sector. The decision problem and the results for this evaluation have been reported in Chapter 6. These are considered the baseline results from which to compare the results using a broader perspective.

7.2.1.2 Step 2 - Broader perspective – healthcare + productivity

For the incorporation of non-health costs and outcomes, the framework proposed by Walker et al. (Walker et al., 2019) is used. It is compatible with CEA and describes an approach to combining the results across multiple dimensions such as health and education, or multiple individuals/groups, and formalises the incorporation of the opportunity costs in the evaluation. See Walker et al. (Walker et al., 2019) for a detailed description.

An example of the framework can be seen in Table 22. This table shows a *within-dimension* and *within-group* approach. Within-dimension net benefit (NB_D) is

estimated across individuals/groups within the dimension (e.g., healthcare or education) incorporating the direct effects of the intervention and the associated opportunity costs. The societal net benefit for the within-dimension approach is then based on a net benefit function in which the within-dimension NBs are aggregated. A within-group approach is estimated in a similar way however the within-group NB (NH_G) incorporating each dimension is estimated for each group or individual. The societal NB function is then estimated by aggregating the NBs for each group.

Table 22 Example of the within-dimension impact inventory

		Dimension 1		Dimension 2		Dimension 3		*Within group*
		DE	OC	DE	OC	DE	OC	
Individuals/ Groups	P_1							NB_{G1}
	P_2							NB_{G2}
	P_3							NB_{G3}
	P_n							NB_{Gn}
Within dimension		NB_{D1}		NB_{D2}		NB_{D3}		

Adapted from Walker et al. (Walker et al., 2019)

Abbreviations: DE, direct effects; NB, net benefit; OC, opportunity cost.

Defining the scope

The first dimension considered in the impact inventory is *health*. The production of health is a fundamental purpose of healthcare systems (Culyer, 1989) and can be considered a goal of the E-SEE Steps programme. Further, the original CEA of E-SEE Steps considered a health care perspective. The second dimension considered is individual's *consumption*, as child health policy makers may be interested in impacts on both health and consumption (Cookson et al., 2021b). It can be used as

an indicator of wellbeing and can indicate impacts on living standards. Finally, the evaluation considers *education* as the final dimension. Educational attainment may improve consumption, but more importantly can be considered an aspect of value in its own right and may improve capabilities, for example; therefore, policies may optimize early childhood education (Low et al., 2005, Marmot, 2013, Woolf et al., 2007, Healey, 2004). The E-SEE Steps trial aimed to enhance infant health, development and wellbeing (Blower et al., 2021b). It was therefore considered reasonable to incorporate lifetime consumption and educational attainment in the evaluation. It should be noted, however, the relevance of these additional domains should be considered in future evaluations of childhood interventions.

The groups affected also need defining. For the purpose of this economic evaluation, the group considered in the impact inventory is the population of England. Despite the health effects only impacting those eligible for E-SEE Steps, the health opportunity costs fall across the entire population. The evaluation considers the whole population as one group. However, in Chapters 1, 4 and 5 the importance of equity as well as efficiency in the evaluation of early childhood interventions was introduced. The evaluation will also consider categorising the population based on a measure of SEP. This is done through the use of income quintiles meaning the impact inventory has 5 groups. LifeSim captures parental household income in the MCS data, therefore our measure of SEP in this evaluation is income quintile at birth. To our knowledge, this will be the first example of the impact inventory in which health equity is incorporated into the evaluation.

Populating the impact inventory

Health

The direct effects (Δh) of the E-SEE Steps programme populating the health dimension are the lifetime QALYs. The costs are the lifetime healthcare costs (Δc_h). As described in Chapter 6, Δh and Δc_h comprise the additive summation of the within-trial results with the extrapolated LifeSim results.

All costs and QALYs are discounted at a rate of 3.5%. The healthcare costs are converted to health opportunity costs using £15,000 per QALY to represent the marginal productivity of the healthcare system (k_h). The health opportunity cost is therefore represented as the $\frac{\Delta c_h}{k_h}$. A scenario is implemented in which a policy threshold of £30,000 per QALY is used to represent k_h as this is used by NICE to determine cost-effectiveness. Table 23 shows how the direct health effects and the health opportunity cost is included in the impact inventory.

Table 23 – Impact inventory for health

		Health		Consumption		Education	
		DE	OC	DE	OC	DE	OC
Individuals/ Groups	P	Δh	$\frac{\Delta c_h}{k_h}$				
		$NB_H = \Delta h - \frac{\Delta c_h}{k_h}$		NB_C		NB_E	

Adapted from Walker et al. (Walker et al., 2019)

Abbreviations: DE, direct effects; NB, net benefit; OC, opportunity cost.

Consumption

Individual consumption (Δc_c) is included in the impact inventory. This represents the complete consumption of goods and services and is based on an individual's lifetime

earnings from employment, interest, pension, savings, wealth and taxes.[21] Lifetime consumption is estimated for each arm of the E-SEE Steps programme. The consumption gains as a result of spending money on E-SEE Steps results in consumption opportunity costs from alternative healthcare interventions foregone. The consumption opportunity costs could be represented by using the marginal productivity of the healthcare sector for consumption ($\frac{\Delta c_h}{k_{hc}}$), i.e., how much consumption is foregone for every £ of healthcare costs. As was used in Walker et al. (Walker et al., 2019) it assumed that £2 of consumption is foregone for every £1 of healthcare expenditure.

Table 24 – Impact inventory for health and consumption

		Health		Consumption		Education	
		DE	OC	DE	OC	DE	OC
Individuals/ Groups	P	Δh	$\frac{\Delta c_h}{k_h}$	Δc_c	$\frac{\Delta c_h}{k_{hc}}$		
		$NB_H = \Delta h - \frac{\Delta c_h}{k_h}$		$NB_C = \Delta c_c - \frac{\Delta c_h}{k_{hc}}$		NB_E	
Adapted from Walker et al. (Walker et al., 2019) Abbreviations: DE, direct effects; NB, net benefit; OC, opportunity cost.							

Education

The educational effects (Δe) are included in the impact inventory in the form of the proportion of university graduates at age 30 years. These educational effects are obtained from the output of the LifeSim model. The education costs (Δc_e) are also required but for the E-SEE Steps study are unknown. It is therefore assumed that the undiscounted incremental education costs of E-SEE Steps compared to SAU is £50.

[21] It is assumed individuals will leave no assets or debts upon death.

This cost is for illustrative purposes only. Further, the marginal productivity of the education sector (k_e) is required. It is assumed that for every £20,000 of additional education costs, there is a 1% decrease in the proportion of university graduates elsewhere. As consumption is included, we need to capture the consumption foregone as a result of education spending (k_{ec}). This is unknown therefore it is assumed that for every £1 of additional education costs, £3 of consumption are foregone elsewhere.

The evaluation in which health, consumption and education are included now considers two decision makers: health and education. Thus, we should consider the marginal productivities of each sector for each outcome i.e., the marginal productivity of the health sector to produce education (k_{eh}) and the marginal productivity of the education sector to produce health (k_{he}). This reflects the fact that the decision to spend health resources may result in education foregone (and vice versa) and these opportunity costs should be reflected. It is assumed k_{eh} represents a 1% decrease in university graduates per £100,000 of additional health costs and k_{he} represents 1 QALY foregone for every £100,000 of additional education costs. These values are assumed to illustrate the impact inventory. The current approach limits the evaluation to three dimensions.

Table 25 - Impact inventory for health, consumption and education

		Health		Consumption		Education	
		DE	OC	DE	OC	DE	OC
Individuals/ Groups	P	Δh	$\frac{\Delta c_h}{k_h}$ +	Δc_c	$\frac{\Delta c_h}{k_{hc}}$ +	Δe	$\frac{\Delta c_e}{k_e}$ +

			$\frac{\Delta c_e}{k_{eh}}$		$\frac{\Delta c_{he}}{k_{ec}}$		$\frac{\Delta c_h}{k_{he}}$
		$NB_H = \Delta h -$ $(\frac{\Delta c_h}{k_{hc}} + \frac{\Delta c_e}{k_{eh}})$		$NB_C = \Delta c_c -$ $(\frac{\Delta c_h}{k_{hc}} + \frac{\Delta c_{he}}{k_{ec}})$		$NB_E = \Delta e -$ $(\frac{\Delta c_e}{k_e} + \frac{\Delta c_h}{k_{he}})$	
Adapted from Walker et al. (Walker et al., 2019) Abbreviations: DE, direct effects; NB, net benefit; OC, opportunity cost.							

7.2.1.3 Step 3: Equity

The evaluation described in this Chapter up to now is limited to efficiency space. That is, we have considered the overall outcomes and costs across the dimensions and have not considered the distribution of the results or which groups benefit as a result of the intervention and which do not. The incorporation of equity into the framework was proposed as being feasible by Walker et al. (Walker et al., 2019) in the original description of the framework yet to date it has not been operationalised. The next section therefore describes the incorporation of equity into this evaluation using the case study of E-SEE Steps described in Steps 1 and 2.

Prior to any evaluation in which health equity is incorporated, an *a priori* assessment of which groups decision-makers are interested in improving health equity (see Chapter 4 and 5 for a discussion of this). In practice that means deciding on the population subgroups *a priori*. For the purpose of this evaluation the subgroups used to categorise the population are income quintile groups.

To allow the incorporation of equity considerations, it may be useful to consider introducing the current level of health (or another domain) for each income quintile. This can be used simply to provide information on the existing level of health in each group or to facilitate an analysis in which decision makers can calculate the level of health before and after an intervention (such as in a DCEA, see Chapter 5). The QALE described in Chapter 4 could serve as a measure of the current allocation of health for each group as it reflects the health expectancy of someone born into an income quintile. It may be useful for decision makers to see the disaggregated outcomes alongside the current allocation of health.

For the impact inventory to fully incorporate health equity, it is desirable to have all of the parameters for the impact inventory estimated by subgroup. Firstly, this means the health effects (Δh); consumption (Δc_c); education effects (Δe); health costs (Δc_h); education costs (Δc_e) for each income quintile group as a result of the E-SEE Steps programme. These results are available from the E-SEE Steps trial results and the LifeSim model with the exception of the education costs, the distribution of which is assumed to be equal across subgroups. The distribution of the education costs is likely to have an impact on the results of an evaluation but as this is an illustrative example the equal distribution is assumed. A policy-maker may want to consider sensitivity analysis in which the distribution of costs is varied.

Secondly, the subgroup-specific marginal productivity of the health care system for health (k_h); the marginal productivity of the health care system for consumption (k_{hc}); the marginal productivity of the health care system for education (k_{eh}); the marginal productivity of the education system for education (k_e); the marginal productivity of

the education system for consumption (k_{ec}); and the marginal productivity of the education system for health (k_{he}) are required. It is assumed that these are equally distributed across all subgroups. The literature does include an estimate of the social distribution of the health opportunity cost across index of multiple deprivation (IMD) quintiles and the results reveal it falls disproportionately on the most deprived in society relative to the least deprived (Love-Koh et al., 2020).

Table 26 shows the impact inventory in which health equity is incorporated and shows the subgroup-specific parameters required. The parameters used in the illustrative impact inventory evaluation of E-SEE Steps are reported in Table 27.

Table 26 - Impact inventory for health, consumption, education and health equity

		CA	Health		Consumption		Education		Net benefit
			DE	OC	DE	OC	DE	OC	
Individuals/ Groups	IncQ1	CA_1	Δh_1	$\frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{h1}} + \frac{\sum_{i=1}^{5}\Delta c_{ei}}{k_{eh1}}$	Δc_{c1}	$\frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{hc1}} + \frac{\sum_{i=1}^{5}\Delta c_{hei}}{k_{ec1}}$	Δe_1	$\frac{\sum_{i=1}^{5}\Delta c_{ei}}{k_{e1}} + \frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{he1}}$	$NB_{Q1} = \sum_{j=1}^{3} x_{Q1j} - y_{Q1j}$
	IncQ2	CA_2	Δh_2	$\frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{h2}} + \frac{\sum_{i=1}^{5}\Delta c_{ei}}{k_{eh2}}$	Δc_{c2}	$\frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{hc2}} + \frac{\sum_{i=1}^{5}\Delta c_{hei}}{k_{ec2}}$	Δe_2	$\frac{\sum_{i=1}^{5}\Delta c_{ei}}{k_{e2}} + \frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{he2}}$	$NB_{Q2} = \sum_{j=1}^{3} x_{Q2j} - y_{Q2j}$
	IncQ3	CA_3	Δh_3	$\frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{h2}} + \frac{\sum_{i=1}^{5}\Delta c_{ei}}{k_{eh2}}$	Δc_{c3}	$\frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{hc3}} + \frac{\sum_{i=1}^{5}\Delta c_{hei}}{k_{ec3}}$	Δe_3	$\frac{\sum_{i=1}^{5}\Delta c_{ei}}{k_{e3}} + \frac{\sum_{i=1}^{5}\Delta c_{hi}}{3}$	$NB_{Q3} = \sum_{j=1}^{3} x_{Q3j} - y_{Q3j}$
	IncQ4	CA_4	Δh_4	$\frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{h2}} + \frac{\sum_{i=1}^{5}\Delta c_{ei}}{k_{eh2}}$	Δc_{c4}	$\frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{hc4}} + \frac{\sum_{i=1}^{5}\Delta c_{hei}}{k_{ec4}}$	Δe_4	$\frac{\sum_{i=1}^{5}\Delta c_{ei}}{k_{e4}} + \frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{he4}}$	$NB_{Q4} = \sum_{j=1}^{3} x_{Q4j} - y_{Q4j}$
	IncQ5	CA_5	Δh_5	$\frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{h2}} + \frac{\sum_{i=1}^{5}\Delta c_{ei}}{k_{eh2}}$	Δc_{c5}	$\frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{hc5}} + \frac{\sum_{i=1}^{5}\Delta c_{hei}}{k_{ec5}}$	Δe_5	$\frac{\sum_{i=1}^{5}\Delta c_{ei}}{k_{e5}} + \frac{\sum_{i=1}^{5}\Delta c_{hi}}{k_{he5}}$	$NB_{Q5} = \sum_{j=1}^{3} x_{Q5j} - y_{Q5j}$

Net benefit	-	-	$NB_H = \sum_{i=1}^{5} \Delta h_i - (\frac{\Delta c_{hi}}{k_{hci}} + \frac{\Delta c_{ei}}{k_{ehi}})$	$NB_C = \sum_{i=1}^{5} \Delta c_{ci} - (\frac{\Delta c_{hi}}{k_{hci}} + \frac{\Delta c_{hei}}{k_{ec}i})$	$NB_e = \sum_{i=1}^{5} \Delta e_i - (\frac{\Delta c_{ei}}{k_{ei}} + \frac{\Delta c_{hi}}{k_{hei}})$	
Adapted from Walker et al. (Walker et al., 2019) In the within-dimension net benefit, x represents the direct health outcome in the relevant dimension, y represents the relevant opportunity cost in the relative dimension. Abbreviations: CA, current allocation; DE, direct effects; NB, net benefit; OC, opportunity cost.						

Table 27 – Parameters used in the impact inventory

Parameter	Value	Source
Health effects (Δh)	Estimated from LifeSim	See Section 6.3.1
Health costs (Δc_h)	Estimated from LifeSim	See Section 6.3.1
Discount rate	3.5%	NICE (2022)(National Institute for Health Care Excellence, 2022)
Time horizon	Lifetime	
Marginal productivity of the health system for health (k_h)	1 QALY foregone per £13,000 of additional health costs	Claxton et al. 2014 (Claxton et al., 2015)
	Scenario: £30,000 per QALY	NICE (2022)(National Institute for Health Care Excellence, 2022)
Marginal productivity of the health system for consumption (k_{hc})	£2 of consumption foregone per £1 of additional health costs	Assumed
Marginal productivity of the health system for education (k_{he})	1% decrease in university graduates per £100,000 of additional health costs	Assumed
Consumption (Δc_c)	Estimated from LifeSim	See Section 6.3.1
Education effects (Δe)	Estimated from LifeSim	See Section 6.3.1
Education costs (Δe_c)	£50	Assumed
Marginal productivity of the education system for education	1% decrease in university graduates per £20,000 of additional education costs	Assumed
Marginal productivity of the education system for consumption (K_{ec})	£3 consumption foregone for £1 additional education costs	Assumed
Marginal productivity of the education system for health	1 QALY foregone for every £100,000 of additional education costs	Assumed

Abbreviations: QALY, quality-adjusted life year.

7.2.1.4 Aggregating the effects

The final stage of the impact inventory is aggregating the effects. A decision should be made to whether this is a within-dimension approach or a within-group approach.

For the impact inventory in which equity is excluded, the analysis only considers one group i.e., the entire population. The analysis therefore uses a within-dimension approach. The societal net benefit function for a within dimension approach (NB_{SWD}) is expressed in equation (11).

$$NB_{SWD} = F(NB_H + NB_C + NB_E) \quad (11)$$

The aggregation of the societal net benefit is through adding the net benefit for each dimension.

For the impact inventory in which equity is included, a within-dimension or a within-group approach could be taken. The societal net benefit function for a within group approach (NB_{SWG}) is achieved through the estimation of the NB for each group (*i*) using equation (12), followed by the aggregation of the within-group NB using equation (13).

$$NB_{SWGi} = F(NB_{Hi} + NB_{Ci} + NB_{Ei}) \quad (12)$$

$$NB_{SWG} = F\left(NB_{SWGQ1} + \cdots + NB_{SWGQ5}\right) \quad (13)$$

The societal net benefit function for a within dimension approach (NB_{SWD}) is achieved through the estimation of the NB for each dimension (*j*) using equation (14), followed by the aggregation of the within-group NB using equation (15).

$$NB_{SWDj} = F\left(NB_{jQ1} + \cdots + NB_{jQ5}\right) \quad (14)$$

$$NB_{SWD} = F(NB_{SWDH} + NB_{SWDC} + NB_{SWDE}) \quad (15)$$

As the impact inventory presented in this chapter is an illustrative example, we have presented no dimension or group weights and have assumed the functions are linear

an additive meaning the within dimension and within group approaches would generate the same results when aggregating. In the equity-informative impact inventory presented in this chapter, a within-group approach is presented without aggregation. This will allow the net benefit of each income quintile to be compared. Due to the absence of group weights applied in the analysis, any aggregation would simply be a mean average of the groups, resulting in the non-equity informative results.

The disaggregated results by group may be sufficient to think about the equity impacts. These results are akin to those reported in an ECEA (see Chapter 3), which would typically show health outcomes and another outcome disaggregated by group. (Verguet et al., 2016). However, it may be useful to show what the resulting social gradients are based on the within-group outcomes. This is achieved through showing the SII of the aggregated results within each group. These results are presented however they are not combined with the current allocation as the outcomes include an aggregation of health, consumption and education and the current allocation is simply health. An alternative approach to aggregation may come in the form of weighting the group-specific outcomes to generate a within dimension result. For example, we may aggregate by weighting the outcomes in the lowest 2 income quintiles to be double that of those in the other income quintiles. These results are also presented.

7.3 Results

Table 28 shows the results of the illustrative evaluation of E-SEE Steps in which the results are limited to a healthcare perspective. These results are reported and

described in Chapter 6. Based on this evaluation E-SEE Steps is considered not cost-effective with a negative iNHB of -0.0193 QALYs.

Table 28 – E-SEE Steps, lifetime time horizon, healthcare perspective

	SAU	E-SEE	Incremental
Costs	£72,483	£72,677	£193
QALYs	42.4986	42.4922	-0.0064
ICER	-	-	**Dom**
iNHB	-	-	**-0.0193**

Assuming κ = £15,000

Abbreviations: ICER, incremental cost-effectiveness ration; iNHB, incremental net health benefit; QALYs, quality-adjusted life years; SAU, service as usual.

7.3.1 Healthcare and broader perspective

To incorporate the non-health costs and outcomes the incremental results are calculated and used to populate the impact inventory along with the parameters detailed in Table 27. Table 29 shows the results of the impact inventory in which health and consumption are included. The results reveal E-SEE Steps resulted in a consumption loss of £1,426 over a lifetime compared to SAU.

Table 29 – E-SEE Steps health and consumption results

	Health (QALYs)		Consumption (£)	
	DE	OC	DE	OC
Population	-0.0064	0.0129	-£1,040	£386
Net benefit (Within-dimension)	NB_H = -0.0193		NB_C = -£1,426	

Assuming κ = £15,000

Abbreviations: DE, direct effects; NB, net benefit; OC, opportunity cost; QALY, quality adjusted life years.

The societal net benefit of the results in Table 29 impact inventory can be aggregated using equation (15) and results in equation (16).

$$NB_{SWD} = F\ (-0.0193\ QALYs, \qquad -£1{,}426) \tag{16}$$

To allow the aggregation of health and consumption in Equation (16), the Department of Health's consumption value of a QALY (v_h =£60,000) (Glover and Henderson, 2010) is used. The societal net benefit when incorporating health and consumption is therefore estimated in equation (17) and shows a net benefit of -£2,584.

$$NB_{SWD} = £60{,}000 \cdot (-0.0193\ QALYs) + (-£1{,}426) = -£2{,}584 \tag{17}$$

Table 30 shows the results of the impact inventory in which health, consumption and education are included. These results show no change in the direct effects of health and consumption and include the additional negative impact on education (-0.001 decrease in proportion of university graduates). The opportunity costs change compared to Table 29 as these include the additional health, consumption and education foregone as a result of resources not available for other health and education interventions. As described in Section 6.2.3.2, this includes the marginal productivities of each sector for each outcome. The results show a health opportunity cost of 0.0134 QALYs, a consumption opportunity cost of £536 and an education opportunity cost of 0.0044 increase in the proportion of university graduates. Thus, resulting in health, consumption and education net benefits of -0.0217 QALYs, -£1,576 and -0.0054 increase in the proportion of university graduates, respectively.

Table 30 – E-SEE Steps health, consumption and education results

	Health (QALYs)		Consumption (£)		Education (% graduates)	
	DE	OC	DE	OC	DE	OC
Population	-0.0064	0.0134	-£1,040	£536	-0.0010	0.0044
Net benefit (Within-dimension)	NB_H = -0.0198		NB_C = -£1,576		NB_E = -0.0054	

Assuming κ = £15,000

Abbreviations: DE, direct effects; NB, net benefit; OC, opportunity cost; QALY, quality adjusted life years.

The societal net benefit of the results in Table 30 impact inventory can be aggregated using equation (15) and results in equation (18).

$$NB_{SWD} = F(-0.0198\ QALYs, \quad -£1{,}576, \quad -0.0054\ \%grads) \tag{18}$$

To allow the aggregation of health, consumption and education we again use the Department of Health's consumption value of QALY (Glover and Henderson, 2010). As the consumption value of a 1% increase in the population graduating university (v_e) is not known, we can estimate it based on the assumption that public sector budgets are efficient and the ratio of the consumption value and marginal productivity of each sector are equal. We can therefore use Equation (19) to estimate v_e:

$$\frac{v_h}{k_h} = \frac{v_e}{k_e} \tag{19}$$

The result is a consumption value of a 1% increase in the population graduating university of £92,308. The societal net benefit when incorporating health and

consumption is therefore estimated in equation (20) and shows a net benefit of -£3,262.

$$NB_{SWD} = £60{,}000 \cdot (-0.0198\ QALYs) + (-£1{,}576) + £92{,}308 \cdot (-0.0054\ \%grads) = -£3{,}262 \quad (20)$$

7.3.2 Healthcare and broader perspective, incorporating health equity

Table 31 shows the SDQ conduct scores and the LifeSim output for each arm and income quintile. As with the method described in Chapter 6, the LifeSim results and the within-trial E-SEE Steps results are summed to generate an estimate of the lifetime health outcomes and costs, and the non-health outcomes and costs. The within-trial results for each income quintile are reported in the DCEA in Chapter 5. The incremental results of each arm and income quintile group are inputted into the impact inventory in

Table 32. The calculations to generate the incremental results are reported in the appendix.

The results of the impact inventory show the incorporation of the current allocation of health in the form of QALE. We can see an absolute gap of 9.98 QALYs between the group with the highest (income Q5) and lowest (income Q2) QALE at birth.

Table 31 – SDQ conduct scores and LifeSim results for each income quintile group

	IncQ1		IncQ2		IncQ3		IncQ4		IncQ5	
	ES	**SAU**	**ES**	**SAU**	**ES**	**SAU**	**ES**	**SAU**	**ES**	**SAU**
SDQ conduct score	2.21	1.36	1.95	2.45	1.74	1.82	1.86	2.20	1.86	1.67
QALYs (disc)	40.32	40.35	40.86	40.84	41.11	41.11	41.49	41.49	42.10	42.11
Health costs, £ (disc)	£73,625	£73,245	£74,030	£74,214	£72,688	£72,700	£68,831	£68,922	£68,926	£68,869
Conduct disorder costs, £	£1,478	£1,408	£1,488	£1,723	£1,639	£1,639	£1,660	£1,660	£1,432	£1,432
Probability of prison	0.0155	0.0133	0.0133	0.0152	0.0118	0.0118	0.0178	0.0178	0.0096	0.0096
Prison costs, £	£29,867	£25,099	£24,644	£28,287	£25,426	£25,426	£31,544	£31,544	£16,499	£16,499
Probability of obtaining a university degree	0.342	0.356	0.380	0.374	0.367	0.367	0.371	0.371	0.476	0.476
Consumption, £	£1,478,050	£1,500,347	£1,615,877	£1,607,149	£1,814,469	£1,813,493	£2,087,761	£2,081,098	£2,586,665	£2,591,532

Residential care costs, £	£3,609	£3,609	£5,820	£5,820	£3,285	£3,285	£3,018	£3,018	£2,605	£2,605

Abbreviations: disc, discounted; ES, E-SEE Steps; IncQ, income quintile; QALYs, quality-adjusted life years; SAU, service as usual;

Table 32 – E-SEE Steps health, consumption and education results across income quintiles

	Health (QALYs)			Consumption (£)		Education (% graduates)	
	CA	**DE**	**OC**	**DE**	**OC**	**DE**	**OC**
IncQ1	67.25	-0.054	0.0105	-£22,297	£450	-0.014	0.0044
IncQ2	67.04	0.026	0.0105	£8,728	£450	0.006	0.0044
IncQ3	71.37	0.011	0.0105	£976	£450	0.000	0.0044
IncQ4	74.93	-0.002	0.0105	£6,663	£450	0.000	0.0044
IncQ5	77.02	-0.006	0.0105	-£4,867	£450	0.000	0.0044
Net benefit (Within-dimension)	-	-		-		-	

Abbreviations: CA, current allocation; DE, direct effects; NB, net benefit; OC, opportunity cost; QALY, quality adjusted life years.

Table 33 - E-SEE Steps net benefit for each income quintile group

	Health (QALYs)		Consumption (£)	Education (% graduates)	Net benefit (within-group)
	CA	**NB_H**	**NB_C**	**NB_E**	**NB_{SWG}**
IncQ1	67.25	-0.0645	-£22,747	-0.0184	-£28,315
IncQ2	67.04	0.0155	£8,278	0.0016	£9,709
IncQ3	71.37	0.0005	£526	-0.0044	£526
IncQ4	74.93	-0.0125	£6,213	-0.0044	£6,213
IncQ5	77.02	-0.0165	-£5,317	-0.0044	-£5,317
Net benefit (Within-dimension)	-	-	-	-	-

Abbreviations: CA, current allocation; DE, direct effects; NB, net benefit; OC, opportunity cost; QALY, quality adjusted life years.

Table 32, the social net benefit for each income quintile is reported in Table 33. The social net benefit calculations for each income quintile group use the same assumptions as the net benefit calculations for the entire population. Equation 21 shows the calculation of the social net benefit for income quintile 1.

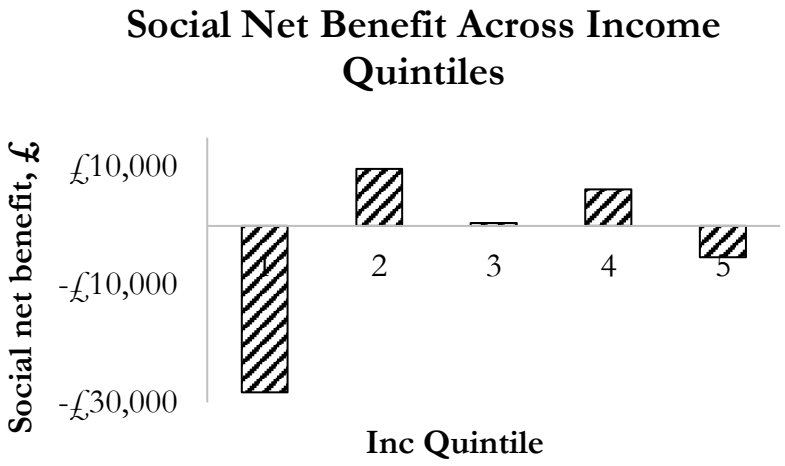
$$NB_{SWDQ1} = £60{,}000 \cdot (-0.0645\ QALYs) + (-£22{,}747)\ + £92{,}308 \cdot (-0.0184\ \%grads) = -£28{,}315 \quad (21)$$

The results in Table 33 show a non-linear pattern in terms of the net-benefit across income quintile groups. The social net benefit is negative in Q1 (-£28,315) and Q5 (-£5,317) and positive in the other quintiles, with the highest net benefit falling in Q2

(£9,709). The results directly reflect the direction and magnitude of the SDQ scores from the E-SEE Steps trial i.e., the largest increase in SDQ conduct score as a result of E-SEE Steps occurred in Q1 (0.85) followed by Q5 (0.19), see Chapter 5 for the E-SEE Steps results.

The social net benefit across each income quintile is displayed in Figure 24. The resulting SII of the social net benefit for each income quintile is £3,355 which represents the difference in social net benefit between those at the top and bottom of the social distribution.

Figure 24 Social net benefit across income quintile



Abbreviation: inc, income.

Finally, as described in the methods, the results can be aggregated using weights. The outcomes in the lowest two income quintile groups are assumed to be double those in the other three to reflect the potential for decision makers to have a pro-poor inequality aversion. This uses the net benefit from Table 33. The results of the within dimension aggregation can be seen in Table 34. The result are presented alongside the results in which each income quintile group is equally weighted.

Table 34 - E-SEE Steps aggregated net benefit

	Health (QALYs)		Consumption (£)	Education (% graduates)	Net benefit (within-group)
	CA	**NB_H**	**NB_C**	**NB_E**	**NB_{SWG}**
Net benefit (Within-dimension) – equal weighting	-	-0.0775	-£13,047	-0.0300	-£17,185
Net benefit (Within-dimension) – pro poor	-	-0.1265	-£27,516	-0.0468	-£35,791

Abbreviations: CA, current allocation; DE, direct effects; NB, net benefit; OC, opportunity cost; QALY, quality adjusted life years.

The results in Table 34 show the net benefit within each dimension when assuming equal weighting and the increasingly negative net benefit in the pro-poor scenario. The weights are assumed and not elicited but this shows an alternative approach to considering equity in the framework.

7.4 Discussion

7.4.1 Principal findings

This chapter has demonstrated the practical aspects of including additional aspects of value into an evaluation of a childhood health intervention. The results reveal a modest impact on net benefit when lifetime consumption is included ($-£2{,}698$) and a slightly larger but again modest net benefit when education is included ($-£3{,}377$). The results do show an impact of introducing consumption and education revealing the value of an intervention may be underestimated if the perspective is limited to the primary system perspective taken, e.g., healthcare.

Consumption and education were included in the evaluation as the literature indicated they may be of interest to early childhood decision-makers (Marmot, 2013, Woolf et al., 2007, Cookson et al., 2021a). The choice of these aspects of value is the purview of decision-makers and it is not suggested that all evaluations of early childhood health policies should be based on health, consumption and education. For example wellbeing may be of interest to decision-makers. Future analyses may consider combining the QALYs and the consumption to report outcomes in 'wellbeing QALYs' (Cookson et al., 2021b).

The incorporation of health equity is an innovative addition to the application of the framework in the literature. The original framework by Walker et al. (Walker et al., 2019) suggested equity relevant characteristics could be included but the case study in this Chapter incorporates equity through a number of approaches. First, the current allocation of expected lifetime health for each of the subgroup populations is included as it may be relevant for decision makers to consider what the existing health gradients are. A limitation of this approach is that any equity weighting is not made explicit, rather decision-makers are merely expected to consider the current allocation of health alongside the net benefit in each group. This approach is closely linked to ECEA (Verguet et al., 2016) in that disaggregated health and additional outcomes are presented for equity-relevant groups. The evaluation includes the current allocation of health and considers *health* equity but decision makers may want to consider the current allocation of consumption and education in addition. The second approach was to consider the SII of the social net benefit for each income quintile group. This more formally allows decision makers to consider the resulting gradient in net benefit, but it does not include the current allocation. The post-

intervention SII of the social net benefit could be compared to the pre-intervention, such as the first stage of a DCEA, but this would require an estimate of the pre-intervention social net benefit based on the current allocation of health, education and consumption. This has not been estimated as part of this chapter but could be considered in future research. These results could then be used for a pre-post analysis or a more formal analysis such as DCEA (Cookson et al., 2017a) or MCDA (Jit, 2018) to allow trade-offs between improvement in net benefit and improvements in net equity across all dimensions. The third approach aggregated the results using weights to generate a single social net benefit as a result of the intervention. The weights could ideally be elicited or at the least made explicit. As in the case of the SII approach, the aggregating approach does not include the current allocation. All three approaches to incorporating equity have their limitations but begin to show decision-makers how equity could be introduced.

The case for using a 'societal perspective' in economic evaluations has been made in order to achieve optimal societal decisions (Drost et al., 2020, Jönsson, 2009). The inclusion of health, consumption and education in the evaluation of a child health intervention should not be considered a 'societal perspective' *per se* as all costs and outcomes related to the intervention are unlikely to be included. However, it is considered a 'broader' perspective and a pragmatic approach to introducing costs and outcomes that may be relevant to a child public health decision maker into an evaluative framework used widely in UK decision-making (i.e., CEA) (National Institute for Health Care Excellence, 2022). Alternative evaluative frameworks, namely CBA and SROI, may lend themselves to evaluating child PHIs with broad/societal perspectives. Cost-benefit analysis was designed to consider a

decision problem in which societal utility is maximised (Drummond et al., 2015) and SROI is designed to measure broader aspects of personal, social and community outcomes to allow cross-sectoral investment decisions (Hamelmann et al., 2017). Their use in decision making is not without challenges (Coast, 2004) (see Chapter 1 for a discussion of the challenges of each evaluative framework). Indeed, reporting of outcomes in monetary terms (as with CBA and SROI) may facilitate the notion that PHIs can be considered investments to save money in the future, but this needs to be interpreted with caution (Buck, 2018). The evaluation presented in this Chapter which takes a CEA and builds upon it to provide health outcomes in QALYs and alternatively reports net monetary benefit making sure to explicitly report the multiple opportunity costs borne by the decision to spend.

7.4.2 Strengths and limitations

A strength of this research is that it demonstrates the first application of the impact inventory to a real-world evaluation demonstrating the impact of broadening the perspective to include additional aspects of value. A considerable limitation is that many of the parameters included in the evaluation are assumed. The marginal productivities of each sector for each outcome are assumed with the exception of the marginal productivity of the healthcare sector for health, which was based on estimated values (Claxton et al., 2015). These assumed parameters many have an impact on the outcome but would be unlikely to change the direction of the results. In the results in which equity was incorporated, the analysis again assumed the distribution of the many parameters were equal across income quintile groups. In reality this is unlikely to be the case. For example, the distribution of the marginal productivity of the health care system has been estimated across index of multiple

deprivation (IMD) quintiles in the England and it was shown to disproportionately higher in more deprived groups (Love-Koh et al., 2020). The consumption value of health has also been shown to differ according to income level (Cookson et al., 2021b) meaning there may be distributional difference across income quintiles. The data requirements for such an evaluation are evidently large as distributional and multi-sector costs and outcomes are required as well as the marginal productivities used to populate the impact inventory. This does raise the question of whether it is possible to capture the impacts of interventions that have impacts across multiple sectors. I would argue that it is possible, albeit a considerable amount of work needs to be done to fully operationalise this framework, but this is something that we can strive towards as decisions regarding whether to fund child health public health interventions are being made and they do have costs and consequences borne across different sectors. Future research could focus on estimating the assumed parameters, allowing future cross-sectoral evaluations to be less data burdensome and rely on fewer assumptions. It may also be useful for future research to consider sensitivity analysis to understand the thresholds at which these effects become important. It is important to understand whether the effects are material and second whether it is worth the analytical effort to estimate them. As a start, the impact of health spending on education outcomes and vice versa could be estimated. The approach to aggregation of the dimensions presents a further limitation. The QALY outcomes from the health sector were based on 'traditional' cost-effectiveness analysis which we have outlined relies on an extra-welfarist normative framework (see Chapter 1). However, to aggregate QALYs and consumption, a common numeraire was required. In this study we used the Department of Health's consumption value of a QALYs (i.e., £60,000) which is estimated using willingness to

pay (Glover and Henderson, 2010), an approach that is grounded in welfarist foundations. This inconsistent approach to valuing outcomes may result in misleading interpretations as the normative framework provides differing societal values of the same outcomes. SROI as an evaluative framework also uses a range of social value estimates which may not be theoretically consistent (Housing Association's Charitable Trust, 2018, Trotter L, 2014) however a considerable limitation of SROI over and above the method presented in this Chapter is that it does not make explicit the opportunity cost, an aspect that is evidently included in this framework.

7.5 Conclusion

The incorporation of wider aspects of social value can have an impact on the assessment of value for money of an early childhood public health intervention. The work presented in this Chapter has shown that it is possible to introduce equity and broader costs and outcomes into an evaluation while making explicit the nature of the costs, outcomes and opportunity costs as well as weights used to aggregate. The combining of multi-sector results into the evaluative framework has been demonstrated but is not without limitations namely in the assumptions due to parameter requirements. Decision-makers tasked with resource allocation decisions of such interventions may consider this case study of the impact inventory but the burden of the limitations will have to be weighed against the limitation of capturing solely health costs and outcomes.

Chapter 8: Discussion

8.1 Thesis Summary

The aim of the research presented in this thesis was to consider the assessment of value for money of early childhood PHIs. The broader aims of the thesis were to outline the methods that have been used to assess value for money of these interventions in a UK context; to consider methods that could be used and to demonstrate the impact and challenges of introducing additional aspects of value on the economic evaluation evidence used in resource allocation decisions. This Chapter draws together the methods and results and attempts to consider the implications for policy and future research.

8.2 Research Findings

This section summarises the findings specific to each chapter and highlights the contribution to the literature.

The systematic literature review conducted in *Chapter 2* demonstrated there is considerably variability in the evidence-base reflecting the value for money of UK-based early childhood PHIs. The interventions identified represented a broad range; however, owing to the methods adopted, a robust statement of value for money was not always possible. The majority of studies adopted a cost-effectiveness analysis framework but under half of all studies (46%; 32/69) reported outcomes in QALYs. The inclusion of the health opportunity cost or a policy threshold was therefore not possible in the non-QALY-based CEAs. The systematic review identified additional frameworks applied in the evidence such as CBA and SROI/ROI, which have been

proposed as candidates for evaluating complex PHIs (Edwards and Lawrence, 2021, Edwards and McIntosh, 2019, McIntosh et al., 2019, Wildman and Wildman, 2019). There was inconsistency in the time horizons and the perspectives adopted in the economic evaluations. An area of consistency, however, was the lack of the incorporation of equity-considerations in evaluations. The two studies adopted an equity-impact analysis (i.e., quantifying the distribution of health outcomes and/or costs) rather than an equity trade-off analysis (i.e. quantifying the trade-offs between improvements in efficiency and equity objectives) (Cookson et al., 2017a).

This systematic review may be useful for decision-makers tasked with resource allocation to consider the robustness of the evidence and the appropriateness of using different types of evaluative frameworks to make determinations of value for money. It may also be useful for researchers to see that despite aspects of value such as equity, non-health costs and outcomes and long term costs and outcomes being important in the context of public health decision making (Frew and Breheny, 2019) they are either inconsistently applied or seldom included.

Chapter 3 introduces the following potential aspects of value for child health PHIs: health equity, broadening the perspective and extending the time horizon of an evaluation. The literature describing the methods available for incorporating equity, extended time horizons and broader perspectives are described.

The application and development of methods for the evaluation of early childhood interventions provided the focus of Chapters 4 to 7.

The analysis conducted in *Chapter 4* explores the issue of equity and adds to the existing literature by describing the variation in QALE by alternative measures of SEP. The specific measures of SEP were income and education as those are widely described in the literature as being indicators of childhood SEP that can influence the inequalities in health observed throughout life (Galobardes et al., 2007). Yet, the distribution of QALE has only been estimated across index of multiple deprivation (IMD). Health-related quality of life weights were estimated from a large dataset (n = 25,320) and combined with mortality statistics to reveal the extent of the existing inequalities across educational attainment and income quintile groups. The resulting social gradients in QALE are steeper across educational attainment groups and shallower across income compared to the literature results estimated across IMD quintiles (Love-Koh et al., 2015).

The SEP distribution of health estimated in Chapter 4 also served as an input to conducting a DCEA of a real-world intervention. This formed the basis of Chapter 5. The E-SEE Steps trial (Bywater et al., 2022) sought to assess if a programme for child social-emotional wellbeing was effective (Bywater et al., 2022) and cost-effective (Cox et al., 2022). The results presented in this Chapter built upon the cost-effectiveness evidence by evaluating the intervention in equity-efficiency space through the use of a DCEA. The analysis built upon the literature by conducting a novel DCEA in which the measure of SEP was varied. For the children, the E-SEE Steps programme was considered not cost-effective but equity improving when evaluated across education groups and income quintile groups. However, it was considered both not cost-effective and equity harming when evaluated across IMD quintile groups. The DCEA literature to-date only considers IMD as the measure of

SEP for UK-based analyses (Ward et al., 2022). This Chapter demonstrates the impact of incorporating equity into the evaluation and along with Chapter 4, shows the impact of changing the groups over which the inequality is considered inequitable. This has implications for decision-makers as it demonstrates the importance of explicitly addressing the question of '*equality between whom?*' when conducting equity-informative analysis.

Chapter 6 demonstrated the first real-world application of the LifeSim model (Skarda et al., 2021). The challenges in linking the E-SEE Steps evidence to LifeSim were detailed. Despite the limitations, the analysis revealed the limited impact the lifetime horizon had on the determination of value for money: reducing from an incremental net health benefit of -0.0176 to -0.0212. The results of the LifeSim model did serve to explain why such a limited impact was observed. Lifetime health costs and QALYs were insensitive to changes in the SDQ conduct score (which was one of the outcomes of E-SEE Steps) when the baseline score was at the normal range (0-3). At the abnormal range (7-10), changes in SDQ conduct score results in large changes in lifetime health costs and QALYs. Thus, the results indicate the groups policy makers may want to consider targeting resources to as they would appear to more cost effective, i.e., those with abnormal SDQ conduct scores, however the costs of the intervention would need to be considered.

Chapter 7 utilised the evidence from the LifeSim model to consider the impact of incorporating broader, non-health costs and outcomes into the decision using the Walker et al. framework (Walker et al., 2019). The incorporation of consumption and educational attainment reduced the net benefit of the E-SEE Steps programme when compared to health alone. This demonstrated the first example of the Walker

framework being used in the childhood intervention literature. The method presented in this Chapter builds upon the Walker framework in which only efficiency is included by incorporating equity. The health, consumption and education results are generated by income quintile and the QALE from Chapter 4 is introduced to represent the current allocation of health for each income quintile group. This represents the first introduction of equity into the Walker framework.

8.3 Discussion of Research Findings

The following section elaborates on the results and themes of the thesis and attempts to place the findings in the context of existing literature. The section is broken up into sub sections discussing the following points that have emerged through the thesis: evaluative frameworks; the nature of public health spending and multiple interventions; spillover effects; early childhood interventions as preventative goods; uncertainty and E-SEE Steps.

8.3.1 Evaluative frameworks

The overall thesis considered the incorporation of equity, non-health costs and outcomes and long term costs and outcomes into the evaluative framework. This was done to reflect value judgements of public health decision makers in England and Wales (Frew and Breheny, 2019). Along with measuring the impacts of an intervention over the life course, their inclusion reflects the discourse in the literature on reasons why improving child health is important. That is, to set the health and trajectories of children throughout their life and close the inequalities in health and social determinants of health (Marmot et al., 2020, Department of Health and Social

Care, 2021). Chapters 5, 6 and 7 demonstrated the impact on the assessment of value as well as an approach to aggregation.

Their aggregation is not without positive challenges, which have largely been described throughout the thesis and will be discussed below. However, there are normative issues too. For example, *should* we be including all of these aspects into resource allocation decisions? What evaluative frameworks *should* we be using?

Which aspects of value should be included?

Choosing what *should* be included centres on which normative approach is adopted: welfarism or extra-welfarism. In this thesis, an extra-welfarist approach is used throughout. Resource allocation decision-making in a UK context has historically been influenced by extra-welfarist ideas (Coast et al., 2008), which differ markedly from welfarist ideas (Sakowsky, 2021, Culyer, 1989, Birch and Donaldson, 2003, Coast et al., 2008, Brouwer et al., 2008) (see Chapter 1). One of the significant seeds from which extra-welfarism grew was the ‘decision-making’ approach to evaluation (Sugden and Williams, 1978) through which the source of values and weights are those of the decision-maker. Therefore, the choice of what should be included is the remit of those tasked with resource allocation decisions.

The decision-maker’s value assessment framework is well defined in England and Wales for clinical interventions (National Institute for Health and Care Excellence, 2022) but they are less well defined for public health. This research leant on the results of a Delphi panel conducted by Frew and Breheny (Frew and Breheny, 2019) in which health, wellbeing and broader outcomes as well as minimising inequalities

were considered important in public health investment decisions (Frew and Breheny, 2019). However, it was not made explicit that educational outcomes or consumption are of value in child health interventions. It was my choice to incorporate these in the broader evaluation. This was in-part due to the illustrative nature of Chapter 7 but also to introduce outcomes that may be of interest to child health decision-makers conscious of the interplay between health, development and human capital (Raghupathi and Raghupathi, 2020) (Bleakley, 2010, Almond et al., 2018b, Conti et al., 2019).

The predominance of extra-welfarism implies decision-makers are those tasked with deciding what is of value. Given there are 42 integrated care boards (ICBs) in England tasked with local health spending, there are many potential decision-makers of which their assessment of value may differ. As bespoke evidence for each ICB is unlikely to be generated, researchers must consider the generalisability of their evidence. The framework provided in Chapter 7 makes explicit the domains and where the effects and costs fall meaning if all evidence is presented in such a framework, decision-makers can make transparent decision while showing which aspects they do not wish to incorporate and those they wish to trade-off. The resource implications of conducting a long-term evaluation of a child health intervention with multiple outcomes may need to be considered, however life course simulation models (such as LifeSim (Skarda et al., 2021)) may ease this burden.

There remains a question regarding whether frameworks other than extra-welfarism are better suited to resource allocation decisions of such complex interventions (Wildman and Wildman, 2019). Proponents of welfarism, which utilises CBA (see Chapter 1), argue that basing decisions on individual utility preferences and

maximising the overall sum of individual utilities (see Chapter 1 for a discussion of Potential Pareto Improvements) results in efficient resource allocation (Seixas, 2017). This is not just efficient allocation of resources to maximise health but to maximise broader social welfare, which in theory is captured in utility judgements (Brouwer et al., 2008). In addition, CBA is operationalised by valuing all outcomes in monetary terms thus facilitating the aggregation of complex outcomes such as health and education. This may appear that welfarism and therefore CBA offer a solution to the evaluation of complex child PHIs. Yet, there are many criticisms of the welfarist approach, including: difficulties with valuing health in monetary terms; the concept that social values are not merely the sum of individual values; the possibility of differential values depending on ability to pay; and maximising utility in a health care system may actually result in negative health outcomes (Seixas, 2017, Brouwer et al., 2008). These challenges have so far seemed insurmountable at national-level decision-making therefore extra-welfarism has dominated. They may not be insurmountable at a local level and it could provide useful information for analysts if research was done to elicit whether local decision-makers favour a normative approach over another.

An alternative approach which is borne out of CBA but does not appear to have a consistent grounding in welfarism or extra-welfarism is ROI and SROI (Edwards and Lawrence, 2021). SROI in particular aims to capture social value not just limited to health. Proponents of SROI argue it allows broader outcomes including capturing ‘well-being’ (Jones et al., 2020, Edwards and Lawrence, 2021). Both ROI and SROI are criticised for not having a consistent grounding in valuation therefore analysts are able to cherry-pick outcomes ensuring a positive ROI. In the systematic review

presented in Chapter 2 all of the ROI/SROI studies were shown to have a positive return on investment. In practice these evaluations largely fail to capture the opportunity cost of spending therefore failing to assess whether the money spent on the intervention could have been better spent elsewhere. The policy implications of this are that caution should be exercised when considering making a decision using the ROI and SROI evidence identified.

The optimal approach is unclear. But what is clear is there is not merely one prescribed approach to evaluating these interventions; there does not appear to be one clear set of values for decision making. This is evidenced through the variable methods adopted in the literature (see Chapter 2) and the degree of ambiguity regarding what public health decision-makers value (Frew and Breheny, 2019). What is unambiguous is that those tasked with public health decision making and NICE-style national health decision making are not always aligned (Hinde et al., 2022, Howdon et al., 2022), meaning simply sticking to a NICE-style assessment of value may result in a sub-optimal allocation of resources.

In this thesis, the multitude of perspectives (i.e.,: i) Healthcare perspective (within-trial); ii) Healthcare perspective (lifetime horizon); iii) Healthcare and consumption perspective; iv) Healthcare, consumption and education perspective; v) Healthcare, consumption and education perspective with equity) demonstrate the implications of potential trade-offs. This may be relevant to consider if other sectors such as education should incur costs of a child public health intervention if the majority of benefits fall in the health sector. The example demonstrated in Chapter 7 showed net health losses and net education losses therefore both decision makers would likely not choose to commission E-SEE Steps. However, alternative analyses may

find health gains and education losses and therefore trade-offs would be required. The use of the framework adopted in Chapter 7 makes explicit the costs, benefits and opportunity costs but does not prescribe how they should be traded-off.

Multiple payers

The analysis adopted in Chapter 7 includes two payers, i.e., a health payer and an education payer, given PHIs may well have benefits felt beyond the health sector (see Chapter 1). Extra-welfarism is largely described as 'health maximising' (Hurley, 2000, Mooney, 2005), potentially undermining the inclusion of multiple outcomes and payers. For example, an education payer may not be interested in maximising health. Although the theoretical basis of extra-welfarist frameworks such as CEA is that the principal output of health services is health (Culyer, 1989), the evaluation need not be limited to health and in theory the maximand can be any object of concern (Brouwer et al., 2008). The incorporation of multiple payers and crucially, opportunity costs, in the Walker framework presented in Chapter 7 operationalises ideas raised by Olsen and Richardson (Olsen and Richardson, 1999) regarding the opportunity costs of public sector resources being broader than health alone. Wildman and Wildman (Wildman and Wildman, 2019) argue that seemingly single payer systems such as the NHS actually resemble multipayer systems with no single perspective funded through general taxation. Thus, the approach adopted in Chapter 7 is flexible regarding the number of decision makers while being explicit about the opportunity costs.

The framework in Chapter 7 assumed two decision makers, two separate budgets each maximising one outcome. It assumes no overlapping or exchangeable budgets.

Decision-makers wanting to use this approach for policymaking may have to pay special attention to this assumption. Should budgets be flexible then alternative opportunity costs may be required as supply-side thresholds[22] used for decision making (i.e., those used in traditional CEA in England and Wales) are predicated on fixed budgets (Sampson et al., 2022). Methods have been described to think about resource allocation and thresholds across multiple flexible budgets (Remme et al., 2017).

Parameters

Marginal productivities

A limitation of the framework adopted is the number of parameters required. Chapter 6 and Chapter 7 revealed many parameters, largely estimates of opportunity costs are missing from the literature. An estimate of the health opportunity costs (k_h) in terms of the marginal productivity of the health care system is available (Claxton et al., 2015). The marginal productivity of the education sector to produce education (k_h) has not been estimated in the literature. Much like the estimation of k_h, a common unit of education is required to estimate k_h. For health, the QALY health metric was used to facilitate comparisons of health outcomes across different conditions. The estimation of k_e would require a common unit of education which may be schooling or learning. A number of the potential options have been discussed in Hinde et al. (Hinde et al., 2019).

[22] There are largely two different approaches to selecting a cost-effectiveness thresholds. 'Supply-side' thresholds are estimated by identifying the opportunity cost of spending limited resources from a fixed budget. 'Demand-side' thresholds are estimated using willingness to pay studies. Note, demand-side thresholds are grounded in welfarism.

For an analysis in which health and education are combined an assessment of the cross-marginal productivities are also required (as introduced in Chapter 7). That is, the marginal productivity of the healthcare sector for education (k_{hc}), i.e. how much education benefit is foregone for every £1 of health care expenditure and the marginal productivity of the education sector for health (k_{ec}), i.e. how much health is foregone for every £1 of education expenditure. These estimates are not available in the literature and therefore assumptions were made. k_{hc} was assumed to be a 1% decrease in university graduates per £100,000 of additional health costs and k_{ec} was assumed to be 1 QALY foregone for every £100,000 of additional education costs (see Chapter 7). Prior to their estimation, the implications for future evaluations depend on whether $k_{hc}$and k_{ec} are likely to have a material impact on the outcomes of the evaluation. If it was predicted they would have a very limited impact, they could be assumed to be zero. However, the literature suggests that this assumption may be an underestimate and would risk overestimating the cost-effectiveness as the opportunity costs are likely to be non-zero. A recent global study looking at the effects of education on mortality found a dose response relationship for years of schooling (Balaj et al.). It showed an average reduction in mortality risk of 1·9% per every additional year of schooling. There are multiple studies outlining the importance of education on health (Raghupathi and Raghupathi, 2020, Grossman, 2006, Ross and Mirowsky, 2010), therefore, it could be perceived that an education intervention will have a considerable impact on health outcome and therefore the opportunity cost should be captured. Likewise, health impacts educational outcomes (Basch, 2011) meaning the marginal productivity of the education sector for health may also be considerable.

An example in the literature of a cross-sectoral evaluation in which health and the criminal justice sector were included assumed no impact of recidivism as a result of health care expenditure and estimated marginal productivity of criminal justice system in producing health (Ramponi et al., 2021). This was achieved by linking QALY losses and costs to each criminal event and then using data on the frequencies of criminal events committed in the UK to express a QALY loss for generic offenders. Future research could adopt this approach although identifying a health loss from a reduction in education outcomes may be difficult given the bidirectional causal nature of education and health. Although the estimation approach is unclear, if this framework is to be used in future decision-making, the magnitude of these parameters requires estimation to avoid making assumptions and potentially biasing the results.

Aggregation parameters

Additional parameters that require estimation are those used to aggregate the within-dimension results. In the analyses presented in this thesis it was assumed health, consumption and education were equally weighted in estimated net benefit function. As the case study showed negative health, consumption and education results, the weights are less contentious as decision makers in both sectors (health and education) are unlikely to consider E-SEE Steps worthwhile from an efficiency perspective. However, in the case of losses in one dimension and gains in another the weights become much more important. The approach adopted does not prescribe weights rather it allows decision makers to aggregate and decide on their own weights, that is both within-dimension and within-group (i.e. for the equity relevant results). Future research could consider how the weights are estimated.

Their derivation may come from the budget allocation of a higher authority to different government departments, e.g. the ratio of the government budget allocation to healthcare versus education, which would be consistent with an extra-welfarist approach (Claxton et al., 2007). Arbitrary decisions regarding the weights should be avoided. Methods such as MCDA make explicit the weights used when decision-making is based on multiple domains. But it has been criticised in the literature for ignoring opportunity costs (Campillo-Artero et al., 2018, Marsh et al., 2018) and failing to incorporate rigorous health economic thinking (Briggs, 2016) meaning weight estimation and the nature of trading off outcomes may need to take a step beyond the MCDA literature.

Conclusion

Economic evaluation should not be prescriptive and the breadth of the evaluation should be based on the evaluative framework. If extra-welfarism is the preferred normative approach, then it is up to decision-makers to decide on the perspective. The framework adopted in this thesis demonstrates bringing various aspects of value into a decision. However, should a decision maker prefer a welfarist approach then social welfare should in theory be captured. For early childhood PHIs it is apparent from the literature that aspects beyond merely the QALY may have value and this thesis provides a way to consider the implications of these.

8.3.2 Multiple interventions – the nature of public health decision-making

The approach adopted in the evaluations in Chapter 5, 6 and 7 evaluate an intervention, in this case E-SEE Steps, in isolation. They provide results that aim to

indicate cost-effectiveness or more broadly value for money of an intervention when compared to a national threshold. There is however a disconnect between the nature of the funding decisions between national decision-making bodies such as NICE which make decisions at arm's length about cost-effectiveness and the integrated ICBs tasked with spending a public health budget to meet the health needs of the population. ICBs may be interested in the affordability of the intervention as well as the cost-effectiveness and the decision to commission a service has implications for the alternative/existing interventions displaced from the budget (Howdon et al., 2022). As this implies those tasked with making public health resource allocation decisions are deciding which combinations of interventions to commission subject to their own budget constraints and decision-making is not concluded when an intervention is deemed to be cost-effective or value for money.

In the context of extra-welfarism, the approach to optimal decision making is via constrained optimisation in which something, in this case health, is maximised subject to the budget constraint. It is worth noting that in theory CBA could be used, however prerequisites including budgets that reflect consumer's willingness-to-pay and a full description of all objects of value render it challenging in the context of public health decision making (Claxton et al., 2007, Sculpher and Claxton, 2012). Methods for maximising a single health outcome (e.g., QALYs) subject to a budget constraint for the context of health decision making are well described, albeit they tend to focus on health benefit packages development in global health contexts (Ochalek et al., 2018, Edwards and McIntosh, 2019). Although it is unclear exactly which approaches ICBs use to spend public health budgets, the global health

methods available could be applied as the theoretical underpinnings hold for a UK context.

An evaluative approach recommended by Public Health England (PHE) for public health budget allocation is PHE's Prioritisation Framework (Public Health England, 2019b). It is a form of MCDA (Baltussen et al., 2019, Thokala et al., 2016, Marsh et al., 2016), which allows the ranking of interventions based on multiple weighted outcomes yet the determination of the weights is subjective. In addition, the evidence recommended for use in the Prioritisation Framework can be found in the (HEER) tool (Public Health England, 2019a) which shows considerable fewer early childhood PHIs compared to the systematic review conducted in Chapter 2. The evidence identified in Chapter 2 could inform budget allocation exercises but there remains plenty of scope for future research to consider how ICBs or similar public health decision-makers can spend a budget.

MCDA is one such approach but this has been criticised (Briggs, 2016) (see Chapter 3). Programme budgeting and marginal analysis (PBMA) is also described as an approach for public health resource allocation (Howdon et al., 2022). PBMA appraises past resource allocation in specific programmes and considers the benefits and costs of investment or disinvestment (Edwards et al., 2014) but it has been criticised for conceptual and operational limitations (Howdon et al., 2022).

What this thesis has emphasised is that decision-makers may need to maximise more than one outcome (i.e. beyond solely health) in a transparent and reproducible way. This is of importance in a policy perspective as demonstrated through discussions with the Department of Health's Start for Life Unit (see Section 8.4.1).

Lofgren et al. (Lofgren et al., 2021) proposed a mathematical optimisation approach to resource allocation in which an optimal combination of interventions were selected to maximise health and financial risk protection subject to a budget constraint. Although this was in the context of Malawi, this perhaps provides a method to consider optimisation of multiple outcomes for future adaptation.

Anecdotally, based on conversations with the Start for Life Unit at the Department of Health and Social Care (see Section 8.4) , there could be a rich vein of future research in providing approaches to spending a budget that meets the goals of public health decision-makers.

8.3.3 Spillover effects

The thesis and discussion of the evaluations so far has detailed value judgments about *which* outcomes and costs are considered to be relevant in the evaluation. The focus was on equity and broader costs and outcomes such as education. Yet, there are also judgments regarding *for whom* the outcomes occur and *on whom* the costs fall. There may be relevant individuals on which these outcomes and costs fall that are not included in the economic evaluation. The term spillover effects is used to denote substantial effects and costs on family members and the wider network of non-family care givers (Basu and Meltzer, 2005, Henry et al., 2023, Grosse et al., 2019). Spillover effects are increasingly prevalent in the health economics literature (Wittenberg et al., 2019) with a number of frameworks and methods to allow their incorporation into evaluations (Al-Janabi et al., 2016, Jacobson, 2000, Al-Janabi et al., 2022, Canaway et al., 2019, Mendoza-Jiménez et al., 2024).

The incorporation of such spillover effects has largely been overlooked in this thesis largely for pragmatic reasons. It is an important topic, however, and one that has implications for early childhood PHIs. Although the inclusion of spillover effects was felt to be beyond the scope of this thesis, their exclusion and ultimately impact does merit further discussion.

In the original economic evaluation of E-SEE Steps the health outcomes and costs for the child and the primary caregiver of the child were estimated (Cox et al., 2022). The cost-effectiveness of E-SEE Steps for the child and for the parent were then estimated as well as the combined cost-effectiveness: this was estimated by summing the costs and QALYs gained. In summary, this approach included the spillover effects of the intervention on the primary caregiver and weighted it equally with the child costs and outcomes. For the DCEA conducted in Chapter 5, two separate evaluations were considered: a DCEA of E-SEE Steps for the child and separately for the primary caregiver. These were not combined as in the original economic evaluation of E-SEE Steps (Cox et al., 2022) as it was unclear *how* to aggregate the results or whether that *should* even be attempted. For example, it is unclear how useful it would be to aggregate when an intervention reduces the health of the most deprived parents but improves the health of their children (i.e. the most deprived children). This was the case with the DCEA results across educational attainment groups (see Chapter 5). A reduction in parental health is likely to negatively impact child health: health shocks negatively impact adult socioeconomic circumstances (García-Gómez et al., 2013) and the socioeconomic circumstances that a child find themselves in impact their health (Galobardes et al., 2004, Galobardes et al., 2006c, Smith et al., 1997). Therefore, valuing the short term

benefits in the child may be neglecting the long term risks as a result of a reduction in their parent's health.

In practical terms, the aggregation of these results would also require weights attached to the child outcomes and the primary caregiver outcomes to facilitate the inclusion of these spillover effects. Weights would be challenging to elicit or estimate in practice. The extra-welfarist approach to basing weights on budget allocation may also not be feasible as any budget assigned to child health may be implicitly aiming to impact adult health as well.

The evaluation in Chapter 6 and 7 did not incorporate the adult outcomes and limited the evaluation to that of the children. The framework presented in Chapter 7 could be adapted to include the adult spillover effects by making explicit the individuals included in the within-individual approach. This would require estimation of the effects as well as weights to allow aggregation.

The incorporation of spillover effects in the evaluation of childhood PHIs is something that does require future research. There are numerous mechanisms through which substantial spillover effects could be experienced including health-related sibling spillover effects (Sjölander et al., 2016, Feinberg et al., 2012, Mallinson and Elwert, 2022), the potential for positive and negative impacts on productivity of the parents (Hubens et al., 2021), and the educational impacts on siblings (Mallinson and Elwert, 2022, Black et al., 2021). Should these impacts be estimated for an intervention, the framework presented in Chapter 7 would allow their explicit incorporation.

8.3.4 Early years interventions as preventative goods

Early years PHIs are concerned with preventing ill health and promoting health behaviour. For example, the E-SEE Steps programme was implemented to improve social and emotional wellbeing as well as health in the early stages of life as these are predictors of outcomes in later life. There are numerous characteristics of preventative health interventions that mean their provision requires special consideration for resource allocation (see Chapter 1). Arrow's seminal paper on market failure of healthcare (Arrow, 1978) detailed healthcare's general characteristics which make valuation and resource allocation of healthcare challenging. Chapter 1 outlines the reasons that preventative interventions require particular consideration over and above those outlined by Arrow. One such reason is the nature of prevention goods being 'merit goods', i.e., the benefit of the good to society is greater than the benefit to the individual. This has implications for the value of PHIs. Neumann et al. (Neumann et al., 2008) suggests the valuing of public health services is in its infancy and work needs to be done or it risks losing out on scare resources.

The valuation of PHIs needs to consider that the benefits to society may be greater than the sum of the individual benefits. There are a number of challenges around valuation in childhood intervention in general (Petrou, 2003, Petrou, 2022). For example, measurement issues in the context of early childhood public health include whether the instrument should be broader than just health outcomes using typical measures such as Child Health Utility 9D (Stevens, 2009) or Infant health-related Quality of Life Instrument (IQI) (Jabrayilov et al., 2019) and capture well-being such as the Quality of Well-Being scale (Seiber et al., 2008). And, given the lifetime time

horizons recommended in public health economic evaluation evidence (Frew and Breheny, 2019) the use of a single common measure for valuation throughout the life course presents methodological limitations (Petrou, 2022). The valuation challenges are evident but the point about childhood prevention goods being ‘merit goods’ may require further research. This suggests that there is perhaps additional intrinsic value in preventative intervention in the form of uncaptured externalities which may be improvements in inequalities and improvement in human capital outcomes.

Public health funding awarded to local authorities has been cut in recent years (Haves, 2024). Investment in prevention is generally good value for money compared to treatment and reallocation of resources to public health expenditure is more productive than NHS expenditure (Martin et al., 2020). Although the case for public health expenditure has been made by Martin et al. (Martin et al., 2020) the value of childhood PHIs has perhaps not been made. They have the potential to reduce widening inequalities and improve outcomes beyond health. The incorporation of these outcomes in evaluations may help to make the case of early childhood PHIs being value for money.

8.3.5 Uncertainty

The methods applied in this research have demonstrated the impact of including additional aspects of value related to childhood public health programmes however the handling of uncertainty has only been explored in-part. In Chapter 4, confidence intervals were estimated for the HRQL weights but the QALE estimates were deterministic. The economic evaluations conducted in Chapters 5, 6 and 7 were also deterministic in nature. One-way sensitivity analyses were conducted to assess the

sensitivity of the outcome to a single parameter or assumption whilst holding all other variables constant. For example, in Chapter 5, 6 and 7 the sensitivity of the results were estimated through altering the cost-effectiveness threshold. The DCEA in Chapter 5 also altered the distribution of the health opportunity cost to assess the impact on the results. In real-life evaluations variables do not vary in isolation meaning the true uncertainty is not fully captured (Briggs, 1999). This thesis was largely about exploring the impact of additional aspects of value on child health evaluations with an eye to considering the methods available in the economics literature and demonstrating their impact. As such, accurately capturing the real-world uncertainty was not considered in the aims of this thesis due to time limitations. Yet, appropriately capturing all forms of uncertainty in an economic evaluation is important (Briggs, 1999, Briggs, 2000, Drummond et al., 2015) particularly if decision-makers are to be fully informed. Therefore, given its importance and the particular role it plays in the economic evaluation of child health owing to analytical issues (Petrou and Gray, 2005), uncertainty is discussed below.

Uncertainty is present in all aspects of an economic evaluation including uncertainty in the sample data informing the evaluation (i.e., E-SEE Steps) and uncertainty in the analytical approach to extrapolating the results beyond the trial (i.e., LifeSim). Uncertainty in the sample data is high, particularly in the E-SEE Steps subgroup results by SEP presented in Chapter 6. The 95% confidence intervals around the estimated QALYs overlap between the E-SEE Steps arm and the SAU arm in all SEP subgroups meaning there is no conclusive evidence of a difference between the arms across subgroups. Using point estimates that differ across arms can therefore be misleading. Uncertainty in the analytic approach can be addressed using various

methods: deterministic sensitivity (which is described above) and probabilistic sensitivity analysis. Deterministic sensitivity analysis has been criticised for having limitations (O'Brien et al., 1994) and a solution is to employ probabilistic sensitivity analysis which involves sampling from the distribution of all parameters over many simulations rather than using the mean. There is abundant uncertainty in both sample data and analytical approach and future analyses may consider addressing this.

A future analysis may consider replicating the DCEA conducted in Chapter 5 using probabilistic sensitivity analysis to try and capture some of the sample data uncertainty. For this analysis, uncertainty in the QALE estimates could be generated through the use of Monte Carlo simulation which involves repeated random sampling from the distribution of the parameters. The results report uncertainty around the costs and QALYs so assuming the distribution would allow probabilistic sensitivity analysis to be conducted. The distribution of results of the DCEA, likely in the form of an ellipsis reported on the equity-impact plane (Briggs, 2000) seen in Chapter 5, would indicate if the intervention were truly equity harming/improving or whether many of the resulting iterations show a contrasting result.

The results in the DCEA are over the E-SEE Steps trial period and a key factor of economic evaluations of child health policies is the need to extrapolate the results to consider the life course. There are myriad parameter and model-structure related potential uncertainties (Manning, 1996, Bojke et al., 2009), all of which may render the results of a complex model such as LifeSim very uncertain. However, LifeSim is not currently equipped to generate estimates of the uncertainty in the results. LifeSim estimates parameters for the various stages of life separately using different dataset

and estimation methods meaning parameter uncertainty in one estimation is compounded over time as it feeds into the next life stage (Skarda et al., 2021). A future life course model may consider estimating parameters from the same cohort over time which would allow formal analysis of parameter uncertainty. Accurately parametrising uncertainty may prove useful in public health decision-making as there may be interest in how uncertain the costs are as budget overspend is a concern for public health decision-making bodies (Howdon et al., 2022). Ultimately, consideration should be given to whether the uncertainty would prove useful. As alluded to above, it may indicate the probability of being cost-effective or equity-harming; it may indicate the potential for budget overspend; or it may be useful in deciding whether future research would be of value, e.g., using value of information (VOI) analyses (Fenwick et al., 2020, Rothery et al., 2020).

The concern with modelling childhood interventions is the potential for butterfly effects, for example a small change in an input parameter (e.g., SDQ conduct score) resulting in a considerable change in life course outcomes. Despite the lack of reported uncertainty in the result, it is reassuring for decision-makers contemplating using LifeSim for policy decisions that the results in this thesis showing the first real-world application of LifeSim revealed a small change in SDQ conduct score resulted in a very small change in lifetime costs and outcomes for low SDQ conduct scores. This generates face validity of LifeSim for decision-makers tasked with considering the life course of a child intervention.

8.3.6 E-SEE Steps

The evaluations conducted in this thesis used E-SEE Steps as a case study. The unaccounted-for uncertainty in the DCEA results (see section 8.3.5) and the limitations in the linking of E-SEE Steps to LifeSim (see Chapter 6) mean the results of economic evaluations presented in this thesis should not be used to justify resource allocation decisions regarding E-SEE Steps without caution. Yet it is worth considering what the findings in the thesis may reveal about E-SEE Steps.

E-SEE Steps was delivered using a proportionate universalism approach (Bywater et al., 2022) to ensure greater care for those of greater disadvantage/need (Carey et al., 2015). The more intensive form of the intervention was provided to those at higher risk of parental depression or for children at higher risk of social-emotional issues. The E-SEE Steps trialists may be interested to see the SEP category of the individuals recruited into the study. Approximately 36% of the trial participants were in the lowest IMD quintile indicating the intervention was reaching more people living in deprived areas. However, the DCEA in Chapter 5 revealed the 44% of all participants were in the highest educational attainment group. This may reflect temporal trends in educational attainment, but it may be demonstrating the inverse care law in action (Hart, 1971). As was made explicit in Chapter 5, the impacts on equity may be acceptable to decision-makers, but they should be explicit across which groups they consider there to be an inequitable inequality *a priori*.

The E-SEE Steps trial had the aim of increasing the health and well-being of all families in order to reduce the gap between the poorest and wealthiest (Blower et al., 2021b). The analyses conducted in Chapter 5 revealed the importance of

considering costs when analysing whether the gap between most and least deprived has been reduced. Spending limited resources on health interventions results in health foregone somewhere else in the population as the foregone costs cannot be used to generate health elsewhere. This ‘health opportunity cost’ is a fundamental aspect of economic evaluation (Drummond et al., 2015) and plays a considerable role when analysing whether an intervention improves health equity. The distribution of the health opportunity costs falls disproportionately on the most deprived groups in society (Love-Koh et al., 2020) so failure to incorporate all of the costs will not give the full picture of the existing inequalities. For example, imagine all five IMD groups gained 1 QALY as a result of an intervention. The costs, however, fall more on the most deprived (e.g. £10,000 on IMD Q1) than the least deprived (£5,000 on IMD Q5) as a results of social variation in health effects of health care expenditure (Love-Koh et al., 2020). Converting the costs to health lost (through the health opportunity costs i.e. £15,000 per QALY) results in unequal health gained as a results: IMD Q1 gains 1 QALY – (2/3 QALY) = 1/3 QALY; IMD Q5 gains 1 QALY – (1/3 QALY) = 2/3 QALY. Therefore, despite generating equal health outcomes in each groups the incorporation of the health opportunity cost of spending and reporting in terms of net health benefit reveals equity-harming impacts.

The study conducted in Chapter 5 demonstrates this through the scenario of equal health outcomes across measures of SEP. The results become equity harming as the estimated distribution of the health opportunity cost is used over the assumption of proportionate distribution. This may serve as a useful case study to future decision-makers tasked with evaluating the equity impacts of an intervention to

remind them that equity-informative economic evaluation such as DCEA (Asaria et al., 2016) may be a necessity.

Finally, E-SEE Steps had the goal of improving the social-emotional wellbeing of children, measured via the SDQ score. The results revealed the intervention was not cost-effective for the children (see Chapter 3). The analysis of E-SEE Steps results reveals that the intervention targeted those with scores falling in the normal region, which is classed as 0-15 for the overall SDQ score and 0-3 for the SDQ conduct score (Oxfordshire County Council, 2015). The results of LifeSim presented in Chapter 6 reveal that reductions in SDQ scores for those in the abnormal ranges are much more productive in terms of reducing lifetime health care costs and improving lifetime health than those in the normal ranges. Figure 23 and Figure 24 show a trend of diminishing marginal returns to reductions in SDQ scores as we move down the baseline SDQ score. Those considering conducting future research on the E-SEE Steps programme may consider targeting the intervention at those with high SDQ score in the abnormal range as this may serve as a more cost-effective use of resources. Albeit, the costs of an intervention targeting this group may be higher and the effects may not be the same as those seen in the E-SEE Steps trial. A proportionate universalism approach (Carey et al., 2015) of this future research may consider using SDQ score to stratify by need.

8.4 Policy implications

Numerous potential policy implications deriving from this research have been described throughout the thesis. There are also realized policy implications too.

8.4.1 Case Study – Start for Life Unit, Department of Health and Social Care

In March 2023, the systematic review from Chapter 2 was published in the *British Medical Bulletin* (Murphy et al., 2023). In June 2023, representatives from the Start for Life programme (Department of Health and Social Care, 2023) at the Department of Health and Social Care (DHSC) expressed interest in discussing the findings from the paper (Murphy et al., 2023). Formal correspondence was initiated, resulting in a series of discussions aimed at elucidating the potential applications of the research findings, in particular how to move forward with potential collaborative avenues as well as using the findings from the systematic literature review (see Appendix). The latter focussed on how improved consistency of evaluative frameworks, outcomes and time horizons can improve decision-making going forward.

The engagement with the Start for Life Unit at DHSC proved instrumental in validating the robustness and relevance of the research questions and the findings of the systematic review. Their insights and feedback provided a valuable perspective on how the research outcomes align with health spending decisions. Furthermore, the discussions allowed for an exploration of potential collaborative avenues that could leverage the research to address existing challenges, proving valuable to my decision-making knowledge base regarding.

Suggestions provided during interactions with the Start for Life Unit allowed us to consider the direction of future research to allow a more refined exploration of the practical implications of the research outcomes. Notably, the Start for Life Unit were more broadly interested in translating the findings from the systematic literature review to help answer broader questions of spending on early childhood PHIs. Much

like the discussion described in Section 8.3.2, there was interest in how methods can inform budget allocation on early childhood interventions. The approaches presented to the Start for Life Unit are described in the Appendix.

8.5 Research Recommendations

The following research recommendations are intended to inform researchers, analysts and decision-makers tasked with resource allocation for the purpose of improving early-childhood public health.

1) Additional aspects of potential value can have an impact on the results of an economic evaluation of an early childhood intervention. By neglecting to include them in an evaluation it means there is an implicit assumption that impacts other than health maximisation have no value in the decision problem. The perspective (e.g., healthcare or healthcare and education) and the potential aspects that may have value (e.g., educational attainment and/or improvements in equity) should be specified *a priori*.

2) It is imperative that there is consistency in the evidence base. For example, studies that report health outcomes in units other than a common measure of health (e.g., QALYs) risk not being able to determine if an intervention represents good value for money as there is no estimate of the opportunity cost with which to compare it to. Further, use of a common measure allows decision-makers to make comparisons of the productivity of each, which is a

necessity if future research endeavours on optimisation methods want to utilise the evidence base.

3) The methods applied in this thesis have shown how additional aspects of value can be operationalised when allocating resources for early childhood PHIs. Yet, there is a clear need for much more effort to be dedicated to health economic methods applicable to preventative interventions. Not least in terms of methods that are aligned with the decision problem and estimation of parameters to facilitate the evaluation of these complex interventions that have the potential to be a very productive use of resources.
4) When incorporating health equity into an economic evaluation of a childhood public health intervention it is important that decision-makers specify *a priori* what they deem to be inequitable in terms of health distribution. Deciding on which measure of SEP is important, which may rely on the literature regarding childhood measures of SEP, and moving away from the status quo has an impact. Deciding on the measure *a posteriori* is not recommended as the evaluation should reflect the decision-makers prior assessment of unfair inequality.
5) Interventions for children that aim to improve social and emotional wellbeing through improving SDQ may want to consider targeting interventions at those with SDQ scores outside the normal range. This may represent a more cost-effective use of resources.

8.6 Conclusions

This thesis addresses questions relevant to resource allocation of early childhood PHIs. The evidence relevant to those making decisions was identified and showed limitations regarding whether they include certain aspects of value. The research conducted in this thesis describes and advances the use of methods available in the health economics literature to demonstrate their use in childhood public health resource allocation decisions. This was conducted first through an exploratory study of a DCEA followed by the adaptation of a published framework. The methods were used to demonstrate the impact on the lifetime effects of an existing UK-based economic evaluation assessing the cost-effectiveness of an intervention for improving social and emotional wellbeing for of an infant.

Findings from this thesis suggest that limiting the approach of an economic evaluation to health maximisation risks providing only a partial picture of whether the intervention could be a good use of resources.

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Appendix

Chapter 2

Search Strategies

Ovid MEDLINE(R) ALL <1946 to August 13, 2021>

via Ovid http://ovidsp.ovid.com/

Date range searched: 1946 to 13th August 2021

Date searched: 16th August 2021

Records retrieved: 2408

The MEDLINE strategy below includes the CADTH economics search filter for Ovid Medline (lines 52-74) and the NICE UK search filter for Ovid Medline (lines 80-90).

Economic Evaluations/Cost/Economic Models - Ovid Medline. Strings attached: CADTH database search filters [Internet]. Ottawa: CADTH; 2016. [Accessed: 16 August 2021]. Available from: https://www.cadth.ca/resources/finding-evidence/strings-attached-cadths-database-search-filters#health

Ayiku L, Levay P, Hudson T, Craven J, Barrett E, Finnegan A and Adams R. The MEDLINE UK filter: development and validation of a geographic search filter to retrieve research about the UK from OVID MEDLINE. Health Information and Libraries Journal, 2017 34 (3): 200-216. (Publisher: Wiley. © 2017 Crown copyright. Health Information and Libraries Journal © 2017 Health Libraries Group.)

1 exp Pediatrics/ (60711)

2 exp Child/ (1996653)

3 exp Infant/ (1181492)

4 exp Infant, Newborn/ (631896)

5 exp Infant, Low Birth Weight/ (36085)

6 exp Infant, Very Low Birth Weight/ (10753)

7 exp Infant, Premature/ (58941)

8 (p?ediatric* or child* or preemie* or baby or babies or infant* or toddler* or neo nat* or neo-nat* or neonat* or newborn* or new-born* or newly born* or newly-born* or preschool* or pre-school* or schoolchild* or school-child* or schoolboy* or school-boy* or schoolgirl* or school-girl* or school-age* or prekindergarten or pre-kindergarten or kindergarten or boy* or girl* or kid* or LBW or VLBW or ELBW or "low birth weight").ti,ab. (2791606)

9 (under adj (five* or "5") adj2 (age* or old*)).ti,ab. (2226)

10 ("birth to 5" or "birth to five").ti,ab. (1388)

11 or/1-10 (3825111)

12 Public Health/ (86906)

13 Health Promotion/ (77265)

14 Health Literacy/ (7074)

15 Health Education/ (62112)

16 "Social Determinants of Health"/ (4516)

17 Child Health/ (3726)

18 Child Development/ (48301)

19 Child Guidance/ (892)

20 Child Welfare/ (22213)

21 Child Abuse/ (23367)

22 Child Nutrition Disorders/ (3672)

23 Infant Health/ (1020)

24 Infant Welfare/ (2777)

25 exp Family Relations/ (96657)

26 Early Intervention, Educational/ (3231)

27 Early Medical Intervention/ (3313)

28 exp Physical Fitness/ (32981)

29 Diet, Healthy/ (5352)

30 Oral Health/ (18053)

31 ((early or early-years or early-life*) adj3 (program* or interven* or scheme* or initiative*)).ti,ab. (46348)

32 ((health* or wellness or welfare or well-being or wellbeing or safety or immuni*) adj5 (program* or interven* or scheme* or initiative* or encourag* or promot* or educat* or literacy or campaign* or improve* or improving)).ti,ab. (463672)

33 ((lifestyle* or diet* or food* or nutrition*) adj3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or target* or alter* or impact*)).ti,ab. (159406)

34 ((behavio?r* or positive* or success*) adj3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or impact*)).ti,ab. (251915)

35 ("best start in life" or "healthy child programme" or "healthy start programme" or "change for children").ti,ab. (543)

36 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((active or physically-active or health*) adj3 (living or life*))).ti,ab. (10533)

37 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 (exercise* or exercising or fitness)).ti,ab. (80371)

38 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (physical* adj2 inactiv*)).ti,ab. (449)

39 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((inactiv* or unhealthy) adj3 (living or life*))).ti,ab. (138)

40 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((weight or body mass or BMI) adj2 (healthy or manage* or control* or loss* or loos* or decreas* or reduc*))).ti,ab. (22088)

41 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (obese or obesity or overweight)).ti,ab. (33832)

42 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((health* or balanced) adj2 (diet* or eating or food or nutrition*))).ti,ab. (9208)

43 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((salt or sugar or calorie*) adj2 (less or lessen or reduc* or restrict*))).ti,ab. (1591)

44 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((fizzy or sugary or sweetened) adj2 (drink or beverage*))).ti,ab. (422)

45 ((breastfeed* or feeding) adj3 (advice or advis* or educat* or support*)).ti,ab. (5385)

46 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (malnutrition or malnourish* or undernourish* or overnutrition)).ti,ab. (3902)

47 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((oral* or dental*) adj2 (health* or care or hygien*))).ti,ab. (10345)

48 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((oral* or dental* or tooth or teeth) adj2 (decay* or disease*))).ti,ab. (1945)

49 ((identif* or detect* or prevent*) adj3 ((domestic* or spousal or child* or caregiver* or care-giver* or parent* or maternal* or paternal* or physical* or emotional*) adj2 (neglect* or abuse* or abusive or violen* or harm or maltreat* or mistreat*))).ti,ab. (2577)

50 or/12-49 (1317434)

51 11 and 50 (370070)

52 Economics/ (27358)

53 exp "Costs and Cost Analysis"/ (248164)

54 Economics, Nursing/ (4005)

55 Economics, Medical/ (9147)

56 Economics, Pharmaceutical/ (3009)

57 exp Economics, Hospital/ (25259)

58 Economics, Dental/ (1919)

59 exp "Fees and Charges"/ (30838)

60 exp Budgets/ (13870)

61 budget*.ti,ab,kf. (31899)

62 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf. (247110)

63 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 (321647)

64 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf. (178877)

65 (value adj2 (money or monetary)).ti,ab,kf. (2636)

66 exp models, economic/ (15742)

67 economic model*.ab,kf. (3633)

68 markov chains/ (15176)

69 markov.ti,ab,kf. (24797)

70 monte carlo method/ (29988)

71 monte carlo.ti,ab,kf. (53152)

72 exp Decision Theory/ (12550)

73 (decision* adj2 (tree* or analy* or model*)).ti,ab,kf. (28075)

74 or/52-73 (788188)

75 (return adj3 investment*).tw. (2469)

76 (SROI or ROI).tw. (11279)

77 or/75-76 (13350)

78 74 or 77 (799559)

79 51 and 78 (23175)

80 exp United Kingdom/ (377664)

81 (national health service* or nhs*).ti,ab,in. (225352)

82 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab. (41374)

83 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jw,in. (2210806)

84 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) 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 not (carolina* or nc)) or ("durham's" not (carolina* or nc)) 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 not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) 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 not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in. (1534733)

85 (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,in. (61019)

86 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in. (226780)

87 (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,in. (28975)

88 or/80-87 (2777779)

89 (exp africa/ or exp americas/ or exp antarctic regions/ or exp arctic regions/ or exp asia/ or exp australia/ or exp oceania/) not (exp United Kingdom/ or europe/) (3062526)

90 88 not 89 (2639366)

91 79 and 90 (2754)

92 exp animals/ not humans/ (4873476)

93 91 not 92 (2741)

94 limit 93 to yr="2000-Current" (2427)

95 remove duplicates from 94 (2408)

Key:

/ = indexing term (Medical Subject Heading: MeSH)

exp = exploded indexing term (MeSH)

? = replaces 0 or 1 character

* = truncation

ti,ab,tw,kf = terms in either title, abstract, textword or keyword heading word fields

jw,in = terms in either journal word or institution fields

adj3 = terms within three words of each other (any order)

Embase <1974 to 2021 August 17>

via Ovid http://ovidsp.ovid.com/

Date range searched: 1974 to 17th August 2021

Date searched: 18th August 2021

Records retrieved: 4120

The Embase strategy below includes the CADTH economics search filter for Ovid Embase (lines 50-68) and the NICE UK search filter for Ovid Embase (lines 74-84).

Economic Evaluations/Cost/Economic Models - Ovid Embase. Strings attached: CADTH database search filters [Internet]. Ottawa: CADTH; 2016. [Accessed: 16 August 2021].

Available from: https://www.cadth.ca/resources/finding-evidence/strings-attached-cadths-database-search-filters#health

Ayiku L, Levay P, Hudson T, Craven J, Finnegan A, Adams R and Barrett E. The Embase UK filter: validation of a geographic search filter to retrieve research about the UK from OVID Embase. Health Information and Libraries Journal, 2019 36 (2): 121-133. (Publisher: Wiley. © 2019 Health Libraries Group)

1 exp pediatrics/ (113669)

2 exp child/ (2769786)

3 exp infant/ (1033796)

4 exp newborn/ (551140)

5 exp low birth weight/ (66137)

6 exp very low birth weight/ (15959)

7 prematurity/ (110110)

8 (p?ediatric* or child* or preemie* or baby or babies or infant* or toddler* or neo nat* or neo-nat* or neonat* or newborn* or new-born* or newly born* or newly-born* or preschool* or pre-school* or schoolchild* or school-child* or schoolboy* or school-boy* or schoolgirl* or school-girl* or school-age* or prekindergarten or pre-kindergarten or kindergarten or boy* or girl* or kid* or LBW or VLBW or ELBW or "low birth weight").ti,ab. (3506590)

9 (under adj (five* or "5") adj2 (age* or old*)).ti,ab. (2821)

10 ("birth to 5" or "birth to five").ti,ab. (1823)

11 or/1-10 (4338575)

12 public health/ (196115)

13 exp health promotion/ (105259)

14 health literacy/ (13958)

15 health education/ (99558)

16 "social determinants of health"/ (11058)

17 child health/ (30025)

18 child development/ (46734)

19 child welfare/ (15505)

20 child abuse/ (31499)

21 exp child nutrition/ (110631)

22 infant welfare/ (1684)

23 exp child parent relation/ (89587)

24 exp early childhood intervention/ (3002)

25 early intervention/ (27619)

26 fitness/ (38503)

27 healthy diet/ (4731)

28 tooth disease/ (32918)

29 ((early or early-years or early-life*) adj3 (program* or interven* or scheme* or initiative*)).ti,ab. (68533)

30 ((health* or wellness or welfare or well-being or wellbeing or safety or immuni*) adj5 (program* or interven* or scheme* or initiative* or encourag* or promot* or educat* or literacy or campaign* or improve* or improving)).ti,ab. (587288)

31 ((lifestyle* or diet* or food* or nutrition*) adj3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or target* or alter* or impact*)).ti,ab. (213174)

32 ((behavio?r* or positive* or success*) adj3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or impact*)).ti,ab. (329737)

33 ("best start in life" or "healthy child programme" or "healthy start programme" or "change for children").ti,ab. (692)

34 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((active or physically-active or health*) adj3 (living or life*))).ti,ab. (14185)

35 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 (exercise* or exercising or fitness)).ti,ab. (106659)

36 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (physical* adj2 inactiv*)).ti,ab. (590)

37 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((inactiv* or unhealthy) adj3 (living or life*))).ti,ab. (173)

38 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((weight or body mass or BMI) adj2 (healthy or manage* or control* or loss* or loos* or decreas* or reduc*))).ti,ab. (33329)

39 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (obese or obesity or overweight)).ti,ab. (48320)

40 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((health* or balanced) adj2 (diet* or eating or food or nutrition*))).ti,ab. (11729)

41 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((salt or sugar or calorie*) adj2 (less or lessen or reduc* or restrict*))).ti,ab. (2069)

42 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((fizzy or sugary or sweetened) adj2 (drink or beverage*))).ti,ab. (511)

43 ((breastfeed* or feeding) adj3 (advice or advis* or educat* or support*)).ti,ab. (6670)

44 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (malnutrition or malnourish* or undernourish* or overnutrition)).ti,ab. (5596)

45 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or

instigat* or invest or benefit* or uptak* or start*) adj4 ((oral* or dental*) adj2 (health* or care or hygien*))).ti,ab. (10903)

46 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((oral* or dental* or tooth or teeth) adj2 (decay* or disease*))).ti,ab. (2094)

47 ((identif* or detect* or prevent*) adj3 ((domestic* or spousal or child* or caregiver* or care-giver* or parent* or maternal* or paternal* or physical* or emotional*) adj2 (neglect* or abuse* or abusive or violen* or harm or maltreat* or mistreat*))).ti,ab. (2992)

48 or/12-47 (1849133)

49 11 and 48 (526075)

50 Economics/ (241804)

51 Cost/ (59613)

52 exp Health Economics/ (895063)

53 Budget/ (30775)

54 budget*.ti,ab,kw. (42271)

55 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kw. (304827)

56 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 (451083)

57 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kw. (251602)

58 (value adj2 (money or monetary)).ti,ab,kw. (3586)

59 Statistical Model/ (166664)

60 economic model*.ab,kw. (5409)

61 Probability/ (120621)

62 markov.ti,ab,kw. (32667)

63 monte carlo method/ (43799)

64 monte carlo.ti,ab,kw. (54829)

65 Decision Theory/ (1782)

66 Decision Tree/ (15443)

67 (decision* adj2 (tree* or analy* or model*)).ti,ab,kw. (39658)

68 or/50-67 (1747244)

69 (return adj3 investment*).tw. (3212)

70 (SROI or ROI).tw. (21379)

71 or/69-70 (24017)

72 68 or 71 (1767789)

73 49 and 72 (47611)

74 exp United Kingdom/ (432881)

75 (national health service* or nhs*).ti,ab,in,ad. (393647)

76 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab. (48979)

77 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland*

or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jx,in,ad. (3363228)

78 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) 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 not (carolina* or nc)) or ("durham's" not (carolina* or nc)) 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 not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) 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 not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in,ad. (2607993)

79 (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,in,ad. (106822)

80 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in,ad. (358831)

81 (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,in,ad. (48980)

82 or/74-81 (4103932)

83 (exp "arctic and antarctic"/ or exp oceanic regions/ or exp western hemisphere/ or exp africa/ or exp asia/) not (exp united kingdom/ or europe/) (3134377)

84 82 not 83 (3884792)

85 73 and 84 (5751)

86 animal/ (1522625)

87 exp animal experiment/ (2728526)

88 nonhuman/ (6628021)

89 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh. (5970209)

90 or/86-89 (9408162)

91 exp human/ (22604851)

92 human experiment/ (551499)

93 91 or 92 (22606761)

94 90 not (90 and 93) (6768070)

95 85 not 94 (5711)

96 limit 95 to yr="2000-Current" (5244)

97 conference.pt. (4926668)

98 96 not 97 (4195)

99 remove duplicates from 98 (4120)

Key:

/ or sh = indexing term (Emtree Subject Heading)

exp = exploded indexing term (Emtree)

? = replaces 0 or 1 character

* = truncation

ti,ab,kw,tw = terms in either title, abstract, keyword or textword fields

jx,in,ad = terms in either journal word, institution, or correspondence address fields

adj3 = terms within three words of each other (any order)

Econlit <1886 to August 05, 2021>

via Ovid http://ovidsp.ovid.com/

Date range searched: 1886 to 5th August 2021

Date searched: 16th August 2021

Records retrieved: 428

The Econlit strategy below includes the NICE UK search filter for Ovid Medline (lines 26-32), which was adapted for use on this database.

Ayiku L, Levay P, Hudson T, Craven J, Barrett E, Finnegan A and Adams R. The MEDLINE UK filter: development and validation of a geographic search filter to retrieve research about the UK from OVID MEDLINE. Health Information and Libraries Journal, 2017 34 (3): 200-216. (Publisher: Wiley. © 2017 Crown copyright. Health Information and Libraries Journal © 2017 Health Libraries Group.)

1 (p?ediatric* or child* or preemie* or baby or babies or infant* or toddler* or neo nat* or neo-nat* or neonat* or newborn* or new-born* or newly born* or newly-born* or preschool* or pre-school* or schoolchild* or school-child* or schoolboy* or school-boy* or schoolgirl* or school-girl* or school-age* or prekindergarten or pre-kindergarten or kindergarten or boy* or girl* or kid* or LBW or VLBW or ELBW or "low birth weight").ti,ab. (35829)

2 (under adj (five* or "5") adj2 (age* or old*)).ti,ab. (19)

3 ("birth to 5" or "birth to five").ti,ab. (5)

4 or/1-3 (35834)

5 ((early or early-years or early-life*) adj3 (program* or interven* or scheme* or initiative*)).ti,ab. (744)

6 ((health* or wellness or welfare or well-being or wellbeing or safety or immuni*) adj5 (program* or interven* or scheme* or initiative* or encourag* or promot* or educat* or literacy or campaign* or improve* or improving)).ti,ab. (21070)

7 ((lifestyle* or diet* or food* or nutrition*) adj3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or target* or alter* or impact*)).ti,ab. (4883)

8 ((behavio?r* or positive* or success*) adj3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or impact*)).ti,ab. (20752)

9 ("best start in life" or "healthy child programme" or "healthy start programme" or "change for children").ti,ab. (10)

10 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((active or physically-active or health*) adj3 (living or life*))).ti,ab. (215)

11 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 (exercise* or exercising or fitness)).ti,ab. (1394)

12 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (physical* adj2 inactiv*)).ti,ab. (0)

13 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((inactiv* or unhealthy) adj3 (living or life*))).ti,ab. (2)

14 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((weight or body mass or BMI) adj2 (healthy or manage* or control* or loss* or loos* or decreas* or reduc*))).ti,ab. (84)

15 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (obese or obesity or overweight)).ti,ab. (299)

16 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((health* or balanced) adj2 (diet* or eating or food or nutrition*))).ti,ab. (318)

17 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((salt or sugar or calorie*) adj2 (less or lessen or reduc* or restrict*))).ti,ab. (11)

18 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((fizzy or sugary or sweetened) adj2 (drink or beverage*))).ti,ab. (12)

19 ((breastfeed* or feeding) adj3 (advice or advis* or educat* or support*)).ti,ab. (30)

20 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (malnutrition or malnourish* or undernourish* or overnutrition)).ti,ab. (132)

21 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((oral* or dental*) adj2 (health* or care or hygien*))).ti,ab. (29)

22 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((oral* or dental* or tooth or teeth) adj2 (decay* or disease*))).ti,ab. (2)

23 ((identif* or detect* or prevent*) adj3 ((domestic* or spousal or child* or caregiver* or care-giver* or parent* or maternal* or paternal* or physical* or emotional*) adj2 (neglect* or abuse* or abusive or violen* or harm or maltreat* or mistreat*))).ti,ab. (16)

24 or/5-23 (47239)

25 4 and 24 (5029)

26 (national health service* or nhs*).ti,ab,kw,in. (962)

27 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jx,in. (61046)

28 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) 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 not (carolina* or nc)) or ("durham's" not (carolina* or nc)) 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 not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) 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 not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in. (108728)

29 (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,in. (4140)

30 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in. (8618)

31 (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,in. (1412)

32 or/27-31 (159238)

33 25 and 32 (457)

34 limit 33 to yr="2000-Current" (428)

35 remove duplicates from 34 (428)

Key:

? = replaces 0 or 1 character

* = truncation

ti,ab = terms in either title or abstract fields

jx,in = terms in either journal word or institution fields

adj3 = terms within three words of each other (any order)

HMIC Health Management Information Consortium <1979 to July 2021>

via Ovid http://ovidsp.ovid.com/

Date range searched: 1979 to July 2021

Date searched: 16th August 2021

Records retrieved: 26

The HMIC strategy below includes the CADTH economics search filter for Ovid Medline (lines 44-60), which was adapted for use on this database.

Economic Evaluations/Cost/Economic Models - Ovid Medline. Strings attached: CADTH database search filters [Internet]. Ottawa: CADTH; 2016. [Accessed: 16 August 2021].

Available from: https://www.cadth.ca/resources/finding-evidence/strings-attached-cadths-database-search-filters#health

1 exp Paediatrics/ (625)

2 exp Pre School Children/ (539)

3 exp Infants/ (1821)

4 Toddlers/ (42)

5 (p?ediatric* or child* or preemie* or baby or babies or infant* or toddler* or neo nat* or neo-nat* or neonat* or newborn* or new-born* or newly born* or newly-born* or preschool* or pre-school* or schoolchild* or school-child* or schoolboy* or school-boy* or schoolgirl* or school-girl* or school-age* or prekindergarten or pre-kindergarten or kindergarten or boy* or girl* or kid* or LBW or VLBW or ELBW or "low birth weight").ti,ab. (37872)

6 (under adj (five* or "5") adj2 (age* or old*)).ti,ab. (61)

7 ("birth to 5" or "birth to five").ti,ab. (33)

8 or/1-7 (38312)

9 Public Health/ (11326)

10 Health Promotion/ (6745)

11 Health Literacy/ (210)

12 Health Education/ (2986)

13 Child Health/ (562)

14 Child Development/ (354)

15 Child Guidance/ (15)

16 Child Welfare/ (220)

17 Child Abuse/ (2148)

18 Infant Care/ (82)

19 exp Family Relations/ (544)

20 Physical Fitness/ (178)

21 Nutrition/ (1885)

22 Oral Health/ (412)

23 ((early or early-years or early-life*) adj3 (program* or interven* or scheme* or initiative*)).ti,ab. (991)

24 ((health* or wellness or welfare or well-being or wellbeing or safety or immuni*) adj5 (program* or interven* or scheme* or initiative* or encourag* or promot* or educat* or literacy or campaign* or improve* or improving)).ti,ab. (30548)

25 ((lifestyle* or diet* or food* or nutrition*) adj3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or target* or alter* or impact*)).ti,ab. (2072)

26 ((behavio?r* or positive* or success*) adj3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or impact*)).ti,ab. (5230)

27 ("best start in life" or "healthy child programme" or "healthy start programme" or "change for children").ti,ab. (124)

28 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((active or physically-active or health*) adj3 (living or life*))).ti,ab. (559)

29 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 (exercise* or exercising or fitness)).ti,ab. (663)

30 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (physical* adj2 inactiv*)).ti,ab. (19)

31 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((inactiv* or unhealthy) adj3 (living or life*))).ti,ab. (7)

32 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((weight or body mass or BMI) adj2 (healthy or manage* or control* or loss* or loos* or decreas* or reduc*))).ti,ab. (243)

33 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (obese or obesity or overweight)).ti,ab. (787)

34 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((health* or balanced) adj2 (diet* or eating or food or nutrition*))).ti,ab. (360)

35 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or

instigat* or invest or benefit* or uptak* or start*) adj4 ((salt or sugar or calorie*) adj2 (less or lessen or reduc* or restrict*))).ti,ab. (16)

36 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((fizzy or sugary or sweetened) adj2 (drink or beverage*))).ti,ab. (13)

37 ((breastfeed* or feeding) adj3 (advice or advis* or educat* or support*)).ti,ab. (181)

38 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 (malnutrition or malnourish* or undernourish* or overnutrition)).ti,ab. (33)

39 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) adj4 ((oral* or dental*) adj2 (health* or care or hygien*))).ti,ab. (310)

40 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) adj4 ((oral* or dental* or tooth or teeth) adj2 (decay* or disease*))).ti,ab. (38)

41 ((identif* or detect* or prevent*) adj3 ((domestic* or spousal or child* or caregiver* or care-giver* or parent* or maternal* or paternal* or physical* or emotional*) adj2 (neglect* or abuse* or abusive or violen* or harm or maltreat* or mistreat*))).ti,ab. (209)

42 or/9-41 (53443)

43 8 and 42 (9507)

44 Economics/ (600)

45 exp "Cost Analysis"/ (340)

46 exp Health Economics/ (3701)

47 exp "Cost Effectiveness"/ (5694)

48 exp Economic Evaluation/ (1451)

49 budget*.ti,ab. (4839)

50 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,ab. (48287)

51 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab. (7533)

52 (value adj2 (money or monetary)).ti,ab. (1189)

53 exp Economic Models/ (169)

54 economic model*.ab. (253)

55 markov.ti,ab. (251)

56 Monte Carlo Methods/ (5)

57 monte carlo.ti,ab. (118)

58 exp Decision Theory/ (18)

59 (decision* adj2 (tree* or analy* or model*)).ti,ab. (640)

60 or/44-59 (54793)

61 (return adj3 investment*).ti,ab. (149)

62 (SROI or ROI).ti,ab. (36)

63 or/61-62 (169)

64 60 or 63 (54847)

65 43 and 64 (1188)

66 limit 65 to yr="2000-Current" (26)

67 remove duplicates from 66 (26)

Key:

/ = indexing term (Subject Heading)

exp = exploded indexing term (Emtree)

? = replaces 0 or 1 character

* = truncation

ti,ab = terms in either title or abstract fields

adj3 = terms within three words of each other (any order)

Cochrane Central Register of Controlled Trials (CENTRAL)

via Wiley http://onlinelibrary.wiley.com/

Date range searched: Issue 8 of 12, August 2021

Date searched: 23rd August 2021

Records retrieved: 4029

The CENTRAL strategy below includes part of the CADTH economics search filter for Ovid Medline (lines 52-73) and part of the NICE UK search filter for Ovid Medline (lines 81-82), both of which were adapted for use on this database.

Economic Evaluations/Cost/Economic Models - Ovid Medline. Strings attached: CADTH database search filters [Internet]. Ottawa: CADTH; 2016. [Accessed: 16 August 2021].

Available from: https://www.cadth.ca/resources/finding-evidence/strings-attached-cadths-database-search-filters#health

Ayiku L, Levay P, Hudson T, Craven J, Barrett E, Finnegan A and Adams R. The MEDLINE UK filter: development and validation of a geographic search filter to retrieve research about the UK from OVID MEDLINE. Health Information and Libraries Journal, 2017 34 (3): 200-216. (Publisher: Wiley. © 2017 Crown copyright. Health Information and Libraries Journal © 2017 Health Libraries Group.)

#1 [mh Pediatrics] 706

#2 [mh Child] 58154

#3 [mh Infant] 33195

#4 [mh "Infant, Newborn"] 16573

#5 [mh "Infant, Low Birth Weight"] 2250

#6 [mh "Infant, Very Low Birth Weight"] 990

#7 [mh "Infant, Premature"] 3943

#8 (p*diatric* or child* or preemie* or baby or babies or infant* or toddler* or neo NEXT nat* or neonat* or newborn* or new NEXT born* or newly NEXT born* or preschool* or pre NEXT school* or schoolchild* or school NEXT child* or schoolboy* or school NEXT boy* or schoolgirl* or school NEXT girl* or school NEXT age* or prekindergarten or pre NEXT kindergarten or kindergarten or boy* or girl* or kid* or LBW or VLBW or ELBW or "low birth weight"):ti,ab 223044

#9 (under NEAR (five* or "5") NEAR/2 (age* or old*)):ti,ab 509

#10 ("birth to 5" or "birth to five"):ti,ab 32

#11 (Edwards and McIntosh-#10) 239541

#12 [mh ^"Public Health"] 260

#13 [mh ^"Health Promotion"] 6089

#14 [mh ^"Health Literacy"] 399

#15 [mh ^"Health Education"] 4049

#16 [mh ^"Social Determinants of Health"] 23

#17 [mh ^"Child Health"] 129

#18 [mh ^"Child Development"] 1985

#19 [mh ^"Child Guidance"] 10

#20 [mh ^"Child Welfare"] 333

#21 [mh ^"Child Abuse"] 370

#22 [mh ^"Child Nutrition Disorders"] 240

#23 [mh ^"Infant Health"] 56

#24 [mh ^"Infant Welfare"] 83

#25 [mh "Family Relations"] 3282

#26 [mh ^"Early Intervention, Educational"] 516

#27 [mh ^"Early Medical Intervention"] 414

#28 [mh "Physical Fitness"] 3503

#29 [mh ^"Diet, Healthy"] 543

#30 [mh ^"Oral Health"] 451

#31 ((early or early NEXT years or early NEXT life*) NEAR/3 (program* or interven* or scheme* or initiative*)):ti,ab 7685

#32 ((health* or wellness or welfare or well NEXT being or wellbeing or safety or immuni*) NEAR/5 (program* or interven* or scheme* or initiative* or encourag* or promot* or educat* or literacy or campaign* or improve* or improving)):ti,ab 70290

#33 ((lifestyle* or diet* or food* or nutrition*) NEAR/3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or target* or alter* or impact*)):ti,ab 37420

#34 ((behavi*r* or positive* or success*) NEAR/3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or impact*)):ti,ab 49659

#35 ("best start in life" or "healthy child programme" or "healthy start programme" or "change for children"):ti,ab 30

#36 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((active or physically NEXT active or health*) NEAR/3 (living or life*))):ti,ab 4358

#37 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 (exercise* or exercising or fitness)):ti,ab 28608

#38 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 (physical* NEAR/2 inactiv*)):ti,ab 79

#39 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 ((inactiv* or unhealthy) NEAR/3 (living or life*))):ti,ab 13

#40 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((weight or body NEXT mass or BMI) NEAR/2 (healthy or manage* or control* or loss* or loos* or decreas* or reduc*))):ti,ab 6561

#41 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 (obese or obesity or overweight)):ti,ab 5356

#42 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((health* or balanced) NEAR/2 (diet* or eating or food or nutrition*))):ti,ab 1974

#43 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((salt or sugar or calorie*) NEAR/2 (less or lessen or reduc* or restrict*))):ti,ab 362

#44 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 ((fizzy or sugary or sweetened) NEAR/2 (drink or beverage*))):ti,ab 160

#45 ((breastfeed* or feeding) NEAR/3 (advice or advis* or educat* or support*)):ti,ab 947

#46 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 (malnutrition or malnourish* or undernourish* or overnutrition)):ti,ab 473

#47 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((oral* or dental*) NEAR/2 (health* or care or hygien*))):ti,ab 1515

#48 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 ((oral* or dental* or tooth or teeth) NEAR/2 (decay* or disease*))):ti,ab 215

#49 ((identif* or detect* or prevent*) NEAR/3 ((domestic* or spousal or child* or caregiver* or care NEXT giver* or parent* or maternal* or paternal* or physical* or emotional*) NEAR/2 (neglect* or abuse* or abusive or violen* or harm or maltreat* or mistreat*))):ti,ab 261

#50 (Drummond et al.-#49) 179460

#51 (#11 and #50) 38754

#52 [mh ^Economics] 41

#53 [mh "Costs and Cost Analysis"] 10920

#54 [mh ^"Economics, Nursing"] 12

#55 [mh ^"Economics, Medical"] 26

#56 [mh ^"Economics, Pharmaceutical"] 65

#57 [mh "Economics, Hospital"] 728

#58 [mh ^"Economics, Dental"] 2

#59 [mh "Fees and Charges"] 258

#60 [mh Budgets] 28

#61 (budget*):ti,ab,kw 1217

#62 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or expenditure? or expense? or financial or finance?):ti,ab,kw 97296

#63 (cost* NEAR/2 (effective* or utilit* or benefit* or minimi* or analy* or outcome?)):ab,kw 35189

#64 (value NEAR/2 (money or monetary)):ti,ab,kw 336

#65 [mh "Models, Economic"] 362

#66 (economic NEXT model*):ab,kw 329

#67 [mh ^"Markov Chains"] 278

#68 (markov):ti,ab,kw 1469

#69 [mh ^"Monte Carlo Method"] 192

#70 (monte carlo):ti,ab,kw 916

#71 [mh "Decision Theory"] 168

#72 (decision* NEAR/2 (tree* or analy* or model*)):ti,ab,kw 2398

#73 {OR #52-#72} 99711

#74 (return NEAR/3 investment*):ti,ab 156

#75 (SROI or ROI):ti,ab 691

#76 {OR #74-#75} 815

#77 (#73 or #76) 100355

#78 (#51 and #77) 5402

#79 (rat or rats or rodent* or mouse or mice or "mus musculus" or "mus domesticus" or murine or murinae or bovine or sheep or ovine or "ovis aries" or porcine):ti,ab,kw 14911

#80 #78 not #79 5361

#81 [mh Africa] 7534

#82 [mh Americas] 26750

#83 [mh "Antarctic Regions"] 12

#84 [mh "Arctic Regions"] 7

#85 [mh Asia] 21466

#86 [mh Australia] 4512

#87 [mh Oceania] 5181

#88 (Grosse et al.-#87) 59504

#89 [mh "United Kingdom"] 6598

#90 [mh ^Europe] 2478

#91 {OR #89-#90} 9062

#92 #88 not #91 58222

#93 #80 not #92 with Publication Year from 2000 to 2021, in Trials 4029

Key:

mh = indexing term, exploded (MeSH)

mh ^ = indexing term, unexploded (MeSH)

* = truncation

? = 1 additional character

ti,ab,kw = terms in either title or abstract or keyword fields

near/3 = terms within three words of each other (any order)

next = terms are next to each other

Cochrane Database of Systematic Reviews (CDSR)

via Wiley http://onlinelibrary.wiley.com/

Date range searched: Issue 8 of 12, August 2021

Date searched: 16th August 2021

Records retrieved: 241

The CDSR strategy below includes part of the CADTH economics search filter for Ovid Medline (lines 52-73) and part of the NICE UK search filter for Ovid Medline (lines 81-82), both of which were adapted by the Information Specialist for use on this database.

Economic Evaluations/Cost/Economic Models - Ovid Medline. Strings attached: CADTH database search filters [Internet]. Ottawa: CADTH; 2016. [Accessed: 16 August 2021].

Available from: https://www.cadth.ca/resources/finding-evidence/strings-attached-cadths-database-search-filters#health

Ayiku L, Levay P, Hudson T, Craven J, Barrett E, Finnegan A and Adams R. The MEDLINE UK filter: development and validation of a geographic search filter to retrieve research about the UK from OVID MEDLINE. Health Information and Libraries Journal, 2017 34 (3): 200-216. (Publisher: Wiley. © 2017 Crown copyright. Health Information and Libraries Journal © 2017 Health Libraries Group.)

#1 [mh Pediatrics] 706

#2 [mh Child] 58154

#3 [mh Infant] 33195

#4 [mh "Infant, Newborn"] 16573

#5 [mh "Infant, Low Birth Weight"] 2250

#6 [mh "Infant, Very Low Birth Weight"] 990

#7 [mh "Infant, Premature"] 3943

#8 (p*diatric* or child* or preemie* or baby or babies or infant* or toddler* or neo NEXT nat* or neonat* or newborn* or new NEXT born* or newly NEXT born* or preschool* or pre NEXT school* or schoolchild* or school NEXT child* or schoolboy* or school NEXT boy* or schoolgirl* or school NEXT girl* or school NEXT age* or prekindergarten or pre NEXT kindergarten or kindergarten or boy* or girl* or kid* or LBW or VLBW or ELBW or "low birth weight"):ti,ab 223044

#9 (under NEAR (five* or "5") NEAR/2 (age* or old*)):ti,ab 509

#10 ("birth to 5" or "birth to five"):ti,ab 32

#11 (Edwards and McIntosh-#10) 239541

#12 [mh ^"Public Health"] 260

#13 [mh ^"Health Promotion"] 6089

#14 [mh ^"Health Literacy"] 399

#15 [mh ^"Health Education"] 4049

#16 [mh ^"Social Determinants of Health"] 23

#17 [mh ^"Child Health"] 129

#18 [mh ^"Child Development"] 1985

#19 [mh ^"Child Guidance"] 10

#20 [mh ^"Child Welfare"] 333

#21 [mh ^"Child Abuse"] 370

#22 [mh ^"Child Nutrition Disorders"] 240

#23 [mh ^"Infant Health"] 56

#24 [mh ^"Infant Welfare"] 83

#25 [mh "Family Relations"] 3282

#26 [mh ^"Early Intervention, Educational"] 516

#27 [mh ^"Early Medical Intervention"] 414

#28 [mh "Physical Fitness"] 3503

#29 [mh ^"Diet, Healthy"] 543

#30 [mh ^"Oral Health"] 451

#31 ((early or early NEXT years or early NEXT life*) NEAR/3 (program* or interven* or scheme* or initiative*)):ti,ab 7685

#32 ((health* or wellness or welfare or well NEXT being or wellbeing or safety or immuni*) NEAR/5 (program* or interven* or scheme* or initiative* or encourag* or promot* or educat* or literacy or campaign* or improve* or improving)):ti,ab 70290

#33 ((lifestyle* or diet* or food* or nutrition*) NEAR/3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or target* or alter* or impact*)):ti,ab 37420

#34 ((behavi*r* or positive* or success*) NEAR/3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or impact*)):ti,ab 49659

#35 ("best start in life" or "healthy child programme" or "healthy start programme" or "change for children"):ti,ab 30

#36 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((active or physically NEXT active or health*) NEAR/3 (living or life*))):ti,ab 4358

#37 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 (exercise* or exercising or fitness)):ti,ab 28608

#38 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 (physical* NEAR/2 inactiv*)):ti,ab 79

#39 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 ((inactiv* or unhealthy) NEAR/3 (living or life*))):ti,ab 13

#40 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or

convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((weight or body NEXT mass or BMI) NEAR/2 (healthy or manage* or control* or loss* or loos* or decreas* or reduc*))):ti,ab 6561

#41 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 (obese or obesity or overweight)):ti,ab 5356

#42 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((health* or balanced) NEAR/2 (diet* or eating or food or nutrition*))):ti,ab 1974

#43 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((salt or sugar or calorie*) NEAR/2 (less or lessen or reduc* or restrict*))):ti,ab 362

#44 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 ((fizzy or sugary or sweetened) NEAR/2 (drink or beverage*))):ti,ab 160

#45 ((breastfeed* or feeding) NEAR/3 (advice or advis* or educat* or support*)):ti,ab 947

#46 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 (malnutrition or malnourish* or undernourish* or overnutrition)):ti,ab 473

#47 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((oral* or dental*) NEAR/2 (health* or care or hygien*))):ti,ab 1515

#48 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR/4 ((oral* or dental* or tooth or teeth) NEAR/2 (decay* or disease*))):ti,ab 215

#49 ((identif* or detect* or prevent*) NEAR/3 ((domestic* or spousal or child* or caregiver* or care NEXT giver* or parent* or maternal* or paternal* or physical* or emotional*) NEAR/2 (neglect* or abuse* or abusive or violen* or harm or maltreat* or mistreat*))):ti,ab 261

#50 (Drummond et al.-#49) 179460

#51 (#11 and #50) 38754

#52 [mh ^Economics] 41

#53 [mh "Costs and Cost Analysis"] 10920

#54 [mh ^"Economics, Nursing"] 12

#55 [mh ^"Economics, Medical"] 26

#56 [mh ^"Economics, Pharmaceutical"] 65

#57 [mh "Economics, Hospital"] 728

#58 [mh ^"Economics, Dental"] 2

#59 [mh "Fees and Charges"] 258

#60 [mh Budgets] 28

#61 (budget*):ti,ab,kw 1217

#62 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or expenditure? or expense? or financial or finance?):ti,ab,kw 97296

#63 (cost* NEAR/2 (effective* or utilit* or benefit* or minimi* or analy* or outcome?)):ab,kw 35189

#64 (value NEAR/2 (money or monetary)):ti,ab,kw 336

#65 [mh "Models, Economic"] 362

#66 (economic NEXT model*):ab,kw 329

#67 [mh ^"Markov Chains"] 278

#68 (markov):ti,ab,kw 1469

#69 [mh ^"Monte Carlo Method"] 192

#70 (monte carlo):ti,ab,kw 916

#71 [mh "Decision Theory"] 168

#72 (decision* NEAR/2 (tree* or analy* or model*)):ti,ab,kw 2398

#73 {OR #52-#72} 99711

#74 (return NEAR/3 investment*):ti,ab 156

#75 (SROI or ROI):ti,ab 691

#76 {OR #74-#75} 815

#77 (#73 or #76) 100355

#78 (#51 and #77) 5402

#79 (rat or rats or rodent* or mouse or mice or "mus musculus" or "mus domesticus" or murine or murinae or bovine or sheep or ovine or "ovis aries" or porcine):ti,ab,kw 14911

#80 #78 not #79 5361

#81 [mh Africa] 7534

#82 [mh Americas] 26750

#83 [mh "Antarctic Regions"] 12

#84 [mh "Arctic Regions"] 7

#85 [mh Asia] 21466

#86 [mh Australia] 4512

#87 [mh Oceania] 5181

#88 (Grosse et al.-#87) 59504

#89 [mh "United Kingdom"] 6598

#90 [mh ^Europe] 2478

#91 {OR #89-#90} 9062

#92 #88 not #91 58222

#93 #80 not #92 with Cochrane Library publication date Between Jan 2000 and Aug 2021, in Cochrane Reviews 241

Key:

mh = indexing term, exploded (MeSH)

mh ^ = indexing term, unexploded (MeSH)

* = truncation

? = 1 additional character

ti,ab,kw = terms in either title or abstract or keyword fields

near/3 = terms within three words of each other (any order)

next = terms are next to each other

NHS EED

via https://www.crd.york.ac.uk/CRDWeb/

Date range searched: Inception to 31st March 2015.

Date searched: 16th August 2021

Records retrieved: 811

1 MeSH DESCRIPTOR Pediatrics 112

2 MeSH DESCRIPTOR Child EXPLODE ALL TREES IN NHSEED 1680

3 MeSH DESCRIPTOR Infant EXPLODE ALL TREES IN NHSEED 1251

4 MeSH DESCRIPTOR Infant, Newborn EXPLODE ALL TREES IN NHSEED 685

5 MeSH DESCRIPTOR Infant, Low Birth Weight EXPLODE ALL TREES IN NHSEED 53

6 MeSH DESCRIPTOR Infant, Very Low Birth Weight EXPLODE ALL TREES IN NHSEED 22

7 MeSH DESCRIPTOR Infant, Premature EXPLODE ALL TREES IN NHSEED 64

8 (pediatric* or paediatric* or child* or preemie* or baby or babies or infant* or toddler* or neo nat* or neo-nat* or neonat* or newborn* or new-born* or newly born* or newly-born* or preschool* or pre-school* or schoolchild* or school-child* or schoolboy* or school-boy* or schoolgirl* or school-girl* or school-age* or prekindergarten or pre-

kindergarten or kindergarten or boy* or girl* or kid* or LBW or VLBW or ELBW) IN NHSEED 3467

9 (under NEAR (five* or 5) NEAR2 (age* or old*)) IN NHSEED 29

10 (birth NEAR (5 or five)) IN NHSEED 33

11 (low NEAR (birth weight or birthweight)) IN NHSEED 74

12 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 3544

13 MeSH DESCRIPTOR Public Health IN NHSEED 68

14 MeSH DESCRIPTOR Health Promotion IN NHSEED 226

15 MeSH DESCRIPTOR Health Literacy IN NHSEED 1

16 MeSH DESCRIPTOR Health Education IN NHSEED 84

17 MeSH DESCRIPTOR Social Determinants of Health IN NHSEED 0

18 MeSH DESCRIPTOR Child Health IN NHSEED 0

19 MeSH DESCRIPTOR Child Development IN NHSEED 9

20 MeSH DESCRIPTOR Child Guidance IN NHSEED 0

21 MeSH DESCRIPTOR Child Welfare IN NHSEED 20

22 MeSH DESCRIPTOR Child Abuse IN NHSEED 7

23 MeSH DESCRIPTOR Child Nutrition Disorders IN NHSEED 5

24 MeSH DESCRIPTOR Infant Health IN NHSEED 0

25 MeSH DESCRIPTOR Infant Welfare IN NHSEED 5

26 MeSH DESCRIPTOR Family Relations EXPLODE ALL TREES IN NHSEED 21

27 MeSH DESCRIPTOR Early Intervention, Educational IN NHSEED 0

28 MeSH DESCRIPTOR Early Medical Intervention IN NHSEED 18

29 MeSH DESCRIPTOR Physical Fitness EXPLODE ALL TREES IN NHSEED 16

30 MeSH DESCRIPTOR Diet, Healthy IN NHSEED 0

31 MeSH DESCRIPTOR Oral Health IN NHSEED 10

32 ((early or early-years or early-life*) NEAR3 (program* or interven* or scheme* or initiative*)) IN NHSEED 113

33 ((health* or wellness or welfare or well-being or wellbeing or safety or immuni*) NEAR5 (program* or interven* or scheme* or initiative* or encourag* or promot* or educat* or literacy or campaign* or improve* or improving)) IN NHSEED 2662

34 ((lifestyle* or diet* or food* or nutrition*) NEAR3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or target* or alter* or impact*)) IN NHSEED 177

35 ((behavior* or behaviour* or positive* or success*) NEAR3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or impact*)) IN NHSEED 297

36 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 ((active or physically-active or health*) NEAR3 (living or life*))) IN NHSEED 62

37 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 (exercise* or exercising or fitness)) IN NHSEED 165

38 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 (physical* NEAR2 inactiv*)) IN NHSEED 0

39 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 ((inactiv* or unhealthy) NEAR3 (living or life*))) IN NHSEED 0

40 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 ((weight or body mass or BMI) NEAR2 (healthy or manage* or control* or loss* or loos* or decreas* or reduc*))) IN NHSEED 11

41 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 (obese or obesity or overweight)) IN NHSEED 44

42 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 ((health* or balanced) NEAR2 (diet* or eating or food or nutrition*))) IN NHSEED 4

43 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 ((salt or sugar or calorie*) NEAR2 (less or lessen or reduc* or restrict*))) IN NHSEED 0

44 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 ((fizzy or sugary or sweetened) NEAR2 (drink or beverage*))) IN NHSEED 0

45 ((breastfeed* or feeding) NEAR3 (advice or advis* or educat* or support*)) IN NHSEED 4

46 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 (malnutrition or malnourish* or undernourish* or overnutrition)) IN NHSEED3

47 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 ((oral* or dental*) NEAR2 (health* or care or hygien*))) IN NHSEED 21

48 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 ((oral* or dental* or tooth or teeth) NEAR2 (decay* or disease*))) IN NHSEED 3

49 ((identif* or detect* or prevent*) NEAR3 ((domestic* or spousal or child* or caregiver* or care-giver* or parent* or maternal* or paternal* or physical* or emotional*) NEAR2 (neglect* or abuse* or abusive or violen* or harm or maltreat* or mistreat*))) IN NHSEED 2

50 #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 3259

51 #12 AND #50 927

52 * IN NHSEED FROM 2000 TO 2015 14762

53 #51 AND #52 811

Key:

MeSH DESCRIPTOR = indexing term: Medical Subject Heading (MeSH)

EXPLODE ALL TREES = exploded indexing term (MeSH)

* = truncation

NEAR3 = terms within three words of each other (only in the order specified).

HTA

via https://www.crd.york.ac.uk/CRDWeb/

Date range searched: Inception to March 2018

Date searched: 16th August 2021

Records retrieved: 447

1 MeSH DESCRIPTOR Pediatrics 112

2 MeSH DESCRIPTOR Child EXPLODE ALL TREES IN HTA 572

3 MeSH DESCRIPTOR Infant EXPLODE ALL TREES IN HTA 317

4 MeSH DESCRIPTOR Infant, Newborn EXPLODE ALL TREES IN HTA 205

5 MeSH DESCRIPTOR Infant, Low Birth Weight EXPLODE ALL TREES IN HTA 8

6 MeSH DESCRIPTOR Infant, Very Low Birth Weight EXPLODE ALL TREES IN HTA 4

7 MeSH DESCRIPTOR Infant, Premature EXPLODE ALL TREES IN HTA 25

8 (pediatric* or paediatric* or child* or preemie* or baby or babies or infant* or toddler* or neo nat* or neo-nat* or neonat* or newborn* or new-born* or newly born* or newly-born* or preschool* or pre-school* or schoolchild* or school-child* or schoolboy* or school-boy* or schoolgirl* or school-girl* or school-age* or prekindergarten or pre-

kindergarten or kindergarten or boy* or girl* or kid* or LBW or VLBW or ELBW) IN HTA 1931

9 (under NEAR (five* or 5) NEAR2 (age* or old*)) IN HTA 4

10 (birth NEAR (5 or five)) IN HTA 1

11 (low NEAR (birth weight or birthweight)) IN HTA 18

12 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 2023

13 MeSH DESCRIPTOR Public Health IN HTA 38

14 MeSH DESCRIPTOR Health Promotion IN HTA 70

15 MeSH DESCRIPTOR Health Literacy IN HTA 6

16 MeSH DESCRIPTOR Health Education IN HTA 30

17 MeSH DESCRIPTOR Social Determinants of Health IN HTA 0

18 MeSH DESCRIPTOR Child Health IN HTA 2

19 MeSH DESCRIPTOR Child Development IN HTA 9

20 MeSH DESCRIPTOR Child Guidance IN HTA 1

21 MeSH DESCRIPTOR Child Welfare IN HTA 8

22 MeSH DESCRIPTOR Child Abuse IN HTA 11

23 MeSH DESCRIPTOR Child Nutrition Disorders IN HTA 1

24 MeSH DESCRIPTOR Infant Health IN HTA 0

25 MeSH DESCRIPTOR Infant Welfare IN HTA 5

26 MeSH DESCRIPTOR Family Relations EXPLODE ALL TREES IN HTA 20

27 MeSH DESCRIPTOR Early Intervention, Educational IN HTA 0

28 MeSH DESCRIPTOR Early Medical Intervention IN HTA 1

29 MeSH DESCRIPTOR Physical Fitness EXPLODE ALL TREES IN HTA 9

30 MeSH DESCRIPTOR Diet, Healthy IN HTA 0

31 MeSH DESCRIPTOR Oral Health IN HTA 7

32 ((early or early-years or early-life*) NEAR3 (program* or interven* or scheme* or initiative*)) IN HTA 42

33 ((health* or wellness or welfare or well-being or wellbeing or safety or immuni*) NEAR5 (program* or interven* or scheme* or initiative* or encourag* or promot* or educat* or literacy or campaign* or improve* or improving)) IN HTA 2721

34 ((lifestyle* or diet* or food* or nutrition*) NEAR3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or target* or alter* or impact*)) IN HTA 104

35 ((behavior* or behaviour* or positive* or success*) NEAR3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or impact*)) IN HTA 231

36 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 ((active or physically-active or health*) NEAR3 (living or life*))) IN HTA 29

37 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 (exercise* or exercising or fitness)) IN HTA51

38 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 (physical* NEAR2 inactiv*)) IN HTA 0

39 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 ((inactiv* or unhealthy) NEAR3 (living or life*))) IN HTA 0

40 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 ((weight or body mass or BMI) NEAR2 (healthy or manage* or control* or loss* or loos* or decreas* or reduc*))) IN HTA 23

41 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 (obese or obesity or overweight)) IN HTA 36

42 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 ((health* or balanced) NEAR2 (diet* or eating or food or nutrition*))) IN HTA 9

43 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 ((salt or sugar or calorie*) NEAR2 (less or lessen or reduc* or restrict*))) IN HTA 0

44 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 ((fizzy or sugary or sweetened) NEAR2 (drink or beverage*))) IN HTA 0

45 ((breastfeed* or feeding) NEAR3 (advice or advis* or educat* or support*)) IN HTA 5

46 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 (malnutrition or malnourish* or undernourish* or overnutrition)) IN HTA 1

47 ((increas* or improv* or encourag* or support* or promot* or influen* or recommend* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR4 ((oral* or dental*) NEAR2 (health* or care or hygien*))) IN HTA 8

48 ((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or deter* or prevent* or avert* or divert) NEAR4 ((oral* or dental* or tooth or teeth) NEAR2 (decay* or disease*))) IN HTA 5

49 ((identif* or detect* or prevent*) NEAR3 ((domestic* or spousal or child* or caregiver* or care-giver* or parent* or maternal* or paternal* or physical* or emotional*) NEAR2 (neglect* or abuse* or abusive or violen* or harm or maltreat* or mistreat*))) IN HTA 3

50 #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 3042

51 #12 AND #50 583

52 * IN HTA FROM 2000 TO 2018 14815

53 #51 AND #52 447

Key:

MeSH DESCRIPTOR = indexing term: Medical Subject Heading (MeSH)

EXPLODE ALL TREES = exploded indexing term (MeSH)

* = truncation

NEAR3 = terms within three words of each other (only in the order specified).

Science Citation Index Expanded

via Web of Science, Clarivate Analytics https://clarivate.com/

Date range searched: 1900 – 16th August 2021

Date searched: 16th August 2021

Records retrieved: 4369

The SCIE strategy below includes the CADTH economics search filter for Ovid Medline (lines 26-33) and the NICE UK search filter for Ovid Medline (lines 38-52), both of which were adapted for use on this database.

Economic Evaluations/Cost/Economic Models - Ovid Medline. Strings attached: CADTH database search filters [Internet]. Ottawa: CADTH; 2016. [Accessed: 16 August 2021]. Available from: https://www.cadth.ca/resources/finding-evidence/strings-attached-cadths-database-search-filters#health

Ayiku L, Levay P, Hudson T, Craven J, Barrett E, Finnegan A and Adams R. The MEDLINE UK filter: development and validation of a geographic search filter to retrieve research about the UK from OVID MEDLINE. Health Information and Libraries Journal, 2017 34 (3): 200-216. (Publisher: Wiley. © 2017 Crown copyright. Health Information and Libraries Journal © 2017 Health Libraries Group.)

55 4,369

#53 NOT #54

Indexes=SCI-EXPANDED Timespan=2000-2021

54 2,806,814

TS=(rat or rats or rodent* or mouse or mice or "mus musculus" or "mus domesticus" or murine or murinae or porcine or sheep or ovine or "ovis aries" or lamb or lambs or ewe or ewes or pig or pigs or piglet or piglets or sow or sows or minipig or minipigs or monkey or monkeys or bovine or cattle or heifer or heifers or chicken or chickens or l ivestock or alpaca* or llama*) Indexes=SCI-EXPANDED Timespan=2000-2021

53 4,450

#37 AND #52

Indexes=SCI-EXPANDED Timespan=2000-2021

52 3,683,748

#38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51

Indexes=SCI-EXPANDED Timespan=2000-2021

51 27,656

AB=(english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) NEAR/5 english))

Indexes=SCI-EXPANDED Timespan=2000-2021

50 38,053

OO=(armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londond erry or "londonderry's" or derry or "derry's" or newry or "newry's")

Indexes=SCI-EXPANDED Timespan=2000-2021

49 49,445

CI=(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")

Indexes=SCI-EXPANDED Timespan=2000-2021

48 227,450

OO=(aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's")

Indexes=SCI-EXPANDED Timespan=2000-2021

47 378,162

CI=(aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's")

Indexes=SCI-EXPANDED Timespan=2000-2021

46 78,169

OO=(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")

Indexes=SCI-EXPANDED Timespan=2000-2021

45 110,138

CI=(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")

Indexes=SCI-EXPANDED Timespan=2000-2021

44 1,610,636

OO=(bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) 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 not (carolina* or nc)) or ("durham's" not (carolina* or nc)) 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 not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not ("new south wales*" or nsw)) or ("liverpool's" not ("new south wales*" or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not ("new south wales*" or nsw)) or ("newcastle's" not ("new south wales*" or nsw)) 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 not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*)))))

Indexes=SCI-EXPANDED Timespan=2000-2021

43 2,625,234

CI=(bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) 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 not (carolina* or nc)) or ("durham's" not (carolina* or nc)) 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 not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not ("new south wales*" or nsw)) or ("liverpool's" not ("new south wales*" or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not ("new south wales*" or nsw)) or ("newcastle's" not ("new south wales*" or nsw)) 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 not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*)))))

Indexes=SCI-EXPANDED Timespan=2000-2021

42 233,425

SO=(gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or "united kingdom*" or (england* not "new england") or "northern ireland*" or "northern irish*" or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*)

Indexes=SCI-EXPANDED Timespan=2000-2021

41 2,587,707

CU=(gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or "united kingdom*" or (england* not "new england") or "northern ireland*" or "northern irish*" or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*)

Indexes=SCI-EXPANDED Timespan=2000-2021

40 328,127

TS=(gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or "united kingdom*" or (england* not "new england") or "northern ireland*" or "northern irish*" or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*)

Indexes=SCI-EXPANDED Timespan=2000-2021

39 190,502

OO=("national health service*" or nhs*)

Indexes=SCI-EXPANDED Timespan=2000-2021

38 29,379

TS=("national health service*" or nhs*)

Indexes=SCI-EXPANDED Timespan=2000-2021

37 19,304

#25 AND #36

Indexes=SCI-EXPANDED Timespan=2000-2021

36 1,847,560

#26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35

Indexes=SCI-EXPANDED Timespan=2000-2021

35 12,023

TS=(SROI or ROI)

Indexes=SCI-EXPANDED Timespan=2000-2021

34 5,514

TS=(return NEAR/3 investment*)

Indexes=SCI-EXPANDED Timespan=2000-2021

33 59,385

TS=(decision* NEAR/2 (tree* or analy* or model*))

Indexes=SCI-EXPANDED Timespan=2000-2021

32 195,759

TS=("monte carlo")

Indexes=SCI-EXPANDED Timespan=2000-2021

31 83,964

TS=(markov)

Indexes=SCI-EXPANDED Timespan=2000-2021

30 7,568

TS=("economic model*")

Indexes=SCI-EXPANDED Timespan=2000-2021

29 3,653

TS=(value NEAR/2 (money or monetary))

Indexes=SCI-EXPANDED Timespan=2000-2021

28 295,528

TS=(cost* NEAR/2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes))

Indexes=SCI-EXPANDED Timespan=2000-2021

27 1,459,439

AB=(economic* or cost or costs or costly or costing or price or prices or pricing or ph armacoeconomic* or pharmaco-
economic* or expenditure or expenditures or expense or expenses or financial or fina nce or finances or financed)

Indexes=SCI-EXPANDED Timespan=2000-2021

26 77,051

TS=(budget*)

Indexes=SCI-EXPANDED Timespan=2000-2021

25 153,267

#4 AND #24

Indexes=SCI-EXPANDED Timespan=2000-2021

24 953,605

#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 O R #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23

Indexes=SCI-EXPANDED Timespan=2000-2021

23 1,267

TS=((identif* or detect* or prevent*) NEAR/3 ((domestic* or spousal or child* or caregiver* or care-giver* or parent* or maternal* or paternal* or physical* or emotional*) NEAR/2 (neglect* or abuse* or abusive or violen* or harm or maltreat* or mistreat*)))

Indexes=SCI-EXPANDED Timespan=2000-2021

22 1,220

TS=((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or det er* or prevent* or avert* or divert) NEAR/4 ((oral* or dental* or tooth or teeth) NEAR/2 (decay* or disease*)))

Indexes=SCI-EXPANDED Timespan=2000-2021

21 6,329

TS=((increas* or improv* or encourag* or support* or promot* or influen* or recomme nd* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((oral* or dental*) NEAR/2 (health* or care or hygien*)))

Indexes=SCI-EXPANDED Timespan=2000-2021

20 3,053

TS=((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or det er* or prevent* or avert* or divert) NEAR/4 (malnutrition or malnourish* or undernourish* or overnutrition))

Indexes=SCI-EXPANDED Timespan=2000-2021

19 5,911

TS=((breastfeed* or feeding) NEAR/3 (advice or advis* or educat* or support*))

Indexes=SCI-EXPANDED Timespan=2000-2021

18 499

TS=((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or det er* or prevent* or avert* or divert) NEAR/4 ((fizzy or sugary or sweetened) NEAR/2 (drink or beverage*)))

Indexes=SCI-EXPANDED Timespan=2000-2021

17 3,209

TS=((increas* or improv* or encourag* or support* or promot* or influen* or recomme nd* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((salt or sugar or calorie*) NEAR/2 (less or lessen or reduc* or restrict*)))

Indexes=SCI-EXPANDED Timespan=2000-2021

16 13,072

TS=((increas* or improv* or encourag* or support* or promot* or influen* or recomme nd* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((health* or balanced) NEAR/2 (diet* or eating or food or nutrition*)))

Indexes=SCI-EXPANDED Timespan=2000-2021

15 33,811

TS=((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or det er* or prevent* or avert* or divert) NEAR/4 (obese or obesity or overweight))

Indexes=SCI-EXPANDED Timespan=2000-2021

14 28,758

TS=((increas* or improv* or encourag* or support* or promot* or influen* or recomme nd* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((weight or "body mass" or BMI) NEAR/2 (healthy or manage* or control* or loss* or loos* or decreas* or reduc*)))

Indexes=SCI-EXPANDED Timespan=2000-2021

13 176

TS=((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or det er* or prevent* or avert* or divert) NEAR/4 ((inactiv* or unhealthy) NEAR/3 (living or life*)))

Indexes=SCI-EXPANDED Timespan=2000-2021

12 421

TS=((decreas* or minimis* or reduc* or discourag* or disincentiv* or dissuade* or det er* or prevent* or avert* or divert) NEAR/4 (physical* NEAR/2 inactiv*))

Indexes=SCI-EXPANDED Timespan=2000-2021

11 72,277

TS=((increas* or improv* or encourag* or support* or promot* or influen* or recomme nd* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 (exercise* or exercising or fitness))

Indexes=SCI-EXPANDED Timespan=2000-2021

10 17,365

TS=((increas* or improv* or encourag* or support* or promot* or influen* or recomme nd* or motivat* or incentiv* or market* or advert* or subsid* or reward* or persua* or convinc* or instigat* or invest or benefit* or uptak* or start*) NEAR/4 ((active or physically-active or health*) NEAR/3 (living or life*)))

Indexes=SCI-EXPANDED Timespan=2000-2021

9 54

TS=("best start in life" or "healthy child programme" or "healthy start programme" or " change for children")

Indexes=SCI-EXPANDED Timespan=2000-2021

8 320,436

TS=((behavior* or behaviour* or positive* or success*) NEAR/3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or impact*))

Indexes=SCI-EXPANDED Timespan=2000-2021

7 178,864

TS=((lifestyle* or diet* or food* or nutrition*) NEAR/3 (intervention* or program* or chang* or modif* or improv* or enhanc* or adapt* or target* or alter* or impact*))

Indexes=SCI-EXPANDED Timespan=2000-2021

6 352,241

TS=((health* or wellness or welfare or well-
being or wellbeing or safety or immuni*) NEAR/5 (program* or interven* or scheme* or initiative* or encourag* or promot* or educat* or literacy or campaign* or improve* or improving))

Indexes=SCI-EXPANDED Timespan=2000-2021

5 43,369

TS=((early or early-years or early-life*) NEAR/3 (program* or interven* or scheme* or initiative*))

Indexes=SCI-EXPANDED Timespan=2000-2021

4 1,995,254

#1 OR #2 OR #3

Indexes=SCI-EXPANDED Timespan=2000-2021

3 231

TS=("birth to 5" or "birth to five")

Indexes=SCI-EXPANDED Timespan=2000-2021

2 3,651

TS=(under NEAR/1 (five* or "5") NEAR/2 (age* or old*))

Indexes=SCI-EXPANDED Timespan=2000-2021

1 1,995,058

TS=(pediatric* or paediatric* or child* or preemie* or baby or babies or infant* or toddler* or "neo nat*" or neo-nat* or neonat* or newborn* or new-
born* or "newly born*" or newly-born* or preschool* or pre-

school* or schoolchild* or school-child* or schoolboy* or school-boy* or schoolgirl* or school-girl* or school-age* or prekindergarten or pre-kindergarten or kindergarten or boy* or girl* or kid* or LBW or VLBW or ELBW or "low birth weight")

Indexes=SCI-EXPANDED Timespan=2000-2021

Key:

TS= terms in either title, abstract, author keywords, and keywords plus fields

TI= search in title field

AB= search in abstract field

CU= search in country/region field

SO= search in publication name field

CI= search in city field

OO= search in organization field

NEAR/3 = terms within three words of each other (any order).

* = truncation

Appendix 2: Data extraction template

1) General
Author
Year
Target population
2) Intervention
Intervention being evaluated
Comparator (counterfactual)
Study design
Study location
Length of follow-up of study
3) Economic evaluation (general)
Evaluative framework used (e.g. CEA, CBE, SROI)
Perspective
Time horizon
Discount rate
3b) Costs
Extent of resource use captured - health and non-health

Source of the cost data
Did the evaluation capture the opportunity costs? If so, what OC was used?
3c) Outcomes
Health outcomes captured
Any outcomes beyond health? (e.g. educational, child development etc.) if so how were they measured?
3d) Incoporation of equity considerations
Was there a formal (quantifiable) incorporation of equity considerations?
If so, what approach was taken?
4) Modelling
Was decision analytic modelling used?
Structural assumptions
5) Recommendation
Was the intervention considered to be cost-effective?
If cross sectoral outcomes included, how were they combined/traded off in decision making?
If equity informative outcomes included, how were equity/efficiency outcomes combined/traded off in decision making?

6) Characterisation of uncertainty
Was the uncertainty in the structural assumptions explored?
Was parameter uncertainty specified?
Were distributions used around parametric extrapolations
Probabilistic sensitivity analysis results presented?
How was uncertainty presented?
Did it influence the conclusion?
Empirical Results
Result of the evaluation (e.g. £/QALY)
Disaggregated costs and outcomes:
Intervention costs
Comparator costs
Intervention outcomes
Comparator outcomes

Appendix 3 – Drummond Checklist

1	**Was a well defined question posed in an answerable form?**
1.1	Did the study examine both costs and effects of the service(s) or programme(s) over an appropriate time horizon?
1.2	Did the study involve a comparison of alternatives?
1.3	Was a perspective for the analysis stated and was the study placed in any particular decision-making context?
1.4	Were the patient population and any relevant subgroups adequately defined?
2	**Was a comprehensive description of the competing alternatives given?**
2.1	Were any relevant alternatives omitted?
2.2	Was (should) a 'do nothing' alternative (be) considered?
2.3	Were relevant alternatives identified for the patient subgroup?
3	**Was the effectiveness of the programmes or services established?**
3.1	Was this done thorugh an RCT? If so, did the trial protocol reflect what would happen in regular practice?
3.2	Were effectiveness data collected and summarized through a systematic overview of clinical studies? If so, were the search strategy and rules for inclusion or exclusion outlined?
3.3	Were observational data or assumptions used to establish effectiveness? If so, were any potential biases recognized?

4	**Were all the important and relevant costs and consequences for each alternative identified?**
4.1	Was the range wide enough for the research question at hand?
4.2	Did it cover all relevant perspectives?
4.3	Were capital costs, as well as operating costs, included?
5	**Were costs and consequences measured accurately in appropriate physical units prior to valuation (e.g. hours of nursing time, number of physician visits, lost work-days, gained life years)?**
5.1	Were the sources of resource utilisation described and justified?
5.2	Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?
5.3	Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?
6	**Were costs and consequences valued credibly?**
6.1	Were the sources of all value clearly identified?
6.2	Were market values employed for changes involving resource gained or depleted?
6.3	Where market values were absent (e.g. volunteer labour), or market values did not reflect actual values (e.g. clinic space donated at a reduced rate), were adjustments made to approximate market value?
6.4	Was the valuation of consequences appropriate for the question posed (i.e. has the appropriate type of types of analysis - cost-effectiveness, cost-benefit - been selected)?
7	**Were costs and consequences adjusted for differential timing?**

7.1	Were costs and consequences that occur in the future 'discounted' to their present values?
7.2	Was a justification given for the discount rate used?
8	**Was an incremental analysis of costs and consequences of alternatives performed?**
8.1	Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?
9	**Was uncertainty in the estimates of costs and consequences adequately characterized?**
9.1	If patient-level data on costs or consequences were available, were appropriate statistical analyses performed?
9.2	If a sensitivity analysis was performed, was justification provided for the form(s) of sensitivity analysis employed and the ranges or distributions of values (for key study parameters)?
9.3	Were the conclusions of the study sensitive to the uncertainty in the results, as quantified by the statistical and/or sensitivity analysis?
9.4	Was heterogeneity in the patient population recognized, for example by presenting study results for relevant subgroups?
10	**Did the presentation and discussion of study results include all issues of concern to users?**
10.1	Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost-effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?
10.2	Were the results compared with those of others who have investigated the same question? If so, were allowances made for potential differences in study methodology?
10.3	Did the study discuss the generalizability of the results to other settings and patient/client groups?

10.4	Did the study allude to, or take account of, other important factors in the choice or decision under consideration (e.g. distribution of costs and consequences, or relevant ethical issues)?
10.5	Did the study discuss issues of implementation, such as feasibility of adopting the preferred programme given existing financial or other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?
10.6	Were the implications of uncertainty for decision making,including the need for future research, explored?

Appendix 4 – Drummond Checklist Results

	Drummond Checklist (Y, N, unclear, n/a)	Achana 2016	Anokye 2020	Atkins 2012	Baguelin 2015	Bamford 2007	Barber 2015	Barlow 2019	Barnardo's 2012a	Barnardo's 2012b	Beck 2021	Bessey 2019	Bessey 2018	Boyd 2016	Brisson 2003
1	Was a well defined question posed in an answerable form?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2	Was a comprehensive description of the competing alternatives given?	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y
3	Was the effectiveness of the programmes or services	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

	established ?														
4	Were all the important and relevant costs and consequences for each alternative identified?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
5	Were costs and consequences measured accurately in appropriate physical units prior to valuation (e.g. hours of nursing time, number of physician visits, lost work-days, gained life years)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

6	Were costs and consequences valued credibly?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
7	Were costs and consequences adjusted for differential timing?	Y	n/a	Y	Y	Y	n/a	n/a	N	N	Y	Y	Y	N	Y
8	Was an incremental analysis of costs and consequences of alternatives performed?	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	N	Y
9	Was uncertainty in the estimates of costs and consequences adequately characterized?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
10	Did the presentatio	Y	N	Y	Y	N	N	N	N	N	N	Y	Y	N	N

	n and discussion of study results include all issues of concern to users?														

	Drummond Checklist (Y, N, unclear, n/a)	Carlton 2008	Chance 2013	Christensen 2013	Christensen 2014	Craig 2011	Davenport 2003	Davies 2003	Davies 2000	Edmunds 2002	Edwards 2007	Ewer 2012	Fayter 2007	Fortnum 2016	Gardner 2017
1	Was a well defined question posed in an answerable form?	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2	Was a comprehensive description of the competing	Y	N	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y

	alternatives given?														
3	Was the effectiveness of the programmes or services established?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
4	Were all the important and relevant costs and consequences for each alternative identified?	Y	Unclear	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
5	Were costs and consequences measured accurately in appropriate physical units prior to	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

	valuation (e.g. hours of nursing time, number of physician visits, lost work-days, gained life years)?														
6	Were costs and consequences valued credibly?	Y	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y
7	Were costs and consequences adjusted for differential timing?	Y	Y	Y	Y	Y	N	N	N	Y	n/a	N	Y	Y	N
8	Was an incremental analysis of costs and consequences of alternatives	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

	performed ?														
9	Was uncertainty in the estimates of costs and consequences adequately characterized?	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
10	Did the presentation and discussion of study results include all issues of concern to users?	Y	N	Y	Y	N	N	N	Y	N	Y	N	Y	N	Y

	Drummond Checklist (Y, N, unclear, n/a)	Grill 2006	Hoddinott 2012	Hodgson 2020	Hollingworth 2012	Jacklin 2007	Jit 2007	Jit 2009	Jit 2010 (previous model)	Kay 2018	Kendrick 2017 i	Kendrick 2017 ii	Kneer 2012	Knowles 2005	Kowash 2006
1	Was a well defined question posed in an answerable form?	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	N
2	Was a comprehensive description of the competing alternatives given?	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
3	Was the effectiveness of the programmes or services established?	Y	Y	Y	Y	Unclear	Y	Y	Y	Y	Y	Y	Y	Y	Y
4	Were all the important and	Unclear	unclear	Y	Y	unclear	Y	Y	Y	Y	Y	Y	unclear	unclear	unclear

	relevant costs and consequences for each alternative identified?														
5	Were costs and consequences measured accurately in appropriate physical units prior to valuation (e.g. hours of nursing time, number of physician visits, lost work-days, gained life years)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
6	Were costs and consequences valued credibly?	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N

7	Were costs and consequences adjusted for differential timing?	Y	n/a	Y	Y	unclear	Y	Y	Y	Y	Y	n/a	Y	unclear	n/a
8	Was an incremental analysis of costs and consequences of alternatives performed?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9	Was uncertainty in the estimates of costs and consequences adequately characterized?	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
10	Did the presentation and discussion	N	N	Y	N	Y	N	N	N	N	Y	N	Y	Y	N

	of study results include all issues of concern to users?														

	Drummond Checklist (Y, N, unclear, n/a)	Martin 2009	McAuley 2004	McIntosh 2003	Melegaro 2004	Morell 2000a (& Morrell 2000b)	Mujica 2006	O'Neill 2017	Pandor 2004 (& Pandor 2006)	Phillips 2011	Pokhriel 2015	Pitman 2013	Renwick 2018	Roberts 2012	Saramago 2014
1	Was a well defined question posed in an answerable form?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

2	Was a comprehensive description of the competing alternatives given?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
3	Was the effectiveness of the programmes or services established?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
4	Were all the important and relevant costs and consequences for each alternative identified?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
5	Were costs and consequences measured	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

	accurately in appropriate physical units prior to valuation (e.g. hours of nursing time, number of physician visits, lost work-days, gained life years)?														
6	Were costs and consequences valued credibly?	Y	Y	Unclear	Y	N	Y	Y	Y	Y	Y	Y	N	Y	Y
7	Were costs and consequences adjusted for differential timing?	Y	n/a	N	Y	N	N	N	N	n/a	Y	Y	n/a	n/a	Y
8	Was an incremental analysis of costs and consequen	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

	ces of alternatives performed?														
9	Was uncertainty in the estimates of costs and consequences adequately characterized?	Y	N	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
10	Did the presentation and discussion of study results include all issues of concern to users?	Y	N	N	N	N	Y	Y	Y	Y	N	Y	Y	N	Y

	Drummond Checklist (Y, N, unclear, n/a)	Simkiss 2013	Simpson 2005	Thomas 2018	Tickle 2016	Trotter 2002	Trotter 2006a	Trotter 2006b	Tudor Edwards 2016	Uus 2006
1	Was a well defined question posed in an answerable form?	Y	Y	N	Y	N	Y	Y	Y	N
2	Was a comprehensive description of the competing alternatives given?	Y	Y	Y	Y	Y	Y	Y	Y	Y
3	Was the effectiveness of the programmes or services established?	Y	Y	Y	Y	Y	Y	Y	Y	unclear
4	Were all the important and relevant costs and consequences for each alternative identified?	Y	Y	unclear	Y	Y	Y	Y	Y	Y
5	Were costs and consequences measured accurately in appropriate	Y	Y	Y	Y	Y	Y	Y	Y	Y

	physical units prior to valuation (e.g. hours of nursing time, number of physician visits, lost work-days, gained life years)?									
6	Were costs and consequences valued credibly?	Y	N	Y	Y	N	Y	N	N	N
7	Were costs and consequences adjusted for differential timing?	N	Y	N	N	Y	Y	Y	n/a	N
8	Was an incremental analysis of costs and consequences of alternatives performed?	Y	Y	unclear	Y	Y	Y	Y	Y	Y
9	Was uncertainty in the estimates of costs and consequences adequately characterized?	Y	Y	Y	Y	Y	Y	Y	Y	N
10	Did the presentation and	N	N	N	Y	N	N	N	Y	N

	discussion of study results include all issues of concern to users?									

Inflated costs

All costs are inflated to 2023 prices using the consumer price index from the Office for National Statistics (Office for National Statistics, 2024a).

Author, Year	Intervention category	Intervention costs	Comparator costs	Incremental costs
Achana 2016 (Achana et al., 2016)	Injury prevention	(A) £7,645 (B) £9,026 (C) £9,052 (D) £10,606	(A) £5,308 (B) £6,920 (C) £7,592 (D) £8,123	- - - -
Anokye 2020 (Anokye et al., 2020)	Breast feeding	£11,499	-	£11,499
Atkins 2012 (Atkins et al., 2012)	Health protection	(1) £1,959 million; (2) £1,406 million	(1) £1,209 million; (2) £1,209 million	-
Baguelin 2015 (Baguelin et al., 2015)	Health protection	£228,777	£215,308	-
Bamford 2007 (Bamford et al., 2007)	Hearing/vision screening	£15.44	£0.34	-
Barber 2015 (Barber et al., 2015)	Health promotion	-	-	£1,462
Barlow 2019 (Barlow et al., 2019)	Reducing risk of abuse/maltreatment	(A) £18,548; (B) £21,172	(A)£12,121; (B) £16,473	-
Barnardo's 2012a (Salisbury et al., 2012)	Parenting support	£84,393.75	-	-
Barnardo's 2012b (Salisbury et al., 2012)	Parenting support	-	-	-
Beck 2021(Beck et al., 2021)	Health protection	-	-	£6,376,256,523
Bessey 2019 (Bessey et al., 2019)	Newborn screening	£8.71m	£4.72m	£4.00m

Bessey 2018 (Bessey et al., 2018)	Newborn screening	£3.65m	£7.81m	-£4.00m
Boyd 2016 (Boyd et al., 2016)	Reducing risk of abuse/maltreatment	(A)£2,541,442, (B)£4,559,094	(A)£255,718, (B)£3,404,473	-
Brisson 2003 (Brisson and Edmunds, 2003)	Health protection	-	-	-
Burke 2012 (Burke et al., 2012)	Newborn screening	£3,404,473	£342,556	-
Carlton 2008 (Carlton et al., 2008)	Hearing/vision screening	£1,299,521	£857,343	-
Chance 2013 (Chance, 2013)	Parenting support & health promotion	£4,770,279	-	-
Christensen 2013 (Christensen et al., 2013)	Health protection	A) £231.1m; b) £232.9m; c) £209.1m; d) £804.5m;	A) £134.8m; b) £134.8m; c) £134.8m; d) £423.8m;	-
Christensen 2014 (Christensen et al., 2014)	Health protection	-	-	-
Craig 2011 (Craig et al., 2011)	Short stature screening	£93	£29	£63
Davenport 2003 (Davenport et al., 2003)	Oral health	(A) £232.05; (B) £230.5; (C) £230.4; (D) £228.9	(A) £124.7; (B) £122.9; (C) £122.2; (D) 120.7	-
Davies 2000 (Davies et al., 2000)	Newborn screening	Unclear	Unclear	Unclear
Davies 2003 (Davies et al., 2003)	Oral health	£250,266.63	-	-
Edmunds 2002(Edmunds et al., 2002)	Health protection	-	-	-
Edwards 2007 (Edwards et al., 2007)	Parenting support	£3,075.73	£75.86	£3,000
Ewer 2012 (Ewer et al., 2012)	Newborn screening	£1,820,225.83	£822,638.13	£997,588
Fayter 2007 (Fayter et al., 2007)	Short stature screening	£14.67m	£9.42m	£5m

Fortnum 2016 (Fortnum et al., 2016)	Hearing/vision screening	£209,638, £232,157	£182,332	-
Gardner 2017 (Gardner et al., 2017)	Parenting support	Unclear	Unclear	-
Griebsch 2007 (Griebsch et al., 2007)	Newborn screening	£2,097,739.26	£948,058.34	£1,149,681
Grill 2006 (Grill et al., 2006)	Hearing/vision screening	£40,780.73	£36,952.75	£3,828
Hoddinott 2012 (Hoddinott et al., 2012)	Breast feeding	£55.26	£28.31	£27
Hodgson 2020 (Hodgson et al., 2020)	Health protection	-	-	-
Hollingworth 2012 (Hollingworth et al., 2012)	Health promotion	£368	£0.00	£368
Jacklin 2007, NICE 2008 (Jacklin et al., 2006, Jacklin et al., 2007)	Breast feeding	-	-	-
Jit 2007 (Jit and Edmunds, 2007)	Health protection	-	-	-
Jit 2009 (Jit et al., 2009)	Health protection	-	-	-
Jit 2010 (Update of 2009 paper with new efficacy evidence) (Jit et al., 2010)	Health protection	-	-	-
Kay 2018 (Kay et al., 2018)	Oral health	-	-	-
Kendrick 2017 I (Kendrick et al., 2017)	Injury prevention	£24,942.94	£23,978.44	£965
Kendrick 2017 ii (Kendrick et al., 2017)	Injury prevention	£46	£22	£24
Knerer 2012 (Knerer et al., 2012)	Health protection	£241,628,691	£248,191,898	-£6,563,207

Knowles 2005 (Knowles et al., 2005)	Newborn screening	£771,264.73	£480,858.72	
Kowash 2006	Oral health	£10,182.15	-	
Lorgelly 2007 (Lorgelly et al., 2008)	Health protection	not reported	not reported	not reported
Martin 2009 (Martin et al., 2009)	Health protection	£117.35 (NHS), £130.06 (societal)	£48.00 (NHS), £95.83 (societal)	£69 (NHS), £34 (societal)
McAuley 2004 (McAuley et al., 2004)	Parenting support	£5,054.74	£8,610.25	£3,556
McIntosh 2003 (McIntosh et al., 2003)	Health protection	£342.88m	£227.19m	£116m
Melegaro 2004 (Melegaro and Edmunds, 2004)	Health protection	£36,599,751.74	£0.00	£36,599,752
Morell 2000a & Morell 2000b (Morrell et al., 2000a, Morrell et al., 2000b)	Parenting support	£1,112.55	£798.93	£315
Mujica Mota 2006 (Mujica Mota et al., 2006)	Parenting support & health promotion	-	-	-
O'Neill 2017 (O'Neill et al., 2017)	Oral health	£1,275.21	£1,012.53	£263
Pandor 2004 (Pandor et al., 2004)+ Pandoor 2006(Pandor et al., 2006)	Newborn screening	£144,107.83	£180,937.36	-£36,830
Phillips 2011 (Phillips et al., 2011)	Injury prevention	£18.80	£0	£18.80
Pitman 2013 (Pitman et al., 2013)	Health protection	a)£24,222m; b) £23,732	£23,970m	-
Pokhrel 2015 (Pokhrel et al., 2015)	Breast feeding	-	-	-

Renwick 2018 (Renwick et al., 2018)	Health promotion	£397.93	£54.59	£343
Roberts 2012 (Roberts et al., 2012)	Newborn screening	£1,820,225	£822,638	£997,588
Saramago 2014 (Saramago et al., 2014)	Injury prevention	£24,941	£25,944	£1,003
Siddiqui 2011 (Siddiqui et al., 2011)	Health protection	-	-	-
Simkiss 2013 (Simkiss et al., 2013)	Parenting support	£848	£0.00	£849
Simpson 2005 (Simpson et al., 2005)	Newborn screening	-	-	£4,689
Thomas 2018 (Thomas, 2018)	Health protection	-	-	-
Tickle 2016 (Tickle et al., 2016)	Oral health	£1,308	£1,038	£269
Trotter 2002 (Trotter and Edmunds, 2002)	Health protection	0-4 months (£20.73m net cost); 5-11 months (£18.86m); 1-4 years (£58.27m)	Unclear but could be assumed to be £0	If we assume £0 for comparator then: 0-4 months (£20.73m net cost); 5-11 months (£18.86m); 1-4 years (£58.27m)
Trotter 2006a (Trotter et al., 2006)	Health protection	a) £1,326,875,158; b) £495,924,727	a) £0; b) £0	a) £1,326,875,158; b) £495,924,727
Trotter 2006b (Trotter and Edmunds, 2006)	Health protection	Strategy 2 £ £1,648m ; Strategy 3a £1246m; S3ab £ 847m; Strategy 4 £446m	£1,246.50m (strategy 1)	-
Tudor Edwards 2016 (Edwards et al., 2016)	Parenting support	-	-	i)£3,412; ii) £3,412; iii) £3,174
Uus 2006 (Uus et al., 2006)	Newborn screening	£54,213	£39,767	£14,446
Costs are inflated to the 2023 costs using the consumer price index from the Office for National Statistics (Office for National Statistics, 2024a). Note, 2023 was selected as this is the most up to date year with all 12 months of CPI data.				

Chapter 3

The following interventions were considered for the case study. The first was the E-SEE Steps evaluation (Bywater et al., 2022). E-SEE Steps is a programme delivered to parents of children under 8 weeks old with the aim of improving the child's social-emotional wellbeing at 20 months of age. E-SEE Steps was evaluated in a randomised controlled trial (RCT) compared to service as usual. The intervention comprised 3 parts: Incredible Years book (IY-B) which was given to all infants and the Incredible Years Infant (IY-I) and Incredible Years Toddler (IY-T) interventions which were delivered under a proportionate universalism approach in which need was based on ASQ:SE-2/PHQ-9 scores. The results of the E-SEE Steps RCT can be seen in Chapter 3.

The second intervention considered for inclusion was the Optimising Family Engagement in HENRY (Health, Exercise, Nutrition for the Really Young) (OFTEN) trial (referred to hereafter as 'HENRY-OFTEN') (Bryant et al., 2021). This was an RCT conducted over a 12-month period and compared HENRY to standard of care. HENRY-OFTEN reported results as a change in Family Eating and Activity Habits Questionnaire (FEAQ) and EQ-5D. The trial was a feasibility study but showed no difference in FEAQ or EQ-5D. As a result, the principal investigator of the HENRY-OFTEN study revealed that a full economic evaluation was planned but due to the null effect this did not happen. Context was provided by the principal investigator as to the reason for the null effect of the trial: 'the trial was conducted at probably the wors[t] possible time it could have been in early years settings (children centre closures/austerity etc.)' (Bryant, 2022, email communication, 26/01/2022).

The third intervention considered for inclusion was the Building Blocks:2-6 study (referred to hereafter as 'BB:2-6') (Robling et al., 2021). This study evaluated the

effectiveness of the Family Nurse Partnership (FNP) compared to usual care in reducing maltreatment, health, developmental and educational outcomes. The results showed no evidence of an intervention effect in the primary outcomes, which was referral to children's social care services. There was no difference in attendance rates for hospital outpatient appointments and early educational attendance. The results of the economic evaluation were reported as a cost-consequence analysis. The principal investigator informed us that as I would be accessing data supplied under license by NHS Digital, amendments to the data sharing agreement (i.e. my access to the data) may incur costs (Robling, 2022, email communication, 28/01/2022).

On reflection, the E-SEE Steps programme was selected as the case study for use in the thesis.

Chapter 4

Mortality rates

The estimated mortality rates from Ingleby et al.

Basecase

	M1	M2	M3	M4
Age group	Degree	A-level	GCSE	No qual
16-24	0.00022059	0.00023866	0.00035149	0.00121773
25-34	0.00037094	0.0004059	0.00056981	0.00173336
35-44	0.00075358	0.0008368	0.00110513	0.00284618
45-54	0.00164706	0.00185669	0.00230588	0.00502484
55-64	0.00401871	0.00460052	0.0053708	0.00989721
65-74	0.01136122	0.01321279	0.01449405	0.02257411
75-84	0.03820559	0.04515273	0.04653132	0.06124484
85+	0.23208476	0.2808753	0.26448234	0.27378774

	F1	F2	F3	F4
Age group	Degree	A-level	GCSE	No qual
16-24	0.00018445	0.00029551	0.00054633	0.00064927
25-34	0.000309	0.0004531	0.00078144	0.00095663
35-44	0.00062545	0.00081992	0.00129295	0.00164378
45-54	0.00136507	0.0016007	0.00230632	0.00304413
55-64	0.00333731	0.00350233	0.00460745	0.00631179
65-74	0.00949721	0.00892496	0.01071258	0.01522647
75-84	0.03232263	0.02722368	0.02980029	0.04392958
85+	0.20060945	0.14462135	0.13872324	0.21521339

	M5	M4	M3	M2	M1
Age group	Q5	Q4	Q3	Q2	Q1
16-24	0.00016384	0.000362	0.00034306	0.0004799	0.00036907
25-34	0.00029642	0.00059429	0.00059961	0.00082103	0.00065083
35-44	0.00065129	0.00115502	0.0012614	0.00168123	0.00138463
45-54	0.00149522	0.00234502	0.00277249	0.00359669	0.00307778
55-64	0.00366639	0.00508415	0.00650818	0.00821737	0.00730671
65-74	0.00981681	0.01203366	0.01668071	0.02049788	0.01894003
75-84	0.02915487	0.0315924	0.04742176	0.05671422	0.05445625
85+	0.14031209	0.12757975	0.21443017	0.24673856	0.25023277

	F5	F4	F3	F2	F1
Age group	Q5	Q4	Q3	Q2	Q1
16-24	0.00017618	0.00051906	0.00027305	0.000231021	0.00025335
25-34	0.00030805	0.00077888	0.0004578	0.000406567	0.00044298
35-44	0.00065238	0.00135813	0.00091941	0.000868072	0.00093811
45-54	0.00146222	0.0025053	0.001954	0.001961683	0.00210267
55-64	0.00356908	0.00503062	0.00452189	0.004827675	0.00513233
65-74	0.00976325	0.01131603	0.01172626	0.013315245	0.01403952
75-84	0.03054598	0.02911271	0.03477923	0.042003159	0.04392501
85+	0.16223825	0.11704501	0.17113246	0.225737635	0.23329808

Scenario analysis in which the 1-4 GCSEs or equivalent group was included in the No qualifications group to make a No qualifications or low-level qualifications group.

	M	M	M	M
Age group	Degree	A-level	GCSE: 5 or more	No quals and low level quals
16-24	0.000220595	0.000238656	0.000341916	0.000789399
25-34	0.000370938	0.000405901	0.000549933	0.001161521

35-44	0.000753578	0.000836805	0.001055868	0.002000287
45-54	0.001647064	0.001856691	0.002180687	0.00372796
55-64	0.004018706	0.004600519	0.005026916	0.007805941
65-74	0.011361222	0.013212788	0.013424741	0.01906873
75-84	0.038205587	0.045152728	0.042645533	0.055830972
85+	0.232084765	0.280875301	0.238710729	0.282020852

	F	F	F	F
Age group	Degree	A-level	GCSE: 5 or more	No quals and low level quals
16-24	0.00018445	0.00029551	0.00060438	0.00056878
25-34	0.000309	0.0004531	0.00085225	0.00083363
35-44	0.00062545	0.00081992	0.00138398	0.00142285
45-54	0.00136507	0.0016007	0.00242184	0.00261747
55-64	0.00333731	0.00350233	0.00474412	0.00539128
65-74	0.00949721	0.00892496	0.0108107	0.01292047
75-84	0.03232263	0.02722368	0.02946193	0.03703411
85+	0.20060945	0.14462135	0.13311075	0.17977456

Missingness

Pattern of missingness in the HSE data.

	Pattern		
Percent	Education group	EQ-5D	Income
72%	1	1	1
17%	1	1	0
6%	1	0	1
3%	1	0	0
1%	0	1	1

<1%	0	1	0
<1%	0	0	1
<1%	0	0	0

The results show 72% of the individuals have all three variables observed. The most common pattern with missing values is when education group and EQ-5D are observed but income is missing (17%). The second most common pattern is when education and income are present but not EQ-5D. Therefore, logistic regression is run to reveal the probability of missingness on the variables of interest for income and EQ-5D.

Income

Income	Odds ratio	Std. err.	P>|z|
Sex	.9453587	.0297105	0.074
Age	.9103903	.0075277	0.000
EQ-5D	1.397653	.0966616	0.000

The model indicates strong evidence that those with higher EQ-5D and higher age group (as the reference group is the youngest age group) are more likely to have the income variable observed. This is strong evidence against the Income variable being MCAR, because we have found variables, which are predictive of missingness.

Exploration of the categorical variable Age confirms that compared to 16-24 year olds, we are more likely to observe the variable up to the age of 64 then from 75 onwards we are less likely to observe it.

	Odds ratio	Std. err.	P>|z|
Age group			

25-34	1.409651	.088748	0.000
35-44	1.823837	.114739	0.000
45-54	1.571762	.0962621	0.000
55-64	1.326741	.080793	0.000
65-74	1.023079	.0626135	0.709
75-84	.7923406	.0525009	0.000
85+	.4592303	.0416551	0.000

EQ-5D

Income	Odds ratio	Std. err.	P>|z|
Sex	1.073566	.0461132	0.098
Age	.8889801	.0100883	0.000
Income	.7941624	.0153062	0.000

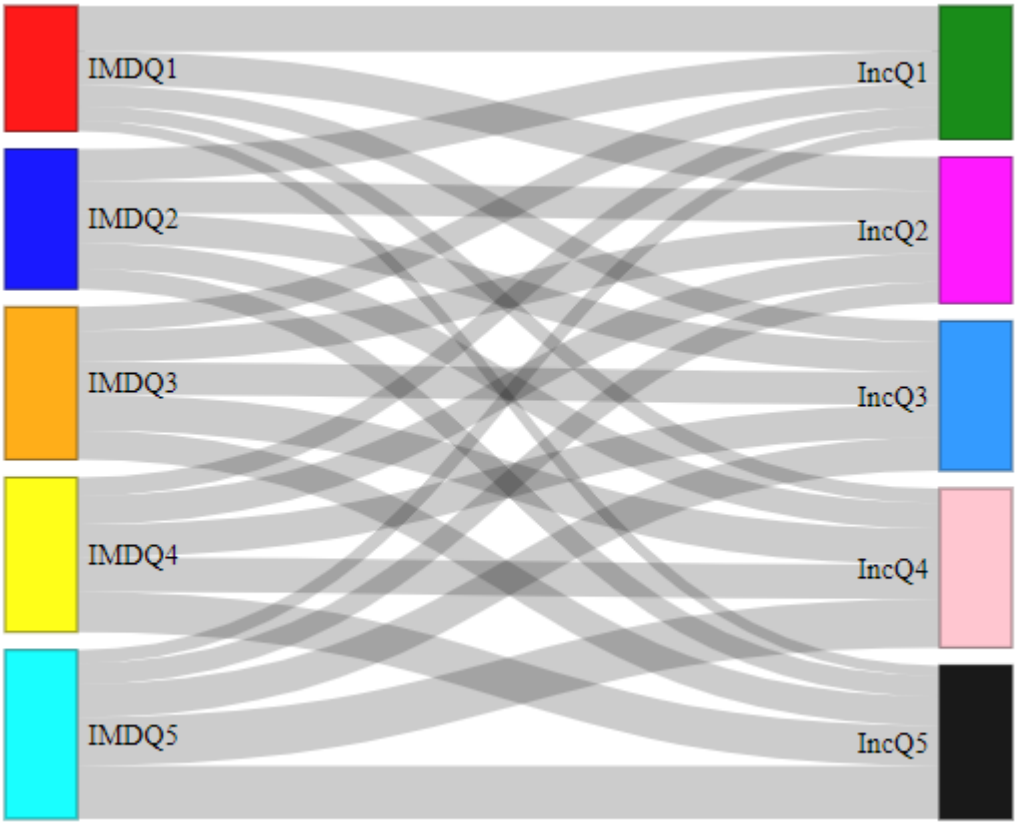
Strong evidence that those in a higher age group (as the reference group is the youngest age group) and a lower income group (as Q1 i.e. highest income quintile, is used as the reference group).

Exploration of the categorical variables Age and income confirm the trend of missingness in the EQ-5D data.

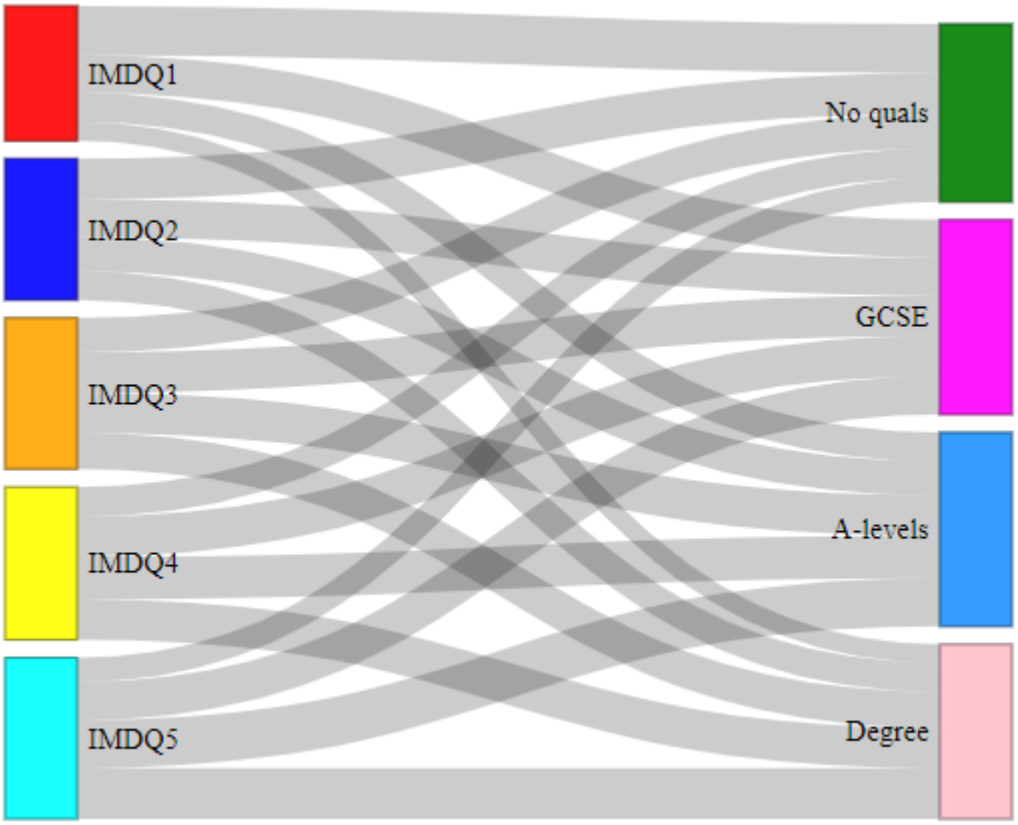
	Odds ratio	Std. err.	P>|z|

Age group			
25-34	1.065274	.098477	0.494
35-44	1.011086	.0894797	0.901
45-54	1.059986	.094165	0.512
55-64	1.191065	.1096713	0.058
65-74	.8645492	.0780995	0.107
75-84	.4728906	.04284	0.000
85+	.3648711	.042962	0.000
Income			
Q4	1.023954	.0978835	0.804
Q3	.7513123	.0683644	0.002
Q2	.550728	.0477331	0.000
Q1	.4446277	.0379765	0.000

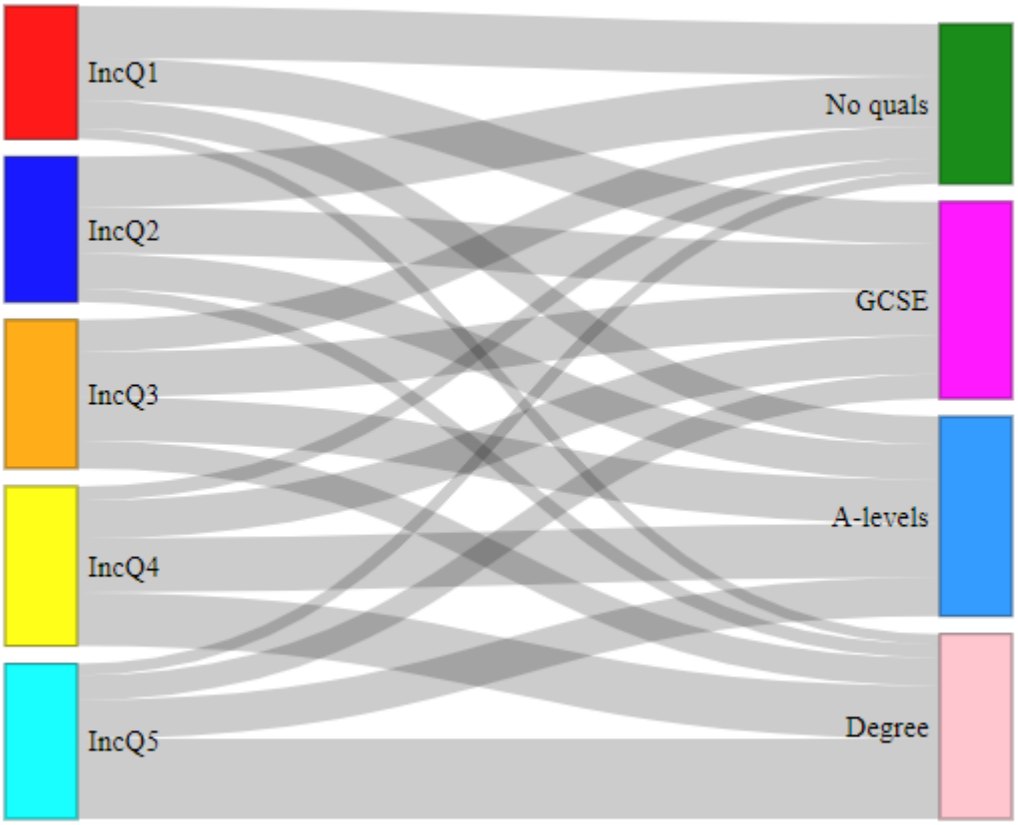
Sankey plots for the HSE



Sankey plot of IMD quintile group and income quintile group



Sankey plot of IMD quintile group and educational attainment group



Sankey plot of income quintile group and educational attainment group

EQ-5D values from the Health Survey for England – scenario analysis

	Education SA	
16-24	0	(.)
25-34	-0.0166*	(0.00735)
35-44	-0.0560***	(0.00711)
45-54	-0.0806***	(0.00706)
55-64	-0.116***	(0.00719)
65-74	-0.102***	(0.00757)

75-84	-0.143***	(0.00882)
85+	-0.156***	(0.0134)
Male	0	(.)
Female	-0.0243***	(0.00361)
Degree or higher	0	(.)
A-levels	-0.0239***	(0.00504)
GCSE; 5 or more	-0.0445***	(0.00535)
No qualifications ~	-0.115***	(0.00532)
Constant	0.978***	(0.00700)
Observations	15305	
R-squared	0.098	

Standard errors in parentheses

* p<0.05, ** p<0.01, *** p<0.001

Alternative estimator: Tobit model

HRQL weights estimated from the regression EQ-5D on age, sex and SEP using a Tobit estimator

Education			Income	
Age				
16-24	0	(.)	0	(.)
25-34	-0.0579***	(0.0126)	-0.0742***	(0.0140)
35-44	-0.136***	(0.0119)	-0.160***	(0.0133)
45-54	-0.182***	(0.0118)	-0.222***	(0.0132)
55-64	-0.252***	(0.0119)	-0.306***	(0.0133)
65-74	-0.237***	(0.0125)	-0.292***	(0.0138)
75-84	-0.316***	(0.0141)	-0.377***	(0.0154)
85+	-0.366***	(0.0201)	-0.436***	(0.0239)
Sex				
Male	0	(.)	0	(.)
Female	-0.0441***	(0.00572)	-0.0429***	(0.00626)
Education				
Degree or higher	0	(.)		
A-levels	-0.0542***	(0.00829)		
GCSE	-0.115***	(0.00820)		
No qualifications	-0.207***	(0.00894)		
Income				
Q5 (highest)			0	(.)
Q4			-0.0321**	(0.00984)
Q3			-0.104***	(0.00996)
Q2			-0.170***	(0.0101)
Q1 (lowest)			-0.260***	(0.0102)
Constant	1.298***	(0.0122)	1.354***	(0.0139)

/

var(e.eqmean) 0.143*** (0.00213) 0.140*** (0.00232)

Observations 22498 18582

R-squared

Standard errors in parentheses

* p<0.05, ** p<0.01, *** p<0.001

The signs on the coefficients are consistent with the relationship observed in the OLS model: lower education and income was associated with lower HRQOL, while ageing and being female are associated with lower HRQOL.

Example QALE lifetable

Age interval	n_x	a_x	M_x	q_x	l_x	L_x	T_x	e_x	u_x	Y_x	N_x	Q_x
0-4	5	0.5	0.0011	0.0055	1.00	4.99	85	84.9	1.000	5	78	77.8
5-9	5	0.5	0.0001	0.0005	0.99	4.97	80	80.3	1.000	5	73	73.2
10-14	6	0.5	0.0001	0.0006	0.99	5.96	75	75.4	1.000	6	68	68.3
16-24	9	0.5	0.0002	0.0015	0.99	8.93	69	69.4	1.000	9	62	62.3
25-34	10	0.5	0.0003	0.0030	0.99	9.90	60	60.5	0.968	10	53	53.4
35-44	10	0.5	0.0007	0.0065	0.99	9.86	50	50.7	0.929	9	43	43.9
45-54	10	0.5	0.0015	0.0148	0.98	9.75	40	41.0	0.895	9	34	34.8
55-64	10	0.5	0.0037	0.0360	0.97	9.51	31	31.5	0.852	8	26	26.4
65-74	10	0.5	0.0098	0.0936	0.93	8.89	21	22.5	0.863	8	17	18.7
75-84	10	0.5	0.0292	0.2545	0.85	7.38	12	14.3	0.819	6	10	11.5
85+	15	0.5	0.1403	1.0000	0.63	4.73	5	7.5	0.781	4	4	5.9

Life table key	
n_x	Range of interval
a_x	Proportion of interval survived by those dying
M_x	Crude mortality rate
q_x	Probability of dying
l_x	Number of cohort alive
L_x	Person years lived
T_x	Person years lived in current and subsequent intervals
e_x	Life expectancy
u_x	Health-related quality of life
Y_x	Quality-adjusted person years lived

N_x	Quality-adjusted person years lived in current and subsequent intervals
Q_x	Quality-adjusted life expectancy

QALE Results

	No qualifications	GCSEs	A-levels or equivalent	Degree and higher
Base case				
Male	61.70	70.70	73.72	76.64
Female	63.20	70.28	73.88	75.90
Combined	62.40	70.47	73.78	76.23
Multiple Imputation				
Male	61.69	70.59	73.66	76.58
Female	63.23	70.21	73.87	75.89
Combined	62.41	70.38	73.75	76.20

Scenario Analyses

	No qualifications + low level qualifications	GCSEs	A-levels or equivalent	Degree and higher
Scenario Analysis 1				
Male	62.20	71.29	73.76	76.68
Female	63.58	70.72	73.76	75.78
Combined	62.83	70.98	73.73	76.18

	No qualifications + foreign qualifications	GCSEs	A-levels or equivalent	Degree and higher
Scenario Analysis 2				
Male	61.80	70.63	73.65	76.58
Female	63.43	70.33	73.94	75.97

Combined	62.56	70.46	73.78	76.24

	No qualifications	**GCSEs**	**A-levels or equivalent**	**Degree and higher + foreign qualifications**
Scenario Analysis 3				
Male	61.81	70.75	73.75	76.32
Female	63.20	70.21	73.79	75.46
Combined	62.45	70.46	73.75	75.85

	Q1	**Q2**	**Q3**	**Q4**	**Q5**
Base case					
Male	67.10	66.40	71.14	75.74	77.87
Female	67.46	67.76	71.66	74.23	76.31
Combined	67.25	67.04	71.37	74.93	77.02
Multiple Imputation					
Male	67.05	66.35	70.94	75.65	77.83
Female	67.38	67.68	71.43	74.12	76.24
Combined	67.18	66.97	71.16	74.83	76.97

	Q1 + n/a	**Q2 + n/a**	**Q3 + n/a**	**Q4**	**Q5**

Scenario Analysis 4					
Male	67.33	66.63	71.38	75.99	78.12
Female	67.50	67.80	71.69	74.28	76.35
Combined	67.38	67.17	71.50	75.07	77.15

	Q1	**Q2**	**Q3 + n/a**	**Q4 + n/a**	**Q5 + n/a**
Scenario Analysis 5					
Male	68.61	67.90	71.84	77.20	79.33
Female	68.83	69.13	72.18	75.54	77.62
Combined	68.68	68.47	71.98	76.31	78.40

Inequality analyses

	QALE: Bottom SEP Group (QALYs) (1)	**QALE: Top SEP Group (QALYs) (2)**	**Absolute Gap (QALYs) (1)-(2)**
Education groups			
Complete case (m)	61.70	76.64	14.93
Complete case (f)	63.20	75.90	12.70
Complete case (c)	62.40	76.23	13.82
MI (m)	61.69	76.58	14.90
MI (f)	63.23	75.89	12.66
MI (c)	62.41	76.20	13.79
SA1 (m)	62.20	76.68	14.47
SA1 (f)	63.58	75.78	12.20
SA1 (c)	62.83	76.18	13.34
SA2 (m)	61.80	76.58	14.78

SA2 (f)	63.43	75.97	12.54
SA2 (c)	62.56	76.24	13.67
SA3 (m)	61.81	76.32	14.51
SA3 (f)	63.20	75.46	12.26
SA3 (c)	62.45	75.85	13.40
Income groups			
Complete case (m)	67.10	77.87	10.77
Complete case (f)	67.46	76.31	8.85
Complete case (c)	67.25	77.02	9.78
MI (m)	67.05	77.83	10.78
MI (f)	67.38	76.24	8.86
MI (c)	67.18	76.97	9.79
SA4 (m)	67.33	78.12	10.78
SA4 (f)	67.50	76.35	8.84
SA4 (c)	67.38	77.15	9.77
SA5 (m)	68.61	79.33	10.72
SA5 (f)	68.83	77.62	8.79
SA5 (c)	68.68	78.40	9.72

Note, the MI results are the base case.
Abbreviations: c, combined; f, female; m, male; MI, multiple imputation; QALE; quality-adjusted life expectancy; QALY, quality adjusted life year; SA, scenario analysis.

Chapter 5

A number of different distributional forms and link functions for the GLM models were assessed based on based on Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC), which provide information on model fit. As outlined by Peraillon et al. (Peraillon et al., 2022), the following distributional forms and link functions were considered for estimating the cost data using a GLM: gamma distribution, log link function; gaussian distribution, log link function; gamma distribution, square root link function; Poisson distribution, log link function. The AIC and BIC are presented in the Table below:

	AIC	BIC
Glm, gamma, log	4836.73	4870.034
Glm, gaussian, log	5300.834	5334.138
Glm, gamma, power0.5	4836.498	4869.802
Glm, poisson, log	509295.6	509328.9

The preferred distributional form and link function for the GLM models used in the base case was the gamma distribution and the log link function. This was based on previous literature (Cox et al., 2022) and the low AIC and BIC.

Regression results

Adult EQ-5D, IMD subgroups

	Coef.	St.Err.	t-value	p-value	[95% Conf	Interval]
randomisation_grp	0.029	0.02	1.46	0.144	-0.01	0.067
eq5d_cw_scr0	0.644	0.069	9.4	0	0.509	0.779
1	-0.031	0.021	-1.5	0.134	-0.071	0.01
2	-0.06	0.024	-2.47	0.014	-0.107	-0.012
age_p	0	0.002	0.12	0.905	-0.003	0.003
gender_child	-0.017	0.015	-1.12	0.262	-0.046	0.013
IMD_Q2	-0.002	0.023	-0.09	0.925	-0.047	0.043
IMD_Q3	0.036	0.023	1.54	0.123	-0.01	0.081
IMD_Q4	0.004	0.021	0.19	0.848	-0.038	0.046
IMD_Q5	0.022	0.025	0.88	0.377	-0.027	0.072
phq_score0	-0.014	0.003	-5.55	0	-0.019	-0.009

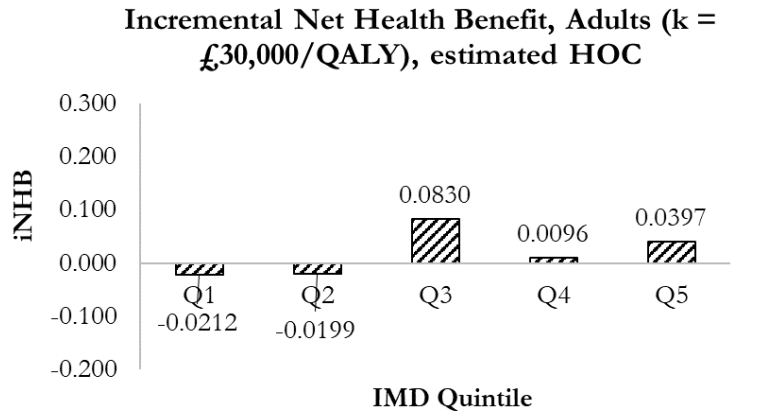
Asq_score0	-0.001	0.001	-0.98	0.326	-0.002	0.001
Constant	0.824	0.082	10.02	0	0.662	0.985

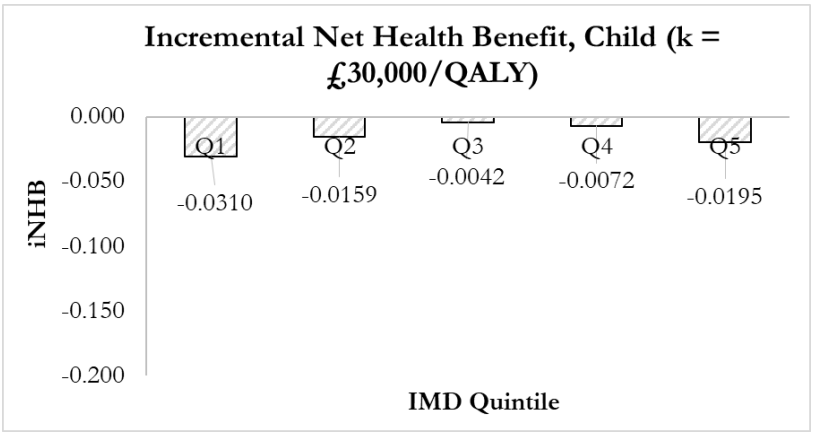
Adult costs, IMD subgroups

	Coef.	St.Err.	t-value	p-value	[95% Conf	Interval]
randomisation_grp	0.298	0.252	1.18	0.238	-0.196	0.791
1	-0.159	0.248	-0.64	0.522	-0.644	0.327
2	-0.178	0.299	-0.6	0.551	-0.764	0.408
age_p	-0.039	0.016	-2.35	0.019	-0.071	-0.006
gender_child	0.163	0.188	0.86	0.388	-0.206	0.531
IMD_Q2	0.118	0.28	0.42	0.673	-0.431	0.668
IMD_Q3	-0.329	0.294	-1.12	0.264	-0.905	0.248
IMD_Q4	-0.455	0.281	-1.62	0.107	-1.008	0.098
IMD_Q5	-0.213	0.318	-0.67	0.502	-0.838	0.411
Constant	8.403	0.583	14.42	0	7.261	9.546

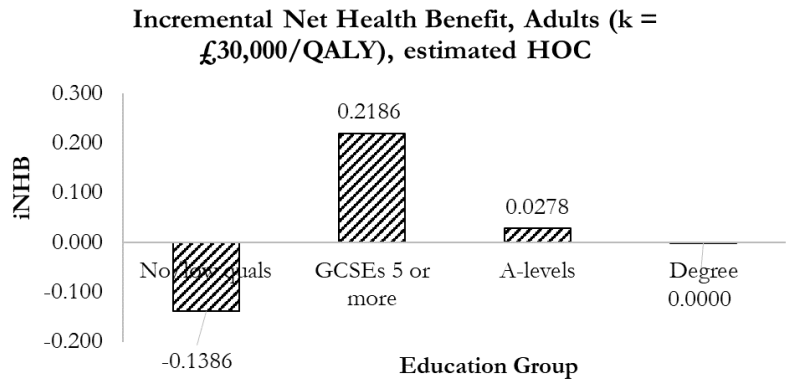
Equity-impact analysis – Love-Koh et al. Health opportunity cost

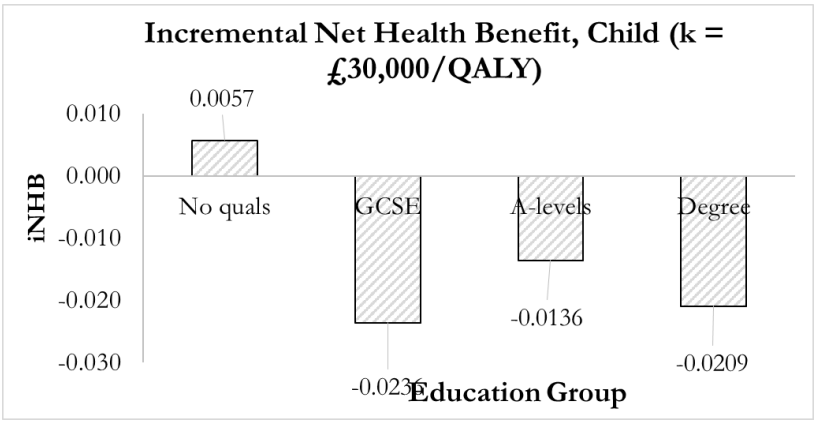
IMD



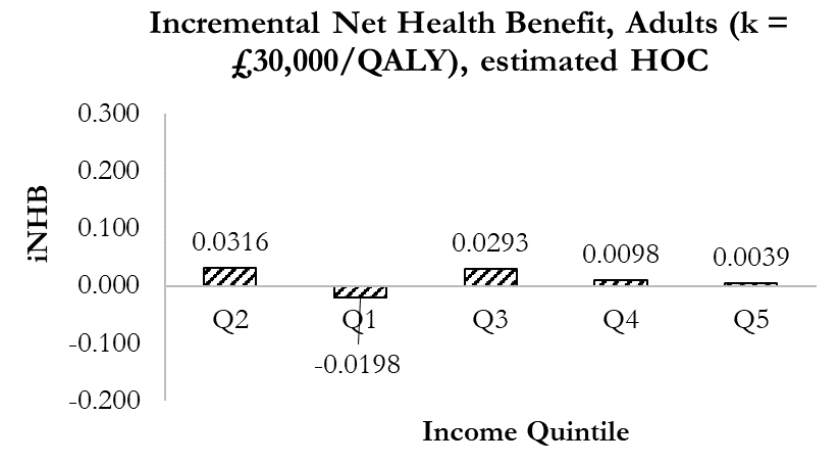


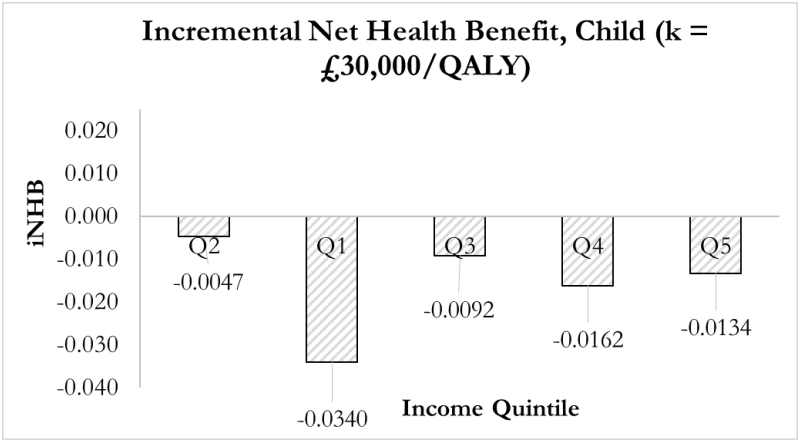
Education




Incremental Net Health Benefit, Child (k = £30,000/QALY)
iNHB
0.010
0.000
-0.010
-0.020
-0.030
0.0057
No quals
GCSE
A-levels
Degree
-0.0136
-0.0209
-0.0236
Education Group

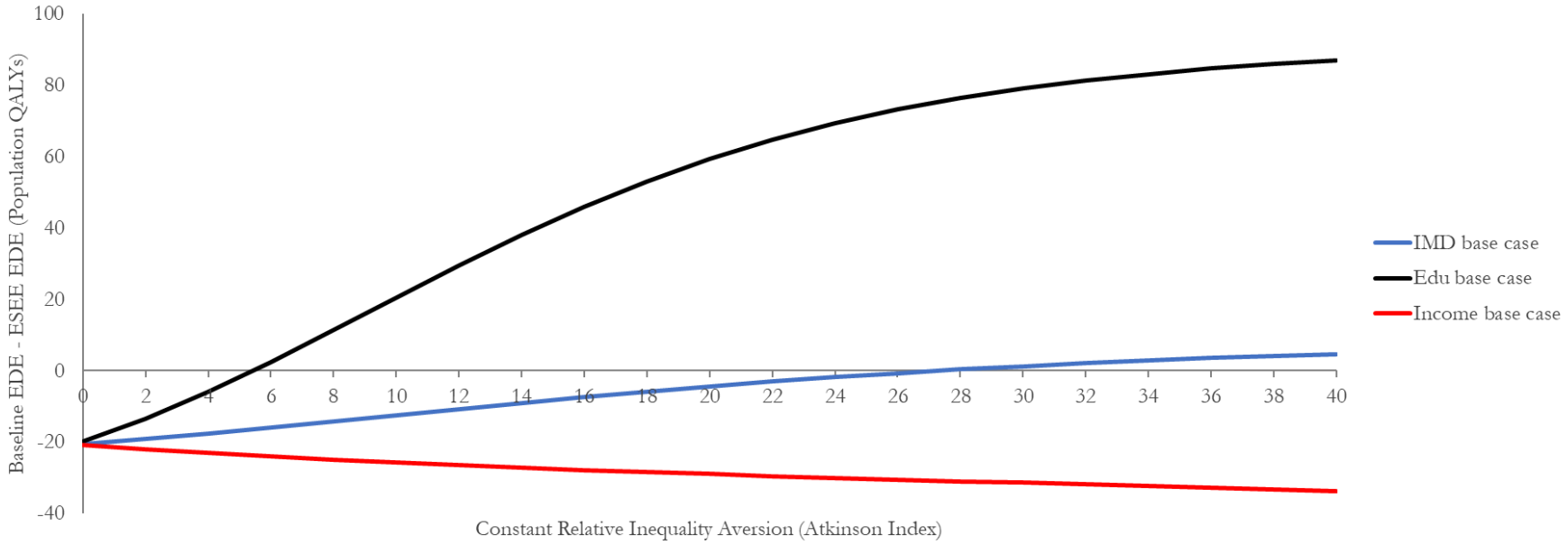
Income


Incremental Net Health Benefit, Adults (k = £30,000/QALY), estimated HOC
iNHB
0.300
0.200
0.100
0.000
-0.100
-0.200
0.0316
0.0293
0.0098
0.0039
Q2
Q1
Q3
Q4
Q5
-0.0198
Income Quintile

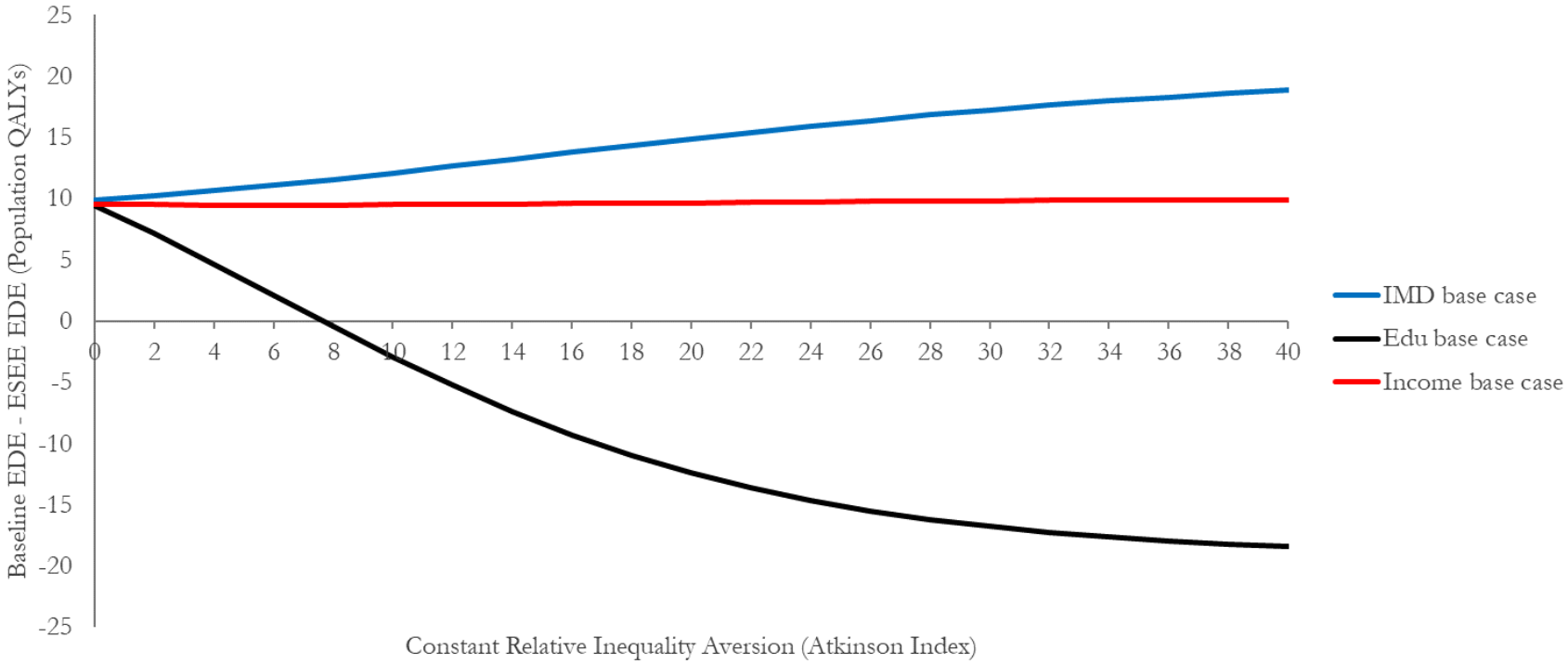

Incremental Net Health Benefit, Child (k = £30,000/QALY)
iNHB
0.020
0.010
0.000
-0.010
-0.020
-0.030
-0.040
Q2
Q1
Q3
Q4
Q5
-0.0047
-0.0340
-0.0092
-0.0162
-0.0134
Income Quintile

Sensitivity analysis of relative inequality aversion (social welfare)

Adults – relative inequality aversion (Atkinson)

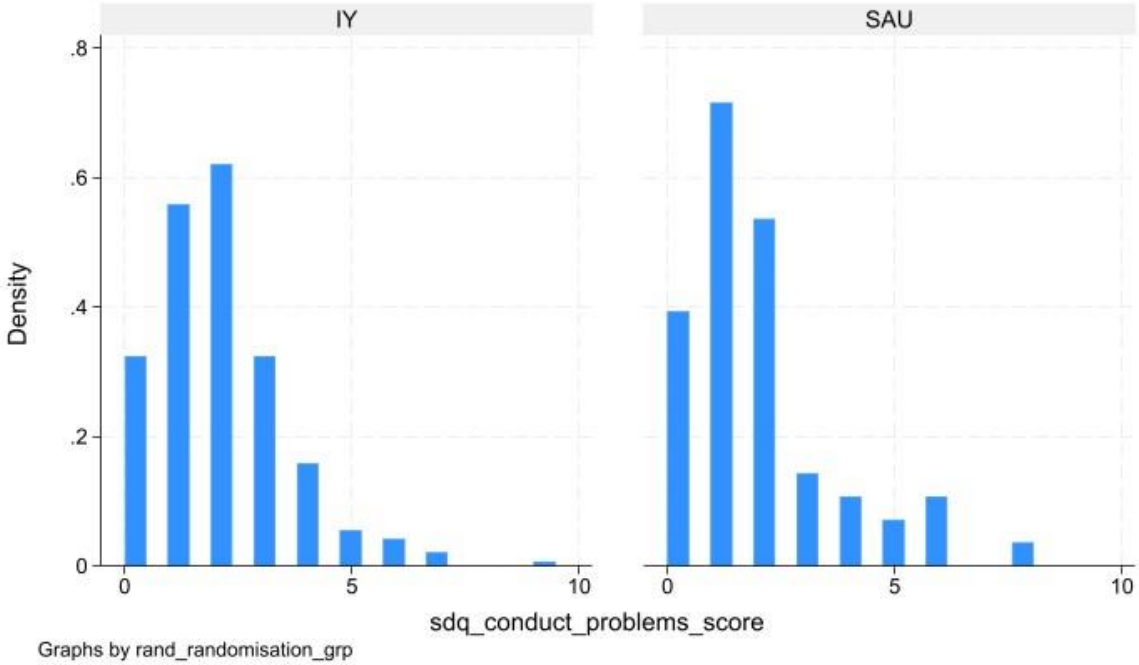


Child – relative inequality aversion (Atkinson)



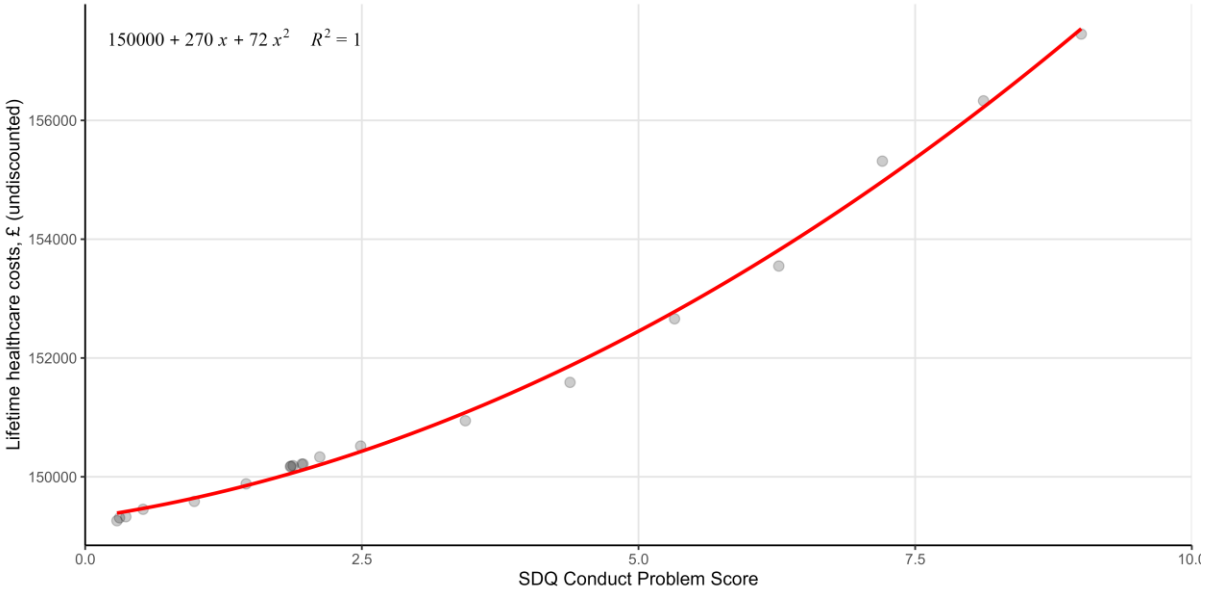
Chapter 6

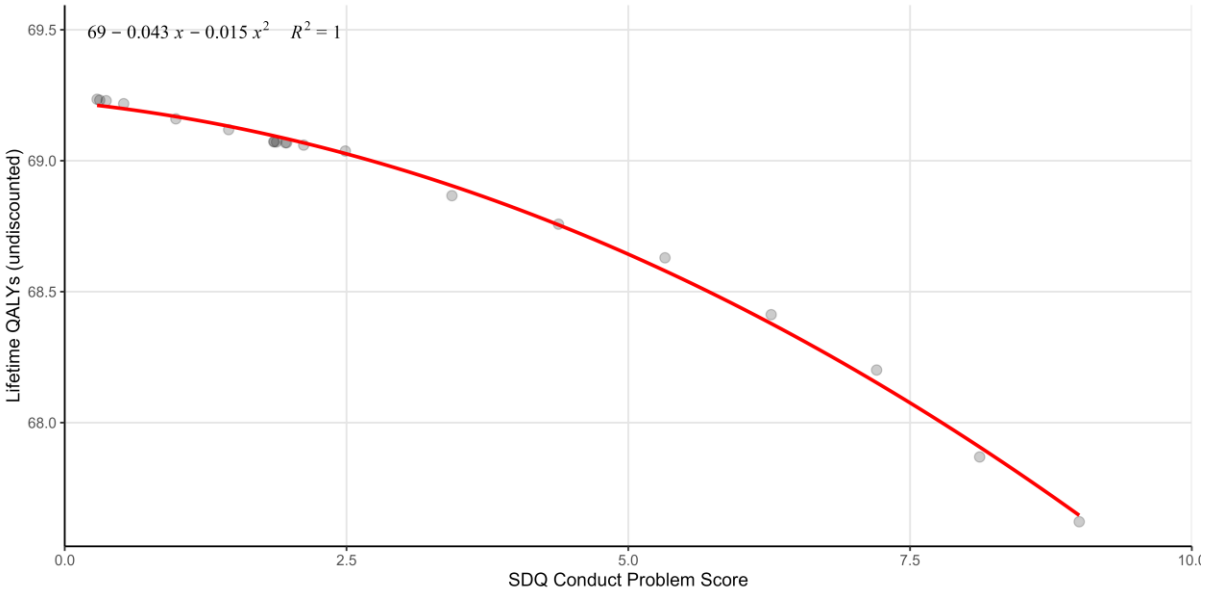
Histograms from the ANOVA of the SDQ Conduct score



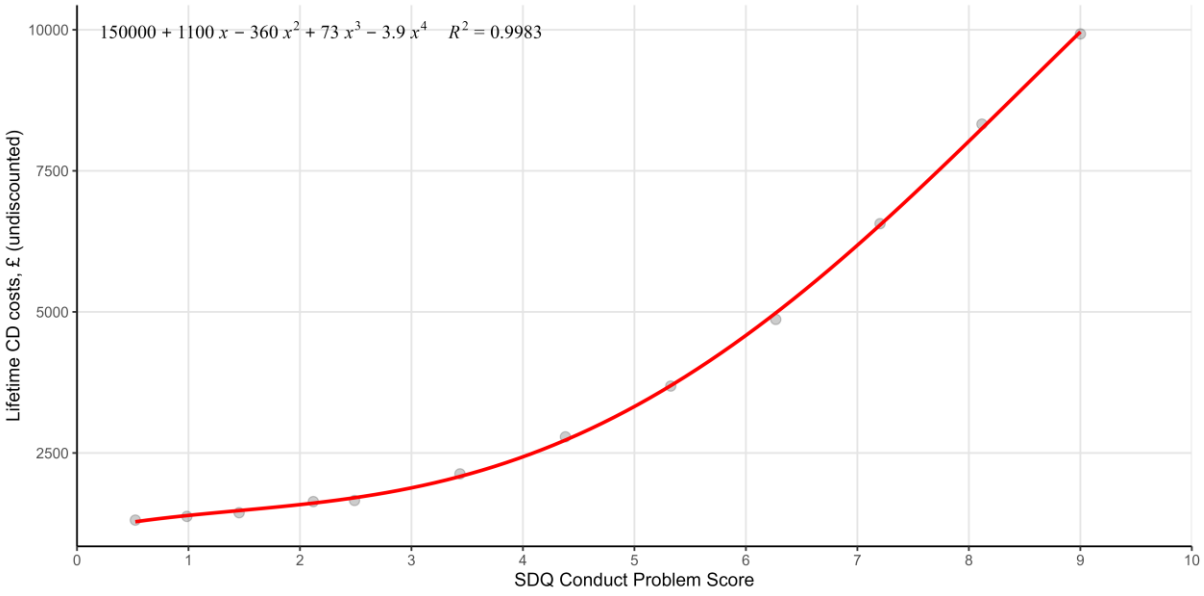
LifeSim results as a function of SDQ score

Undiscounted lifetime healthcare costs and QALYs

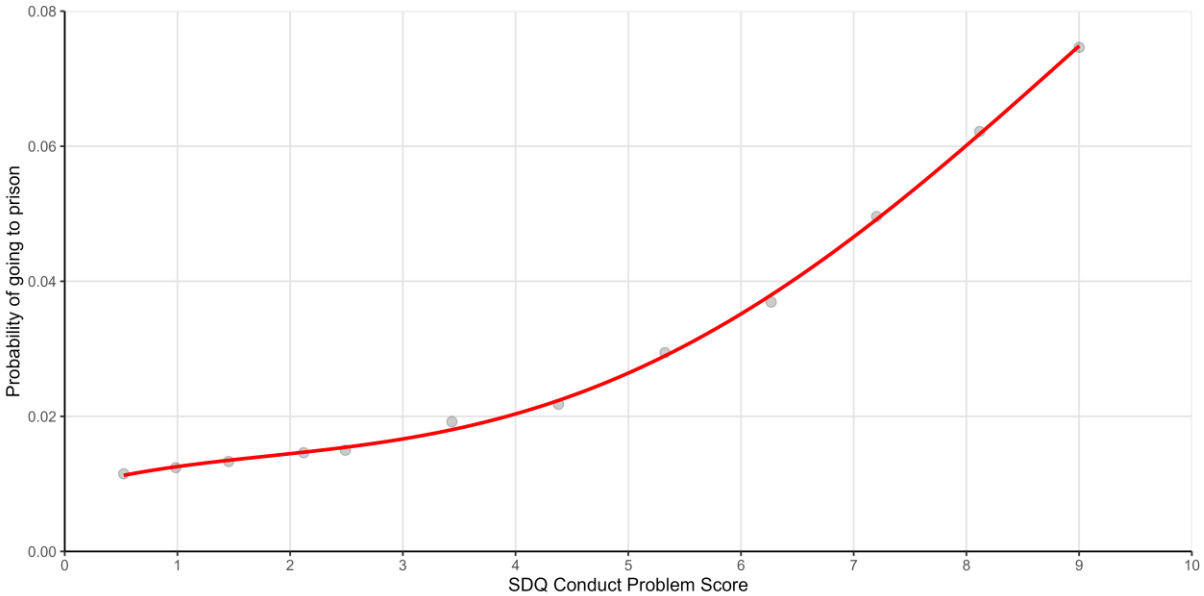




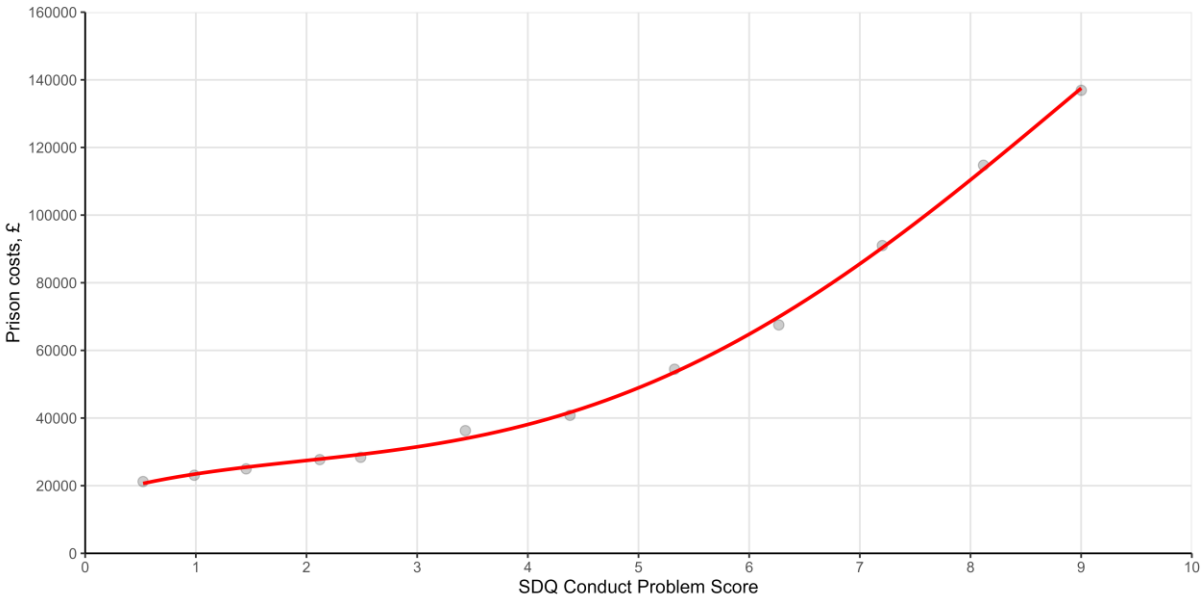
Conduct disorder costs



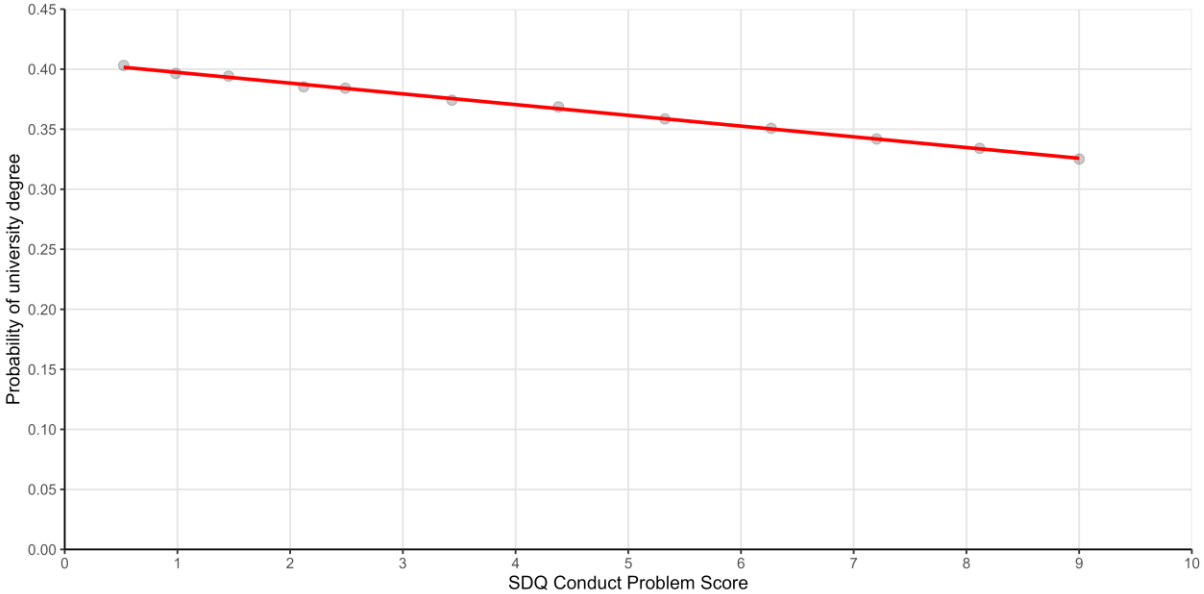
Probability of prison



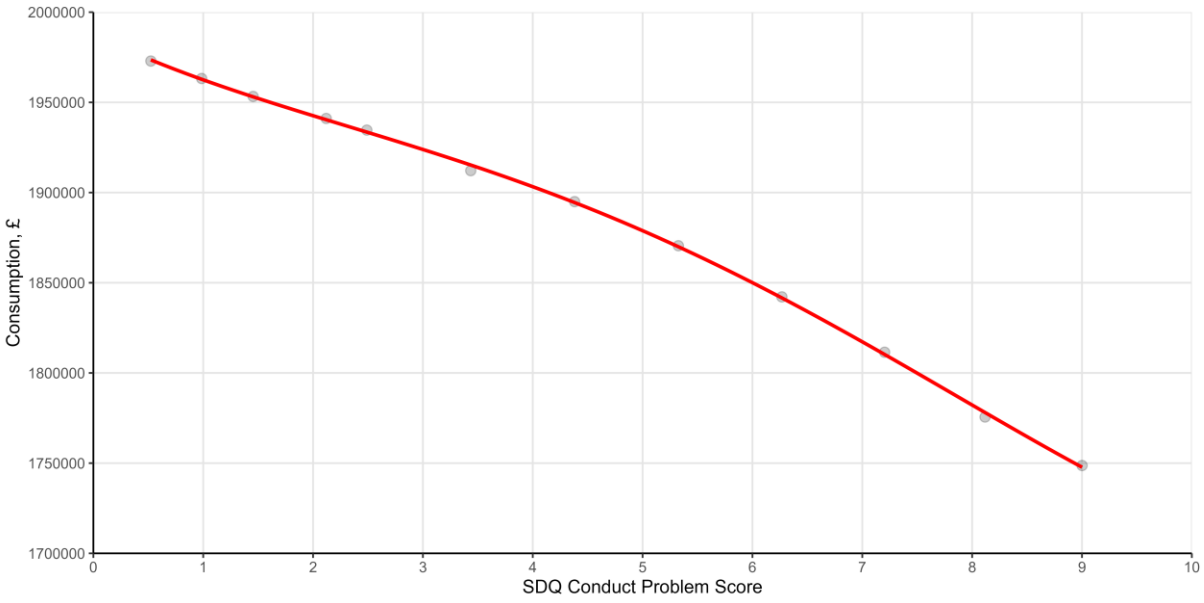
Prison costs



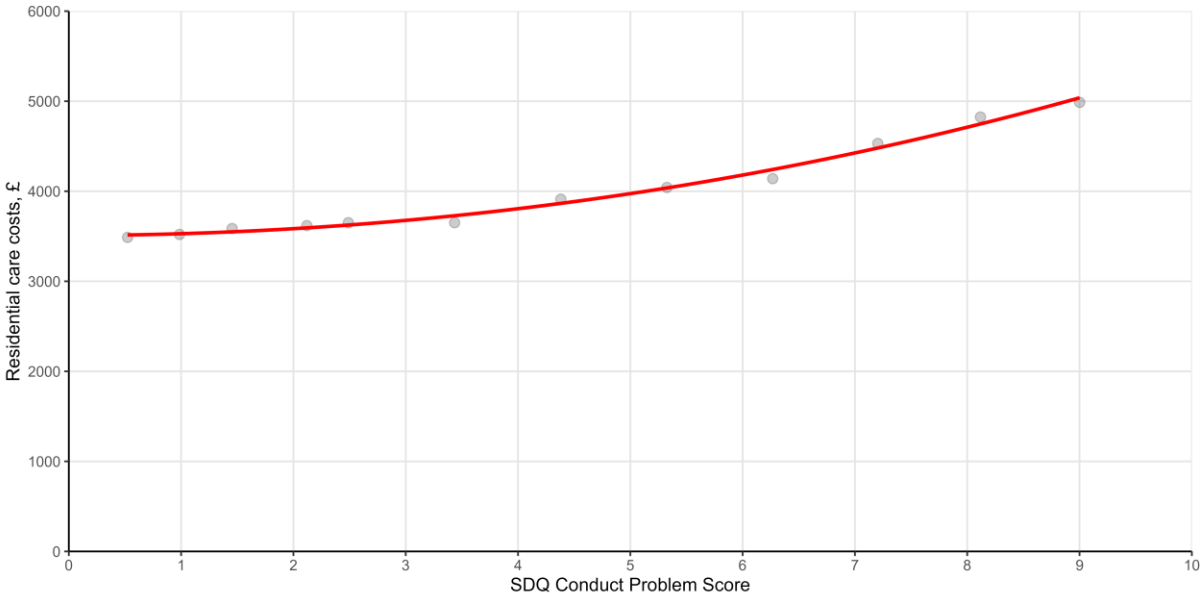
Probability of obtaining a university degree



Lifetime consumption



Residential care costs



E-SEE Steps, within-trial time horizon, healthcare perspective assuming a k = 30,000

	SAU	E-SEE	Incremental
Costs	£1,000	£1,177	£177
QALYs	1.27420	1.26957	-0.0046
ICER	-	-	**Dom**
iNHB	-	-	**-0.0105**

Assuming κ = £30,000

Abbreviations: ICER, incremental cost-effectiveness ration; iNHB, incremental net health benefit; QALYs, quality-adjusted life years; SAU, service as usual.

E-SEE Steps, lifetime time horizon, healthcare perspective

	SAU	E-SEE	Incremental
Costs	£72,483	£72,677	£193
QALYs	42.4986	42.4922	-0.0064
ICER	-	-	**Dom**
iNHB	-	-	**-0.0128**

Assuming κ = £30,000

Abbreviations: ICER, incremental cost-effectiveness ration; iNHB, incremental net health benefit; QALYs, quality-adjusted life years; SAU, service as usual.

Chapter 7

Impact inventory calculations

The calculation of the net benefit of the evaluation in which health and consumptions are incorporated is as follows:

	Health (QALYs)		**Consumption (£)**	
	DE	OC	DE	OC
Population	-0.0064	$0.0129 = \frac{£193}{£15{,}000/QALY}$	-£1,040	£386 = 2·£193
Net benefit (Within-dimension)	**NB_H** = -0.0064 - 0.0129 = **-0.0193**		**NB_C** = -£1,040 - £386 = **-£1,426**	

Assuming κ = £13,000
Abbreviations: DE, direct effects; NB, net benefit; OC, opportunity cost; QALY, quality adjusted life years.

The calculation of the net benefit of the evaluation in which health, consumptions and education are incorporated is as follows. Note, the opportunity costs change here as we now incorporate the marginal productivity of each sector for each outcome.

	Health (QALYs)		**Consumption (£)**		**Education (% graduates)**	
	DE	OC	DE	OC	DE	OC
Population	-0.0064	$0.0153 = \frac{£193}{£15{,}000} + \frac{£50}{£100{,}000}$	-£1,040	£536 = 2·£193 + 3·£50	-0.0010	$0.0044 = \frac{£50}{£20{,}000} + \frac{£193}{£100{,}000}$

Net benefit (Within-dimension)	**NB_H** = -0.0064 – 0.0134 = **-0.0198**	**NB_C** = -£1,040 - £536 = **-£1,576**	**NB_E** = -0.0010 – 0.0044 = **-0.0054**

Assuming κ = £13,000
Abbreviations: DE, direct effects; NB, net benefit; OC, opportunity cost; QALY, quality adjusted life years.

Scenario analysis results using k = £30,000

E-SEE Steps, lifetime time horizon, healthcare perspective

	SAU	E-SEE	Incremental
Costs	£72,483	£72,677	£193
QALYs	42.4986	42.4922	-0.0064
ICER	-	-	**Dom**
iNHB	-	-	**-0.0128**

Assuming κ = £30,000

Abbreviations: ICER, incremental cost-effectiveness ration; iNHB, incremental net health benefit; QALYs, quality-adjusted life years; SAU, service as usual.

E-SEE Steps health and consumption results

	Health (QALYs)		Consumption (£)	
	DE	OC	DE	OC
Population	-0.0064	0.0129	-£1,040	£386
Net benefit (Within-dimension)	NB_H = -0.0128		NB_C = -£1,426	

Assuming κ = £30,000

Abbreviations: DE, direct effects; NB, net benefit; OC, opportunity cost; QALY, quality adjusted life years.

E-SEE Steps health, consumption and education results

	Health (QALYs)		Consumption (£)		Education (% graduates)	
	DE	OC	DE	OC	DE	OC
Population	-0.0064	0.0134	-£1,040	£536	-0.0010	0.0044
Net benefit (Within-dimension)	NB_H = -0.0133		NB_C = -£1,576		NB_E = -0.0054	

Assuming κ = £30,000

Abbreviations: DE, direct effects; NB, net benefit; OC, opportunity cost; QALY, quality adjusted life years.

Social net benefit

$$NB_{SWD} = £60{,}000 \cdot (-0.0133\ QALYs) + (-£1{,}576) + £92{,}308 \cdot (-0.0054\ \%grads) = -£2{,}873$$

Chapter 8

Letter from the Start for Life Unit, DHSC

Dear Reader,

We at the Start for Life Unit in the Department of Health and Social Care contacted Peter Murphy for discussion around the findings from his published systematic literature review entitled 'Methods of assessing value for money of UK-based early childhood public health interventions: a systematic literature review'. The meetings focused on discussing methods that could help strengthen the case for investment in early years and the way in which the findings from the systematic literature review can help inform decision making. The review and subsequent discussions with Peter provided significant insight for the Start for Life Unit into methodological approaches used to demonstrate value for money and how improved consistency of evaluative frameworks used, outcomes and time horizons can improve decision making going forward. As a result of the discussions, future collaboration between the Centre for Health Economics and the Start for Life Unit are being planned.

Note that these views are my own and do not represent the views of the Start for Life Unit or the Department of Health and Social Care.

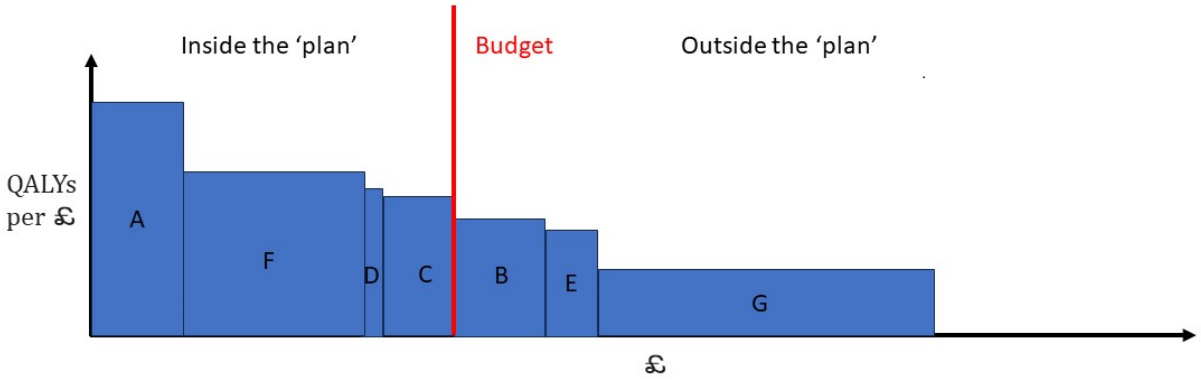
Yours sincerely

Umar Yunis-Guerra, Economic Advisor in the Start for Life Unit

The Start for Life Unit discussed the broader issue of how best to spend an allocated budget on early childhood PHIs. Leaning on methods available, the ‘cost-effectiveness bookshelf’ described by Culyer (Culyer, 2016) was proposed as a starting point to think about the incorporation of health economic evidence in spending decisions. Much of the theory of the bookshelf approach has focused on decision problems in low- and middle-income countries (Love-Koh et al., 2019, Culyer, 2016) but the methods could apply to public health decision-making.

The bookshelf approach allows population health promoters to select a set of interventions that maximise health subject to a budget constraint. Books are used to represent the available interventions and the placing of the books on the bookshelf according to set rules illustrates those interventions that should and should not be funded. An illustration and description of the bookshelf approach is provided in below.

Cost-effectiveness ‘bookshelf’ illustration and description



Imagine a decision maker has a number of different interventions/policies (or ‘books’) to choose from. These are represented by books A to G on the ‘bookshelf’ above. The health generated by each intervention is measured and reported in a common unit of health e.g. QALYs or life years gained. The cost of each intervention is reported in £. The costs should include all of the costs associated with the implementation and delivery of the intervention.

The book height represents the number of QALYs produced per £ (QALYs per £). The width of the book represents the total cost or the ‘budget impact’ (£). The area of the spine of the book therefore represents the number of population QALYs produced.

The approach assumes the decision maker aims to maximise health subject to the budget constraint (represented by the red line or the ‘bookend’).

The bookshelf approach asserts that health is maximised if we stack the books from tallest to shortest from left to right. Those books on the left side of the bookend represent the interventions that should be included in the plan or funded by the budget, and those on the right side represent those that should not be included or funded. The book to the left of the bookend represents the marginal intervention and represents the marginal cost of health. This book represents the book that should be displaced should a more cost-effective intervention be considered for inclusion/funding, which would be represented by the new book being taller than Book C.

A rapid literature search was conducted to find real-world examples of the implementation of the cost-effectiveness bookshelf approach for defining services provided through public funding. The search identified only one example by Ochalek et al. (Ochalek et al., 2018), which was used to support the development of a health benefits package in Malawi. Although the context is different, there are things that

can be learned through this example such as the approach to maximising health and the nature of the evidence required. Ochalek and colleagues approached this decision problem by maximising health subject to the budget constraint. This thesis has outlined the importance of incorporating additional aspects of value therefore the decision problem may need to incorporate health equity and non-health costs and outcomes.

The sections below outlines the proposed use of the bookshelf approach to help inform decision making in the Start for Life Unit. The approach uses hypothetical interventions and evidence to illustrate the method.

Description of the worked example of the bookshelf approach

First, an illustrative example is presented with hypothetical early childhood interventions in which a health care decision-maker is maximising health subject to a budget constraint. Second, this approach will introduce the additional criteria that have been deemed important to capture in child health interventions i.e., long-term costs and outcomes, non-health costs and outcomes and impacts on inequality. Finally, the feasibility of conducting the illustrative analyses with the evidence identified in systematic review in Chapter 2 will be discussed.

Step 1: Applying the bookshelf approach to maximising health in early childhood

To select a set of interventions, the cost-effectiveness bookshelf approach requires a list of all of the potential interventions available for selection. Interventions can range from targeted public health interventions to those for the general population. In all cases, the health outcomes need to be reported in a common numeraire to allow

comparisons to be made as well as the inclusion of the health opportunity cost. The reporting of outcomes of an intervention without a common unit of health means comparisons cannot be made. For the purpose of this analysis, QALYs are used as the common unit of health to reflect health decision making in England and Wales (National Institute for Health Care Excellence, 2022). The illustrative example considers 10 hypothetical early childhood interventions shown in Table 35.

The interventions included those for health promotion, breast feeding, oral health, hearing/vision screening, vaccination and new-born screening. They were for a range of ages from new-borns to 5-year-olds and were a mixture of targeted and universal interventions. It is assumed the evidence for each of these included intervention and comparator costs and QALYs; the size of the eligible population; a measure of equity impact (based on change in SII); and educational impact (based on change in % of individuals graduating from university).

Table 35

	Population (a)	Intervention category (b)	Universal/ Targeted (c)	Intervention (d)	Comparator (e)	Intervention costs (f)	Comparator costs (g)	Intervention QALYs (h)	Comparator QALYs (i)	Incremental costs (j)	Incremental QALYs (k)	ICER (l)
1	1 year olds	Health promotion	Targeted	Preschool Health	Usual practice	£150	£30	0.06	0.052	£120	0.008	£15,000
2	Newborns	Breast feeding	Targeted	Breast feeding promotion	Routine care	£648	£100	0.09	0.07	£548	0.02	£27,400
3	5 year olds	Oral health	Targeted	Five Smile	Routine care	£155	£100	0.4	0.22	£55	0.18	£306
4	4 year olds	Hearing/vision screening	Universal	Hearing Screening	No screening	£10	£2	0.98	0.97	£8	0.01	£800
5	1 year olds	Vaccination	Universal	VZV Vaccination Programme	No vaccination	£258	£159.12	0.0052	0.0017	£99	0.0035	£28,286
6	Newborns	Vaccination	Universal	MenB1 - meningitis B vaccine	Routine vaccination strategy	£15	£10	0.0008	0.0002	£15	0.0008	£18,750
7	Newborns	Vaccination	Universal	MenB2 - meningitis B vaccine	Routine vaccination strategy	£31	£8	0.0002	0.0002	£31	0.0002	£155,000
8	Newborns	Newborn screening	Universal	CF Screening	No screening	£600	£100	0.9	0.6	£500	0.3	£1,667
9	2 year olds	Health promotion	Universal	Toddler Good Food	No promotion	£500	£100	0.005	0.004	£400	0.001	£400,000
10	2 year olds	Injury prevention	Targeted	Safe House	Usual care	£21,000	£19,000	1	0	£2,000	1	£2,000

The hypothetical evidence shown in Table 1 reflects the nature of evidence available in the literature. For example: the evidence is estimated across a number of different populations; there are competing interventions for the same population and disease area; some interventions are targeted and others universal; and the comparators differ.

The first step is to estimate the net health benefit (NHB) for each intervention listed in the table using the following formula:

$$NHB = Incremental\ QALYs - \frac{Incremental\ costs}{\lambda}$$

Where λ represents the policy threshold, which may represent the health opportunity cost. For the purpose of this illustrative example, λ is assumed to be £20,000.

Particular attention needs to be paid to the comparator for the estimation of the incremental costs and QALYs. If the decision problem allows the prescription of a completely new set of interventions then the comparator should be 'no intervention'. If, however, the decision problem is allowing new interventions to be considered in place of specific existing interventions (e.g. the current standard of care) then the comparator should represent the existing standard of care with incremental costs and QALYs estimated relative to this (Culyer, 2016).

For the purpose of this analysis, it is assumed the Start for Life Unit are funding an entirely new set of interventions meaning incremental costs and QALYs should be relative to a 'no intervention' strategy. Table 3 shows a modified version of Table 2 in which the incremental costs and QALYs are estimated relative to 'no intervention'. In

the case of interventions 4, 5, 8 and 9, these are already incremental on a ‘no intervention’ strategy and therefore the incremental costs and QALYs are retained. For all other interventions it is assumed the comparator costs and QALYs have a value of 0 meaning the intervention costs and QALYs can be used to represent the incremental values.

Table 36

(a)	Intervention costs (f)	Comparator costs (g)	Intervention QALYs (h)	Comparator QALYs (i)	New incremental costs (m)	New incremental QALYs (n)	NHB (per person) (o)	Population size (p)	NHB (population) (q)
1	£150	£0 assumed	0.06	0 assumed	£150	0.06	0.0525	263,956	13858
2	£648	£0 assumed	0.09	0 assumed	£648	0.09	0.0576	255,134	14696
3	£155	£0 assumed	0.4	0 assumed	£155	0.4	0.3923	281,356	110362
4	£10	£2	0.98	0.97	£8	0.01	0.0096	687,213	6597
5	£258	£159.12	0.0052	0.0017	£99	0.0035	-0.0015	659,890	-957
6	£15	£0 assumed	0.0008	0 assumed	£15	0.0008	0.0001	637,834	32
7	£31	£0 assumed	0.0002	0 assumed	£31	0.0002	-0.0014	637,834	-861
8	£600	£100	0.9	0.6	£500	0.3	0.2750	637,834	175404
9	£500	£100	0.005	0.004	£400	0.001	-0.0190	681,032	-12940
10	£21,000	£0 assumed	1	0 assumed	£21,000	1	-0.0500	272,413	-13621

The incremental costs and QALYs reflect the per person estimates, therefore the result is the per person NHB. This can be scaled up to the population level based on the eligible population size which is estimated based on the age of the cohort and whether the population is targeted or universal. The population for each age group is obtained from the ONS (Office for National Statistics, 2024). If the intervention is targeted then it is assumed the eligible population is 2/5 of the population in the age band (i.e. to represent the two most deprived quintiles receiving it).

The population net health benefit (q) is estimated by multiplying the per person net health benefit by the size of the eligible population (p). The interventions are then ranked in descending order according to the per person net health benefit. The population costs (r) provide estimates of the productivity of the intervention (i.e. the NHB) however the costs used for the purpose of budget allocation should be the financial costs borne by the health sector over the relevant budgetary time period (s). This has been assumed to be 3 years to reflect typical budgetary time horizons in public health decision making (Howdon et al., 2022). Note, cost-effectiveness studies in the literature may report the cost over the lifetime of the individual therefore estimating the costs to match a budgetary time horizon (i.e., 3 years in this example) may be difficult. The population cost over the three years is estimated (t). The cumulative cost (u) indicates the point at which the budget has been spent. It is assumed interventions are divisible.

Intervention Number (a)	NHB (per person), QALYs (o)	NHB (population), QALYs (q)	Cost (population) (r)	Individual financial cost over 3 year time horizon (s)	3-year financial cost of the intervention (t)	Cumulative financial cost (u)
3	0.392	110362	£43,610,180	£11	£7,033,900	£7,033,900
8	0.275	175404	£382,700,400	5	£11,481,012	£18,514,912
2	0.058	14696	£165,326,832	25	£1,275,670	£19,790,582
1	0.053	13858	£39,593,400	50	£2,903,516	£22,694,098
4	0.010	6597	£6,872,130	2	£34,360,650	£57,054,748
6	0.000	32	£9,567,510	1	£637,834	£57,692,582
7	-0.001	-861	£19,772,854	12	£7,654,008	£65,346,590
5	-0.001	-957	£170,251,620	18	£1,319,780	£66,666,370
9	-0.019	-12940	£340,516,000	25	£17,025,800	£83,692,170
10	-0.050	-13621	£5,720,673,000	10	£2,724,130	£86,416,300

The approach described above bases the rank ordering and the budgetary impact of each intervention on the point estimate and has not accounted for uncertainty. There will be inherent uncertainty in the results introduced at all stages of the evaluative process (Drummond et al., 2015) and basing decisions on point estimates alone will prevent policy makers from having the full picture. (Briggs, 2000)

The cost-effectiveness bookshelf is populated using published estimates of costs and QALYs from the literature meaning analysts are limited by the availability of the evidence. The uncertainty around the costs and benefits may be reported in the literature in the form of sensitivity analyses meaning it may be possible to reproduce the bookshelf using the 'most pessimistic' and 'most optimistic' results which reflect the lower and upper bounds of the incremental costs and QALYs. A recent addition to the literature which relies on value of information (VOI) analyses (Wilson, 2015), known as the VOI-HBP tool (Schmitt et al., 2021) quantifies the value of resolving the uncertainty through research in terms of population NHB.

The optimisation described takes a unisectoral health maximisation approach and assumes the health budget reflects the resources allocated to healthcare; the cost of the intervention falls entirely on the health budget; and interventions are evaluated solely on their impact on population health (Remme et al., 2017). However, there may be many interventions that do not satisfy the above criteria namely public health interventions for children (see Chapters 1 to 6). The potential additional aspects of value that broaden the objective function from health maximisation are considered below.

Step 2: Applying the bookshelf approach to maximising additional benefits in early childhood

There may be a number of additional aspects of value specific to early childhood interventions that decision makers may want to consider beyond simply maximising health. These may include but are not limited to: improving health equity and

improving non-health outcomes e.g. educational attainment, minimising criminal justice system costs or productivity. The systematic review reported in Chapter 2 revealed the availability of the health equity and non-health outcomes reported in the literature of economic evaluations of early childhood public health interventions.

Health Equity

Let us assume that health equity information was reported for the hypothetical interventions reported in this case study. The health equity information is reported as change in the slope index of inequality (SII). As described in Chapter 5, the SII is the coefficient of a simple one variable regression of QALE (Q) on the fractional rank (r) and forms the inequality measure reported in a distributional cost-effectiveness analysis. An SII of 0 indicates no inequality and the higher the SII, the greater the health gradient (or inequality) across the distribution. A reduction in the SII therefore indicates the existing inequality in health has been reduced. The SII is measured across social groups based on socioeconomic position (SEP). The SEP groups have not been defined in this illustrative example but the measure of SEP should be consistent across all evaluations. See Chapter 4 for a discussion of SEP. Table 4 shows changes in the SII for the hypothetical interventions in the case study. Following a similar prioritisation approach as shown in Step 1, the interventions in Table 4 have been ranked from highest to lowest according to a change in the SII.

Table 37

Intervention Number (a)	Change in SII ($x10^4$) (v)	3-year financial cost of the intervention (t)	Cumulative financial cost (u)
3	1.08	£7,033,900	£7,033,900
5	0.79	£1,319,780	£8,353,680

1	0.3	£2,903,516	£11,257,196
10	0.1	£2,724,130	£13,981,326
6	0.06	£637,834	£14,619,160
9	0.04	£17,025,800	£31,644,960
2	0.02	£1,275,670	£32,920,630
8	0.001	£11,481,012	£44,401,642
7	-0.41	£7,654,008	£52,055,650
4	-0.45	£34,360,650	£86,416,300

Abbreviations: SII, slope index of inequality.

Note, in this table a positive change in SII indicates a reduction (an improvement) in the existing SII.

Following the same approach as in Step 1, the budgetary costs of each intervention allow us to calculate the cumulative cost, which indicates the point at which the budget has been spent. It is assumed interventions are divisible. It is assumed that interventions are evaluated solely on their impact on improving health inequalities. Under this assumption, interventions 3, 5, 1, 10, 6, 9, 2, 8 and a proportion of 7 are selected to maximise health subject to the health sector budget, which has been set at £50m.

Non-health costs and benefits

Public health interventions may be expected to have impacts that fall outside of the health care sector. We consider the interventions introduced in the illustrative example to be public health interventions, in that they have public health as their primary objective but they may have impacts outside of the health care sector, referred to as ‘spillover effects’. Note, these are distinct from ‘non-health interventions’, which do not have health as a primary objective but do have impacts

on the health sector (Remme et al., 2017). The incorporation of ‘public health interventions’ into the cost-effectiveness bookshelf relies on different assumptions compared to ‘non-health interventions’.

Let us assume that each intervention has captured non-health benefits in the form of educational benefits. These are reported in units of a change in the proportion of university graduates as a result of the intervention. Following a similar prioritisation approach as above, the interventions in Table 5 have been ranked from highest to lowest according to the educational benefits and the 3-year financial costs falling on the health sector are estimated.

Table 38

Intervention Number (a)	Education benefits, change in % of university graduates (w)	3-year financial cost of the intervention (t)	Cumulative financial cost (u)
10	5.00%	£2,724,130	£2,724,130
5	3.00%	£1,319,780	£4,043,910
1	2.00%	£2,903,516	£6,947,426
2	0.50%	£1,275,670	£8,223,096
7	0.40%	£7,654,008	£15,877,104
8	0.30%	£11,481,012	£27,358,116
3	0.10%	£7,033,900	£34,392,016
9	0.01%	£17,025,800	£51,417,816
6	0.00%	£637,834	£52,055,650
4	-1.00%	£34,360,650	£86,416,300

It is assumed that interventions are evaluated solely on their educational impacts. Under this assumption, interventions 10, 5, 1, 2, 7, 8, 3 and a proportion of 9 are selected to maximise health subject to the health sector budget, which has been set at £50m. The educational outcomes captured in Table 5 can not be considered the true productivity of the interventions as they fail to account for the education opportunity cost of spending. The ranking of the educational outcomes of the interventions could not be considered as the educational productivity of the intervention as it fails to account for the education opportunity cost of funding this educational intervention. This assumes a health decision maker has education maximisation as their objective. Note, there may be an education decision-maker perspective that ranks entirely on education outcomes alone.

The results of the three optimisations are reported in Figure 1 to Figure 3. Figure 1 shows that a decision maker maximising health subject to the budget would select interventions 3, 8 and 2 (see appendix for descriptions of the interventions). However, if maximising health equity a decision maker would choose to fund interventions 3, 5, 1, 10, 6 and part of 9, assuming interventions are divisible which may raise horizontal equity concerns. Finally, a decision maker maximising educational benefits would select interventions 10, 5, 1, 2, 7 and part of 8. It is important to note this final optimisation assumes a health decision maker is solely maximising educational benefits which is unlikely to reflect real life.

Figure 1 Cost effectiveness bookshelf when maximising health

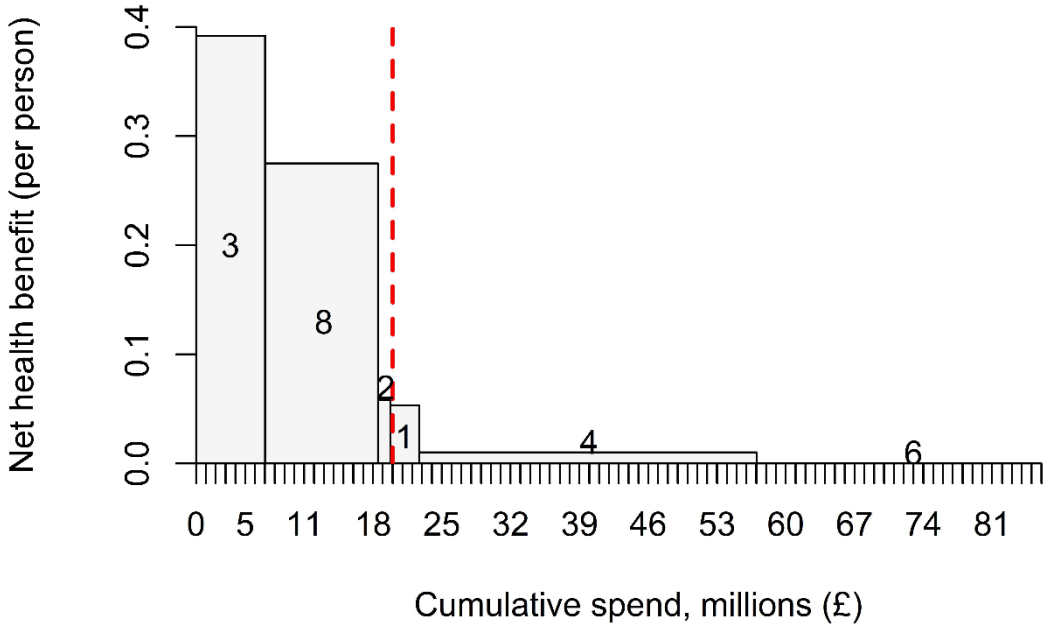


Figure 2 Cost effectiveness bookshelf when maximising health equity

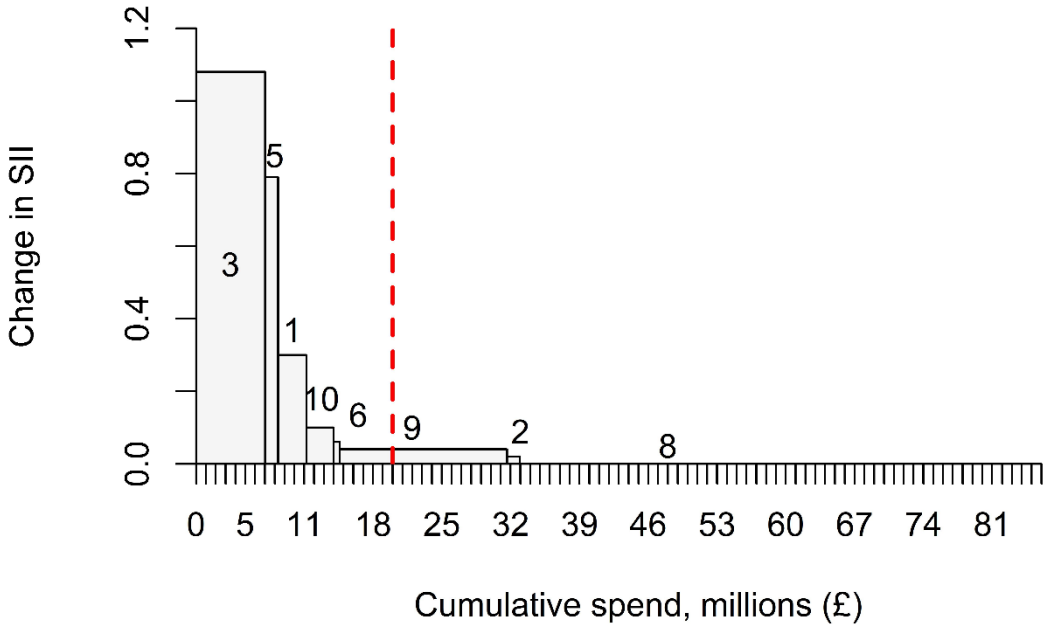
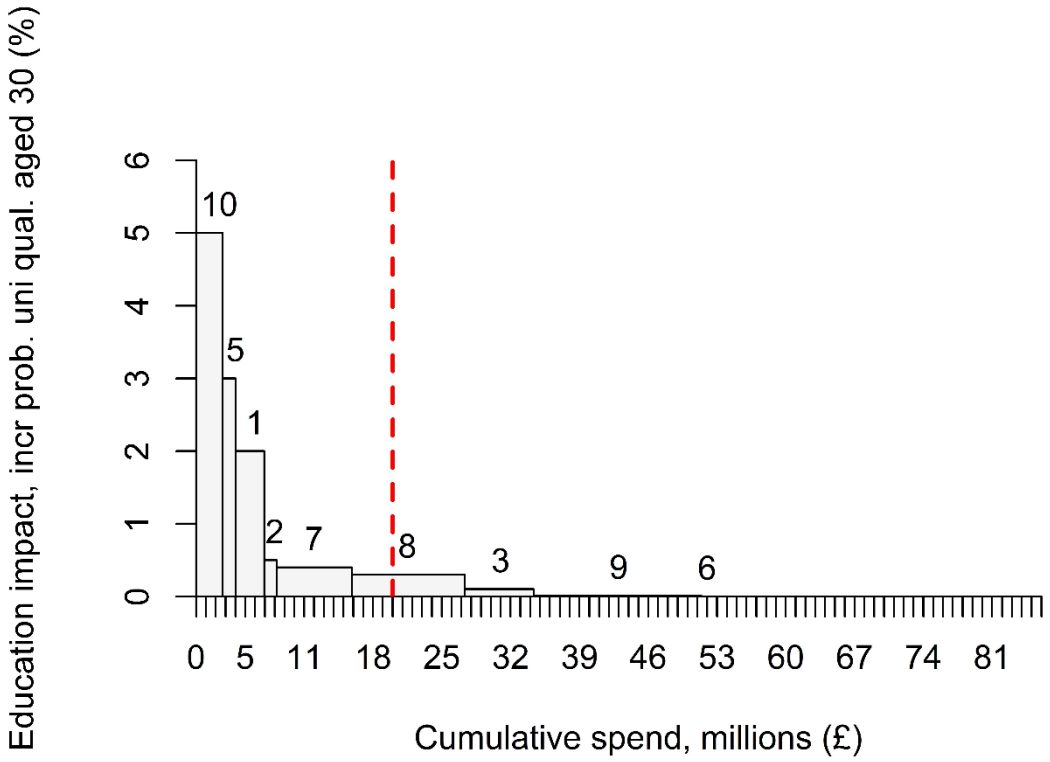


Figure 3 Cost effectiveness bookshelf when maximising education



The illustrative optimisations show the varying results when using the bookshelf method to consider different optimisations. Table 6 shows how the rank ordering of the interventions change for each of the optimisations. If a decision maker chooses to allocate resources based on one outcome in their objective function (i.e., maximising health or maximising health equity) then they should see Figure 1 to Figure 3 and select accordingly. If, however, a decision maker seeks to maximise more than one outcome, there is currently no prescribed method as how to do that. They may consider choosing the interventions that are consistently considered to be 'inside the plan'. They may consider the rank orderings of each intervention in the three optimisations and select those that are consistently ranked high across three outcome measures. For example, Table 6 shows how the rank orderings of the

interventions change across outcome measures and how the interventions 'inside the plan' differs.

Table 6 – Interventions funded using the bookshelf approach

Rank	Health	Inequalities	Education
1	3	3	10
2	8	5	5
3	2	1	1
4	1	10	2
5	4	6	7
6	6	9	8
7	7	2	3
8	5	8	9
9	9	7	6
10	10	4	4

Yet, caution should be used as resource allocation decision-making based on rank ordering or league tables has been criticised (Drummond et al., 1993). Further, it is unclear how a decision makers should weight the different outcome measures and attributing no weighting would imply a weight of 33.3% to each outcome. This approach begins to overlap with MCDA (Baltussen et al., 2019, Thokala et al., 2016, Marsh et al., 2016), which has been described and criticised in Chapter 3 and Section 8.3.2.

This illustrative example shows the Start for Life Unit and a wider audience that the process of spending a budget in which a decision maker maximises more than just health outcomes is difficult and further research is needed. The literature has not yet considered how a decision-maker may seek to allocate resources when maximising health and health equity/educational attainment. A recent study by Lofgren et al.

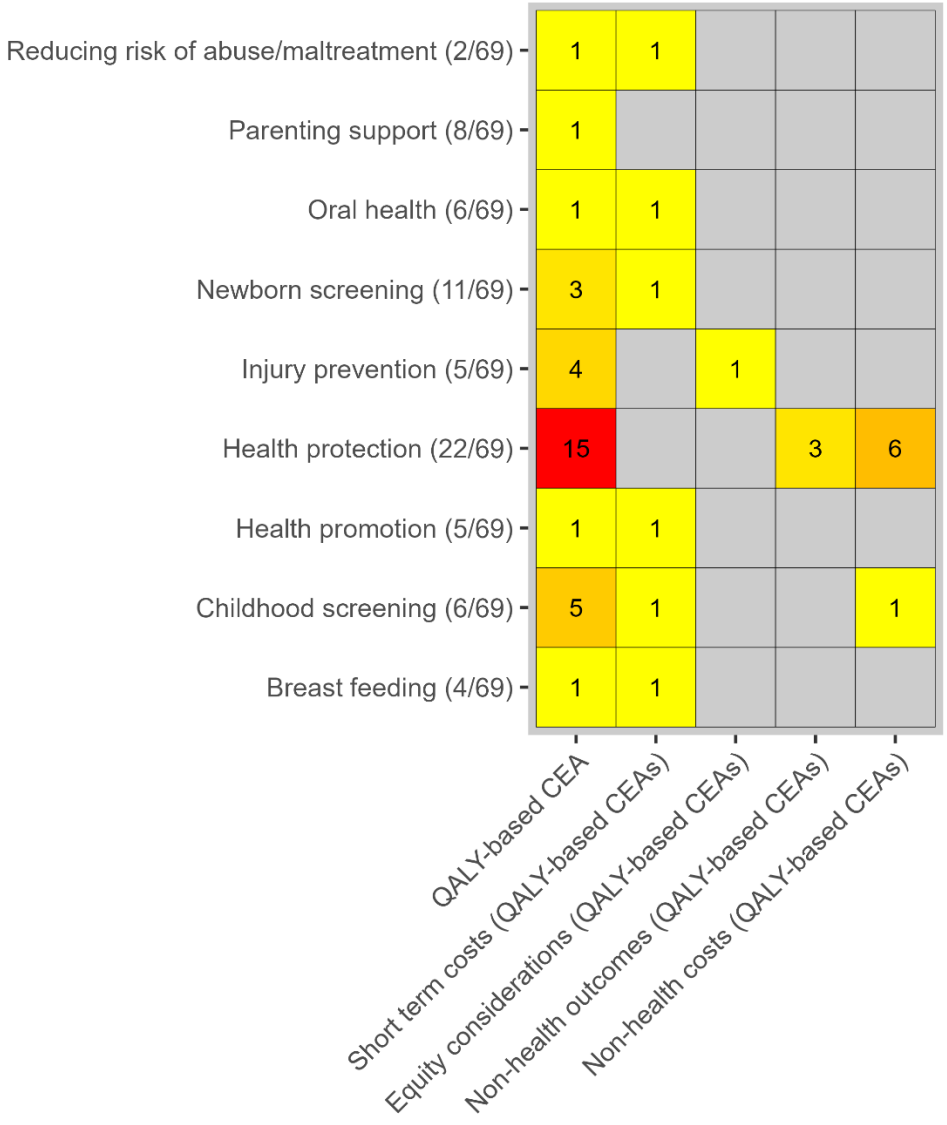
(Lofgren et al., 2021) has demonstrated how a health benefit package in Malawi could be developed when considering maximising health and financial risk protection. Indeed, the process of maximising health-alone is challenging. For example, costs are required for a budgetary time horizon (e.g., 3 years in this example) and the extraction of this from typical cost-effectiveness literature may be challenging as costs are rarely reported in disaggregated terms. In addition, evidence of an intervention in the literature is likely to be incremental evidence generated with reference to a comparator. The comparator provided in the literature may not be generalisable with the comparator being considered in the decision problem.

Real world evidence base

The systematic review conducted in Chapter 2 identified all of the health economic evidence of early childhood PHIs available in a UK context. The question then becomes whether this evidence could be used to select interventions that a decision-maker may choose to spend their budget on using the principles above. Of the 77 evaluations identified, only 32 reported outcomes in QALYs; a common outcome is required to implement the bookshelf (Culyer, 2016). Figure 4 shows an evidence map of the 32 studies included in the SLR (shown in the 'QALY-based CEA' column). The figure then shows how many of the 32 have short-term costs; equity considerations; non-health outcomes and non-health costs, which would all be required for a decision-maker to implement the bookshelf approach described above. The results reveal only six studies had short-term costs, only one study had equity considerations, and only a small proportion included costs and outcomes. The relevance of the evidence base is therefore limited for such a decision-making

approach in a UK context. Future research must consider the evidence requirements of decision-makers if resource allocation of early childhood health interventions is to incorporate health equity and a broader perspective.

Figure 4 – Evidence map of the studies identified in the systematic review



Conclusion

The involvement of the Start for Life Unit in the research process has highlighted the significance of the findings beyond the academic realm. It has also shown the short comings in the methods and the evidence when comparing the requirements of national style decision makers and those tasked with local public health decisions (Howdon et al., 2022, Hinde et al., 2022). The Start for Life Unit's interest and active participation underscore the potential of the research conducted throughout this thesis to contribute to evidence-based policymaking and real-world applications.

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