**Economic Analysis Plan**

**Main trial analysis**

**Enhancing Social-Emotional Health and Wellbeing in the Early Years (E-SEE):**

**A Community-based Randomised Controlled Trial and Economic Evaluation of the Incredible Years Infant and Toddler (0-2) Parenting Programmes**

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# Overview

This document outlines the economic analysis plan for the assessment of the parenting programme evaluated in the main Enhancing Social-Emotional Health and Wellbeing in the Early Years (E-SEE) trial. E-SEE is a community-based randomised controlled trial evaluating the Incredible Years Infant (IY-I) and Toddler (IY-T) Parenting Programme delivered as a proportionate universal intervention compared with services as usual (SAU) for parents of children aged 0-2 years from predominately disadvantaged areas in England. The IY intervention comprises The Incredible Babies book (offered to everyone), and IY-Infant (10 weeks, 2hours/week) and IY-Toddler (12 weeks, 2hours/week) group programmes offered to parents above a predefined threshold on the Patient Health Questionnaire (PHQ-9) and/or the Ages and Stages Questionnaire: Social Emotional, Second Edition (ASQ:SE-2).

The economic analysis of the E-SEE trial will assess the cost-consequences and the cost-effectiveness of providing the proportionate delivery of the IY intervention compared with services as usual [1]. Outcomes will include quality-adjusted life-years (QALYs), in line with current UK guidance for economic evaluations [2], and other measures of parental and child social and emotional wellbeing as defined by PHQ-9 and ASQ-SE-2 scores. The analysis will be performed from a public sector perspective, while a wider perspective also encompassing the financial impacts on the individuals themselves will also be considered (e.g. wage losses due to absence from work and transportation expenses). The base case analysis will be performed over the 18 month trial period. If differences exist between trial arms which may result in the cost-effectiveness being expected to differ over the longer term, extrapolation of trial results will be conducted with longer time horizons explored as scenarios. Cost-effectiveness results will be expressed in terms of incremental cost-effectiveness ratios, showing the cost per additional QALY compared to the next less costly strategy, and incremental net health benefits to show the difference between the health generated with a strategy and the health which could be generated elsewhere in the health care system using the same resources (at thresholds of £13,000, £20,000 and £30,000 per QALY [2, 3]. Cost consequence results will also be presented.

# Study design and interventions

Primary caregivers and co-parents of children aged 8 weeks or less at baseline were identified by self-referral, children’s centre staff, health visitors and parent advisory committees in predominately disadvantaged areas in England. At baseline, all parents were randomly allocated to either a proportionate delivery model of the IY parenting programme or to SAU.

At baseline, all intervention parents received a book (The Incredible Babies Book) (universal level). Depending on level of need, as indicated by parent depression scores at follow up 1 (PHQ-9 score at 2 months), parents were invited to participate in the IY-I programme. Depending on level of need, as indicated by parent depression scores at follow-up 2 (PHQ-score at 9 months) or elevated scores of child social and emotional problems (ASQ:SE2 at 9 months), parents were invited to participate in the IY-T programme.

Briefly, the parenting programmes IY-I and IY-T have been developed for parents of children aged 0-3 years, and are all accompanied by a book, reflecting the content of the programmes. The book provides information to parents on how to promote and understand a baby’s physical, emotional and language development. It includes activities and journal pages. The IY-I group-based programme involves parents attending a 2-hour session, once a week, for 10 weeks. The IY-T group-based programme involves parents attending a 2-hour session, once a week, for 12-14 weeks. Both the IY-I and the IY-T are manual-based and delivered in a group format by two trained facilitators.

# Data collection

Both outcome and resource use data will be collected at baseline (postpartum), 2, 9 and 18 months follow-up post-baseline.

# Outcomes

A range of primary and secondary outcomes for both parents and children will be collected throughout the trial. The economic analysis will report a descriptive summary for each child and parental outcome deemed relevant (see below) and present cost-effectiveness and cost-consequence analyses.

**Primary outcomes**

The following primary outcomes will be presented in a cost-effectiveness analysis framework consistent with current UK guidance for economic evaluations [2]. The health-related quality of life weights and survival data will be combined to estimate QALYs over the 18 month trial period for the children and parents [4]. An area under the curve approach using linear interpolation between time points will be used when estimating QALYs for both children and parents.

***Children***

Paediatric Quality of Life Inventory (PedsQL) Infant – a measure of health-related quality of life (HRQoL) for children aged 13-24 months, completed by the primary caregiver at the 18 month FU only. Currently, it is not possible to directly estimate HRQoL scores for the estimation of quality-adjusted life-years (QALYs) from PedsQL scores. Instead mapping methods will be used to generate EQ-5D utility scores from the PedsQL scores. Given that PedsQL was not completed at baseline (due to the measure being inappropriate at this age) we will explore alternative assumptions for baseline HRQoL of infants for the estimation of QALYs including: i) the HRQoL score being constant over the 18month duration, and; ii) the baseline score for QALY estimation being the mean value across all infants measured at 18 months.

***Parents***

EQ5D-5L – Completed by the primary caregiver at every time point (baseline, 2, 9 and 18 months FU). EQ5D-5L measures changes in HRQoL in parents using five levels of severity across five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) [5, 6]. EQ5D scores can be transformed into HRQoL scores by using UK social tariffs obtained from a sample of the general population which assigns values to each health state described by the EQ5D [7]. Consistent with guidelines for economic evaluation, we will map EQ5D-5L scores to HRQoL values based on a population survey using the EQ-5D-3L instrument and estimate QALYs using these values [8]. Patient HRQoL scores will be used to estimate QALYs over the 18 month FU period of the trial using the area under the curve method. As a scenario analysis we will directly use EQ5D-5L scores to estimate QALYs.

**Secondary outcomes**

The following secondary outcomes will be presented in a cost-consequence analysis framework, which is relevant to inform decision-makers where costs and outcomes of an intervention fall on different domains.

***Children***

*Strengths and Difficulties Questionnaire* (SDQ) – assesses prosocial and emotional and behavioural problems in children. The preschool version is designed for use with children aged between 2 and 4 years. It is completed by the primary caregiver at the 18 month FU, and therefore prior to the age group the SDQ has been validated for [9].

*Ages & Stages Questionnaire – Social and Emotional (ASQ:SE-2)* – a measure of social and emotional wellbeing that is used as the primary outcome for children in the trial. Completed by the primary caregiver at every time point: baseline, 2, 9 and 18 months FU [10].

***Parents***

*Patient Health Questionnaire (PHQ-9)* – a measure to establish the level of depression and assess need for the IY-I and IY-T levels of the intervention, completed by the primary caregiver at every FU time point [11].

# 3.2. Costs

Costs in both trial arms will be estimated from a public sector perspective, and a broader perspective encompassing the financial impacts on the individuals. Costs will be calculated for each participant in the trial based on resource items and associated relevant unit costs.

# 3.2.1. Intervention cost

A micro costing framework will be used to estimate the cost of delivering the IY intervention. Intervention costs will include the set-up and training of practitioners and costs associated with the delivery of the interventions (e.g. materials, time contacting caregivers outside of the sessions, number and duration of sessions, administrative time, transportation costs, provision of crèche facilities, venue rental, food and catering, supervision time etc.). This information will be retrieved from the trial manager/project documentation. For the base case, the full costs of training practitioners will be included. If the intervention was widely implemented, practitioners would be able to deliver the intervention to multiple groups and over a longer time period, as such alternative assumptions will be explored about the average cost per parent of the training of practitioners.

# 3.2.2. Resource use

The economic consequences of compromised outcomes in early childhood are likely to fall on different sectors of the society, such as the health care and social care sectors, as well as incur costs to families and carers. Data on resources used by participants will be collected at each measurement time point throughout the trial, baseline, 2, 9 and 18 months FU, through a face-to-face interview with the primary caregiver. The data collection is done retrospectively, via the administration of the Revised Client Service Receipt Inventory (CSRI) [12, 13], which asks about service contacts over a time period preceding the date of the interview. At baseline, the CSRI will cover the preceding six months, and at the remaining measurement points, the duration of the recall period will be denoted by the length of time since the last CSRI administration.

The CSRI collects data on resource use in the public sector (with a particular focus on healthcare) and out of pocket expenses incurred by caregivers and absence from employment of caregivers. The following items are included in the questionnaire: childcare, parenting classes, visits to general practitioner, nurse, district nurse, psychologist, psychiatrist, other counsellors/therapists, social worker, mental health nurse, accident and emergency, outpatient visits and inpatients stays, and health visitors. It also includes absence from employment and transportation questions. Descriptive statistics per trial condition and resource item/type of provider will be presented for each measurement point over the trial period.

# 3.2.3. Unit costs

Unit costs for the relevant resources will be sourced from published sources. Resources related to the health and social care sector will be costed using published national sources, such as the NHS reference costs [14] and the Personal Social Services Research Unit (PSSRU) Unit Costs of Health and Social Care [15]. Unit costs for childcare will be retrieved from a national survey on costs of childcare [16]. Productivity losses due to absence from work will be calculated using the human capital approach where caregivers time off work is multiplied by their salary [17]. Resources will be costed using the latest reference year available at the time of analysis (expect to be 2018/19).

# 3.2.4. Total costs

Average costs per caregiver, per child and per family for each trial arm will be summarised and presented both by item and by aggregated total cost estimates at each measurement point during follow up and over the full 18 month trial period. Costs will be calculated for each participant in the trial as the product of resource units by relevant unit costs. Total cost for the intervention arm will also include the total cost of setting up and delivering the intervention.

# Methods for analysis

The within trial analysis will be conducted on an intention to treat (ITT) basis and encompass cost-effectiveness analyses using the primary outcomes outlined in section 3.1, namely, QALYs measured using the EQ-5D-5L for parents and PedsQL scores for children, both mapped onto EQ-5D-3L scores (via crosswalk algorithms). A secondary analysis will include a cost-consequence analysis presenting costs and outcomes in a disaggregated format, i.e. ASQ:SE-2 and SDQ for children and PHQ-9 for parents (see secondary outcomes in section 3.1).

# Costs and outcomes

Costs are not normally distributed with a non-negative distribution which is usually skewed. With this in mind, generalised linear models (GLM) will be used to analyse costs while controlling for baseline covariates [18]. The GLM approaches allow the consideration of other distributions and functional forms to fit the costs data. QALYs will also be analysed using GLMs.

Adjusted mean outcomes and costs and mean outcome and cost differences between intervention and control will be presented. Analyses will be performed using Stata version 15.1.

# Missing data

Where resource use, cost and outcomes are missing, multiple imputation (MI) will be performed to replace each missing observation with a set of imputed values following the method recommended by Faria et al for the imputation of economic data [19]. Predictive mean matching will be used to ensure imputed values are in the appropriate range (e.g. no negative costs or EQ-5D scores greater than 1) with MI by chained equations (MICE) and Rubin’s rules [20] applied for the subsequent analysis of multiple data sets [21]. All analyses will be conducted in Stata.

# Cost-effectiveness analysis

The cost-effectiveness of the proportionate model of the IY programme versus SAU will be investigated based on the differences in QALYs gained by both children (as calculated from PED-QL) and caregivers (as calculated from the EQ-5D) over the trial period. These outcome differences will be compared with differences in costs measured from the public sector perspective and presented as both incremental cost-effectiveness ratios (ICER) and incremental net health benefits (NHB). Net health benefit will be presented at three measures of health opportunity cost: £13,000 per QALY, based on recent empirical estimates [3], together with £20,000 and £30,000 per QALY reflecting the range used by NICE [2]. An annual discount rate of 3.5% will be applied to both costs and outcomes [2]. The probability of the intervention being cost-effective (i.e. having the highest positive net health benefit) at each cost-effectiveness threshold will be calculated using Monte Carlo simulation. Uncertainty around the incremental cost and outcome estimates will be represented on cost-effectiveness planes. Cost-effectiveness acceptability curves will be used to present the decision uncertainty by reporting the probability that implementing the IY intervention will be cost-effective at different cost-effectiveness thresholds [1, 22]. Given that financial impacts on individuals (parents) do not fall on the public sector budget we will report how incorporating these costs impact on the cost-effectiveness results [23].

# Cost-consequence analysis

The E-SEE trial assesses a range of outcomes for children (e.g. ASQ:SE-2 and SDQ) and for parents (e.g. PHQ-9 ) (see outcomes in section 3.1). A cost-consequence analysis framework is helpful to inform decision-makers where costs and outcomes of an intervention fall on different domains which may be of interest. All costs and outcomes will be presented in a descriptive and disaggregated way, where costs and outcomes per caregiver/child will be presented for each cost and outcome item in terms of average and incremental values across trial arms. Total costs will also be presented.

# Sensitivity analysis

Several sensitivity analyses will be conducted to assess the impact of different assumptions on the study results. We will consider the following scenarios, among others:

* Complete case analysis
* Alternative sources of unit cost data
* EQ5D-5L scores used to estimate parental QALYs
* A 1.5% discount rate for costs and QALYs
* Public and payer’s perspective
* Alternative extrapolation methods (if conducted – see Section 4.6)

# Extrapolation

Ineffective parenting strategies and parental emotional distress are known to impact negatively on child social and emotional wellbeing over both the short and long term [24, 25]. Child mental ill-health has both a large disease and financial burden to the children themselves, their families and society. Such issues are associated with lower school attainment and dropouts, alcohol and drug abuse, criminal behaviour, adult mental health problems, and unemployment to name a few [26, 27]. If significant differences in child social and emotional wellbeing are observed in the trial we may explore links between the trial primary and secondary outcomes and longer-term outcomes, and investigate the longer-term cost-effectiveness of the intervention. This may be conducted using an existing framework for life course economic evaluation for evaluating training programmes for parents, or instead simply exploring alternative scenarios in relation to the expected duration of benefit, along with threshold analyses showing the duration of observed benefit required in order for the IY parenting programme to be deemed cost-effective.

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