Protocol for cost-effectiveness analysis of a randomised trial of mHealth coaching (Bump2Baby and Me) compared to usual care for healthy gestational weight gain and postnatal outcomes in at-risk women and their offspring

Laura Pirhonen Nørmark (laura.pirhonen@sund.ku.dk)  
University of Copenhagen

Fionnuala M McAuliffe  
University College Dublin, National Maternity Hospital

Helle Terkildsen Maindal  
Aarhus University

Sharleen O’Reilly  
University College Dublin, National Maternity Hospital

Anna Davies  
University of Bristol

Christy Burden  
University of Bristol

Timothy Skinner  
University of Copenhagen

Karsten Vrangbaek  
University of Copenhagen

Emily Callander  
University of Technology Sydney

Study protocol

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Abstract

Background

Gestational diabetes mellitus (GDM) and overweight are associated with an increased likelihood of complications during birth and for the newborn baby. These complications lead to increased immediate and long-term healthcare costs as well as reduced health and wellbeing in women and infants. This protocol presents the health-economic evaluation to investigate the cost-effectiveness of Bump2Baby and Me (B2B&Me), which is a health coaching intervention delivered via smartphone to women at risk of gestational diabetes.

Methods

Using data from the B2B&Me randomised controlled trial, this economic evaluation compares costs and health effects between the intervention and control group using the incremental cost-effectiveness ratio. Direct healthcare costs, costs of pharmaceuticals and intervention costs will be included in the analysis, body weight and quality-adjusted life years will serve as the effect outcomes. To investigate the long-term cost-effectiveness of the trial, a Markov model will be employed. Deterministic and probabilistic sensitivity analysis will be employed.

Discussion

GDM is a growing public health concern affecting both short and long-term health outcomes and healthcare costs. Identifying cost-effective options for prevention is an international global priority. This protocol describes the methods for calculating the short-term and long-term cost-effectiveness of an intervention aimed at preventing GDM, overweight and obesity amongst women during pregnancy and the first year postpartum.

Trial registration

Australian New Zealand Clinical Trials Registry ACTRN12620001240932. Registered on 19th November 2020

1. Background

Maternity care is a high cost and high volume form of healthcare. Previous studies noted the need to promote high-value maternity care to improve health outcomes whilst curtailing escalating costs (1-4). The changing demographics of women seeking maternity care add complexity with increasing age, body mass index (BMI) and medical conditions (5, 6). Gestational diabetes mellitus (GDM) is a condition of concern, with a global prevalence of between 5 and 18% (7, 8).

GDM is associated with increased likelihood of pregnancy complications including pre-eclampsia, infection, obstructed labour, caesarean delivery and postpartum hemorrhage (9-12). GDM also increases
long-term chronic condition risk for type 2 diabetes and hypertension as well as other complications related to cardiovascular diseases (13-16). Pre-term birth and special or intensive care nursery admission increases for infants born to women with GDM (12). Additionally, overweight and obesity in pregnancy leads to higher risk of complications during delivery as well as higher risk of adverse maternal and infant outcomes (17, 18). All these outcomes reduce overall short and long-term health and wellbeing of women and infants, they also come at sizable costs to health funders (12, 19, 20). Due to the increased risk for type 2 diabetes and cardiovascular diseases because of GDM, the short-term and long-term direct healthcare costs as well as indirect costs are expected to be substantial (21, 22). As such the GDM prevention potentially offers an opportunity to improve maternity care value – provided the proposed interventions are cost-effective.

Cost-effectiveness analysis is a well-founded and widely used method within health economics where costs and outcomes of a specific intervention are compared to an alternative (23). The cost-effectiveness analysis produces an incremental cost-effectiveness ratio. This identifies the additional outcomes that are produced by an intervention and the additional costs of achieving them. This ratio can then be compared to established willingness to pay thresholds and to similar interventions to evaluate the cost-effectiveness and comparative effectiveness of the studied intervention.

The planned cost-effectiveness analysis described in this protocol will be used to evaluate the costs and health outcomes of the Bump2Baby and Me (B2B&Me) intervention compared with usual care. The results from the analysis will serve as a foundation for healthcare policy makers in the decision making surrounding the implementation of the B2B&Me intervention in healthcare practice for pregnant women in risk of gestational diabetes. More specifically, the analysis will inform about the value of the intervention within the publicly funded health and social care systems across Ireland, the UK, Spain, and Australia.

2. Study design

A cost-effectiveness analysis of the B2B&Me intervention compared with usual care will be conducted. The design of the economic evaluation, as described in this protocol, follows the recommendations of the International Society for Pharmacoeconomics and Outcomes Research Randomised Controlled Trial Cost-Effectiveness Analysis (ISPOR RCT-CEA) Task Force (24) and ISPOR Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (25).

3. Comparison groups

3.1 Intervention

The intervention consists of mHealth coaching support delivered through a smartphone application from the time of randomization up until one year postpartum. The coaching support will be delivered through the application and will use both synchronous and asynchronous video and text messages including automated reminder and motivational messaging as well as specific health information connected to the
participants’ journey through pregnancy and first year post-partum. The intervention group will have access to a variety of resources associated with gestational weight gain and postpartum weight management, infant feeding and active play, and diabetes prevention. The intervention group are also able to connect with other women going through pregnancy and postpartum care using the virtual social network feature in the smartphone application.

More specifically, the intervention will consist of the following six components: 1) **Synchronous mHealth coaching**: two individual coaching sessions delivered by the mHealth coach together with follow-up summary video message containing goals discussed during the meeting, one at randomization and one 6-8 weeks postpartum. An additional third session will be offered to individuals diagnosed with GDM to review and adjust lifestyle goals. 2) **Asynchronous mHealth coaching**: Interactions between the coach and the individual through text and video messaging once a week during the first 4 weeks and bi-weekly until birth. Postpartum interactions will be conducted weekly for one week and bi-weekly until the end of the intervention period (12 months postpartum). 3) **Automated push notifications**: Standardized messages tailored to individual goals, child feeding practices and preferences instructing the individual to follow through on goals, reminders to register goal achievements and motivational messages after achieving goals. 4) **Personalised educational content**: Covering topics within breastfeeding, healthy eating, physical activity, emotional wellbeing, and best practice infant feeding. 5) **Additional support content**: Automated push notifications once a week for additional content available in the app. The push notifications will provide individuals with specially designed online resources for recipes, information, tips for food and activity choices, breastfeeding resources and links to relevant support agencies. 6) **Virtual social network**: Opportunity to connect with other women in the intervention group through the smartphone application and thereby enable social engagement and support.

### 3.2 Usual care

The control group receives usual care according to the maternity care at each site (ref to implementation protocol manuscript when published where it is described in detail). In addition, the control group participants will be provided with links to standard information sources on gestational diabetes and lifestyle. Both intervention and usual care will receive electronic newsletters updating them on the study progress.

### 4. Data

#### 4.1 Trial design

B2B&Me is a multicentre single-blind randomised controlled implementation trial with the aim of testing the innovation of a mHealth app and personalized health coaching with integrated health service screening for high-risk women in pregnancy, until one year postpartum. The details of the trial are reported elsewhere (26) but are briefly accounted for here. The study will aim to recruit around 800 women across four hospital sites, National Maternity Hospital Dublin, Ireland, San Cecilio University Hospital Granada, Spain, Southmead Hospital Bristol, England, Monash Medical Centre, Melbourne,
Australia. The intervention will be implemented at each hospital site with pregnant women aged 18 and older attending maternity services screened for risk of developing GDM using the validated Monash GDM Screening Tool around their first antenatal visit. Individuals scoring 3 or higher on the tool will be invited to participate if they meet the inclusion and exclusion criteria below.

The inclusion criteria are: women attending a participating maternity service for maternity care, scoring of 3 or higher on the Monash GDM screening tool, smartphone owner, and not currently in a health behaviour change clinical trial. The exclusion criteria are: previously diagnosed diabetes (type 1 or type 2), greater than 24 weeks gestation, current multiple pregnancy (e.g. twin, triplets), cancer (not in remission), severe mental illness, substance abuse or myocardial infarction in the last three months, difficulty with using the English language for the Irish, English and Australian sites and Spanish for the Spanish site, and not owning a smartphone capable of hosting the intervention app.

At the baseline visit demographics will be collected via questionnaire including maternal age, ethnicity, gravidity, parity, relationship status, educational attainment, employment status (of the participant and relevant partner), housing status, childcare responsibilities and prior medical history. Maternal height (cm) and weight (kg) will be extracted from medical records and participants will be invited to weigh themselves weekly on a Bluetooth-enabled scales provided by the study. Blood pressure will be measured during the baseline visit. Online questionnaires will be completed within one week of the baseline visit. The questionnaires will collect data on diet, physical activity, breastfeeding attitudes, health status (EQ-5DL), psychological health, sleep quality, health literacy and willpower. The questionnaires will be completed within a week of final study visit (12 months postpartum). Additional questionnaires on infant development, health status, diet and physical activity as well as anthropometry on infant length (cm), weight (kg), and head circumference (cm) will be completed at the final visit. At 3, 6, 9 months a questionnaire will be completed on healthcare visits and out-of-pocket costs postpartum.

4.2 Effect outcomes

The two main health outcomes for the economic evaluation will be health-related quality of life measured using the quality-adjusted life years (QALY) approach and maternal body weight (kg) 12 months postpartum. QALYs are a summary health outcome measure routinely utilised for economic evaluation integrating quantity and quality of life into a single index (27). QALYs will be calculated based on responses from the EQ-5D-L questionnaire sent out to patients in the clinical trial and country-specific value sets will be applied (28-31).

Effects (QALYs and weight) for the economic evaluation will be measured on individual patient level at baseline and 12 months postpartum. Additional effect outcomes (maternal and infant) can be employed if necessary, depending upon the analysis of the trial clinical effects.

4.3 Cost outcomes
The cost-effectiveness analyses will be performed from a health sector perspective. Cost categories for the economic evaluation include the value of all antenatal healthcare consumption, postpartum healthcare consumption related to diet, activity and weight for both baby and mother, costs of pharmaceuticals in pregnancy, and the cost of the intervention itself.

Information on utilisation of health services and utilisation of pharmaceuticals will be collected at the individual level. The antenatal services will be captured from the electronic case report forms (eCRFs) maintained by hospital sites. If participants visited hospitals or health providers other than the trial sites, the number of diagnostic and treatment procedures will be obtained based on self-report. Information on type of visit, frequency and out-of-pocket postpartum healthcare visit costs relating to diet, physical activity and weight management for the participant and their infant will be collected through online questionnaires at 3 months, 6 months, 9 months and 12 months postpartum. Valuation of the resources identified and measured will be done using country-specific unit costs for healthcare services. Each contact (face-to-face visit, phone contact etc.) will be assigned a unit cost based on type of visit and type of healthcare professional. Costs for the intervention itself will be collected by the company providing the smartphone application (Liva Healthcare) and will contain costs related to the implementation of the application in participating countries healthcare systems. Costs will be presented in 2023 Euros.

5. Methods

5.1 Cost-effectiveness analysis

Well established health-economic methods will be employed in order to estimate the cost-effectiveness of the clinical trial (32). A cost-effectiveness analysis enables the calculation of gains in treatment effect of a specific intervention (the B2B&Me intervention in this case) with its additional costs and compares the treatment effects and costs to a comparator (usual care in this case). Comparing treatment effects and costs between two alternatives results in an incremental cost-effectiveness ratio (ICER) will be calculated as follows:

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ICER = \frac{C^{D2B} - C^{UC}}{E^{D2B} - E^{UC}}
\]

where \( C^{D2B} \) and \( C^{UC} \) are the mean costs among participants in the B2B&Me and usual care arms while \( E^{D2B} \) and \( E^{UC} \) are the mean effects (QALYs or body weight). Depending on the effect measure chosen, the ICER expresses the additional costs per unit decrease in body weight or per additional QALY gained if B2B&Me is used by pregnant women in risk of gestational diabetes. Concluding whether or not the intervention or the comparator is the cost-effective alternative depends on the societal willingness to
pay (for a specific country) i.e., if the ICER is below the willingness-to-pay threshold the intervention will be regarded as cost-effective.

5.1.1 Short-term cost-effectiveness analysis

Short-term cost-effectiveness analysis will be employed using data from the clinical trial. Conducting analysis employing both pooled data from all countries included in the trial as well as country-specific estimates will contribute to a comparative analysis of the health systems and contextual factors affecting cost-effectiveness across countries. The results of the analysis will conclude if the B2B&Me intervention is a cost-effective alternative to usual care for pregnant women at risk of gestational diabetes.

5.1.2 Long-term cost-effectiveness analysis

A clinical trial and the subsequent data collection often spans over a relatively short period of time. Health economic modelling can be employed so that results from clinical trials are extrapolated beyond the reach of clinical data and thereby providing important insights to potential long-term benefits (and costs) of an intervention. To estimate the long-term cost-effectiveness of the B2B&Me intervention, a Markov cohort model will be employed. First, data collected during the clinical trial will be employed in the model and thereafter the data will be extrapolated to estimate the long-term cost-effectiveness. The model runs the two arms (intervention and usual care arm) simultaneously and participants move through the states in predetermined cycles. The model will be populated with parameter values collected from the clinical trial and from the published literature, if needed. Transition probabilities (how patients move from one state to another), state-dependent quality of life weights and state-dependent costs will be calculated.

5.2 Sensitivity analysis

We plan to perform both deterministic sensitivity analysis as well as probabilistic sensitivity analysis for both short-term and long-term cost-effectiveness analyses.

5.2.1 Deterministic sensitivity analysis

Deterministic sensitivity analysis will be performed both for the short-term and the long-term cost-effectiveness analysis (33). The deterministic sensitivity analysis for the one-year cost-effectiveness analysis will be performed by re-calculating and presenting the ICER for different subgroups. One-way deterministic sensitivity analysis will be performed for the long-term cost-effectiveness analysis by varying the following parameters in the simulation model: 1) discount rate for costs 2) discount rate for effects, and 3) transition probabilities between states.

5.2.2 Probabilistic sensitivity analysis
In order to investigate the probability of achieving an incremental cost-effectiveness ratio that falls below a specific willingness-to-pay threshold, probabilistic sensitivity analysis can be performed (34, 35). We plan on, both pertaining to the short-term and the long-term cost-effectiveness analysis, implementing a bootstrap procedure to examine the likelihood of cost-effectiveness at different thresholds. A bootstrap procedure entails drawing random samples with replacement from the available data many times, for example 5000 times. This method produces an estimate of the distribution of the ICER. The results from the probabilistic sensitivity analysis will then be presented in a cost-effectiveness acceptability curve (CEAC) and a cost-effectiveness (CE) plane (36). The CEAC displays the estimated probability that the B2B&Me intervention will be deemed cost-effective compared to usual care at any given willingness-to-pay threshold level for the ICER (37, 38). The CE-plane presents all incremental effect and incremental cost pairs that are produced by the bootstrapping procedure graphically and illustrates whether most of the pairs result in cost-effectiveness for the intervention or the comparator.

5.3 Missing data

Participants will be followed-up at specific points in time, but some participants may be lost to follow-up. In addition, data may be missing for some participants for example if the EQ-5D-L questionnaire is not filled out at a follow-up point. These problems will be handled by applying multiple imputation methods (39-41).

5.4 Discounting

Costs and effects in the long-term cost-effectiveness analysis will be discounted using a discount rate of 3%.

6. Discussion

This protocol aims to describe the methods for conducting cost-effectiveness analysis of the B2B&Me intervention compared with usual care to inform decision-makers about its incorporation into routine care. This will be achieved by comparing the costs and outcomes associated with the intervention, including all background health service use of women during pregnancy, birth, and postpartum covering the long-term impacts of the intervention. The methods employed for the short-term analysis will consist of a cost-effectiveness analysis using trial data. The long-term analysis will employ a Markov cohort model using trial data and published literature to present the long-term cost-effectiveness of the intervention compared to usual care. Deterministic and probabilistic sensitivity analysis will be employed. Gestational diabetes is a growing area of concern, affecting both health outcomes and costs for funders. Identifying cost-effective options for prevention is an international priority. Cost effectiveness and cost saving has been shown for other pregnancy interventions aiming to reduce excessive weight gain, GDM and large for gestational age infants (42, 43).

Indirect costs (productivity losses) will not be collected during the trial. Therefore, the (short-term) cost-effectiveness analysis will only include costs for healthcare consumption (healthcare visits and
pharmaceuticals) during pregnancy and one-year postpartum as well as costs for the intervention. It is assumed that the productivity losses incurred during the trial period are negligible due to maternity leave after pregnancy. However, these costs are planned to be collected from the published literature and included in the long-term cost-effectiveness analysis to inform the long-term cost-effectiveness of health-coaching support for women with high-risk pregnancy.

**Abbreviations**

B2B&Me - Bump2Baby and Me  
BMI - Body mass index  
CE-plane - Cost-effectiveness plane  
CEAC - Cost-effectiveness acceptability curve  
CHEERS - ISPOR Consolidated Health Economic Evaluation Reporting Standards  
GDM - Gestational diabetes  
ICER - Incremental cost-effectiveness ratio  
ISPOR RCT-CEA - International Society for Pharmacoeconomics and Outcomes Research Randomised Controlled Trial Cost-Effectiveness Analysis Task Force  
QALY - Quality-adjusted life years

**Declarations**

**Ethics approval and consent to participate**

The National Maternity Hospital Human Research and Ethics Committee was the primary approval site (EC18.2020) with approvals from University College Dublin HREC-Sciences (LS-E-20-150-OReilly), Junta de Andalucia CEIM/CEI Provincial de Granada (2087-M1-22), Monash Health HREC (RES-20-0000-892A) and NHS Health Research Authority and Health and Care Research Wales (HCRW) (21/WA/0022). Informed consent will be obtained from all subjects and/or their legal guardian(s).

**Consent for publication**

Not applicable

**Availability of data and materials**

Data can be made available upon reasonable request to the corresponding author.
Competing interests

The authors have no competing interests.

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Authors’ contributions

LPN planned and wrote the manuscript with the support of EC and KV. All authors have been involved in critically revising the manuscript, have given final approval of the version to be published and agree to be accountable for all aspects of the work. All authors read and approved the final manuscript.

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