The BUMPES study

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Health Economics Analysis Plan

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Contributors: **Oya Eddama, NPEU, University of Oxford**
Oliver Rivero-Arias, NPEU, University of Oxford
Peter Brocklehurst, UCL

This document describes the health economics analysis plan and the presentation of results of the BUMPES economic evaluation. The aim of this document is to introduce the key aspects of data collection and the analysis that will be carried out as part of the health economic evaluation of this project. This document includes a brief summary of the aims of the BUMPES study, the aims of the cost-effectiveness analysis, and the proposed health economic methods to analyse and present the results of the economic evaluation.

Background

Epidural analgesia is the most effective form of pain relief for women in labour. [1] However, epidural analgesia is associated with an increased risk of C-section, instrumental vaginal delivery (IVD), and perineal trauma requiring surgical repair. There has been interest in position during second stage of labour for women with an epidural, in order to prevent instrumental deliveries and increase the number of spontaneous vaginal delivery (SVD). However, this issue has so far not been adequately addressed. The longer-term impacts of IVD/C-sections are profound and can include urinary and faecal incontinence in the mother, decreased quality of life, as well as other bowel problems. [21] There are also possible effects on the infant associated with different modes of delivery. The aim of the BUMPES trial is to evaluate whether a policy of enabling upright position compared to a policy of lying down amongst nulliparous women with a low dose epidural who enter second stage decreases the incidence of IVD and increases the incidence of SVD.

The economic evaluation of the BUMPES trial will evaluate the health care costs and quality of life of women randomised to an upright or lying down position in the second stage of labour with an epidural, up until one year after birth. Therefore, we aim to evaluate whether one position compared to the other one is associated to improvements in quality of life or savings to the National Health Service (NHS) therefore representing value for money of scarce resources.

1. The BUMPES Randomised Controlled Trial

Full details of the primary and secondary objectives of the BUMPES study, trial design, eligibility, and son can be obtained from the main study protocol and the statistical analysis plan study that are available in separate documents. Briefly, BUMPES is a pragmatic multicentre randomised controlled trial (RCT) assessing the effectiveness of: 1) an upright maternal position (intervention group) which would maintain the pelvis in a vertical plane as possible; and 2) a lying down maternal position (control group) which would maintain the pelvis in a horizontal plane as possible. Both interventions begin during the second stage of labour with the intention of continuing the allocated position up until the birth. The BUMPES study will evaluate postnatal maternal and neonatal morbidity and well-being assessed one year after birth.

2. The BUMPES Economic Evaluation

3.1 Objective of the BUMPES Economic Evaluation

A summary of the components of the BUMPES economic evaluation is presented in Table 1.The BUMPES economic evaluation will compare the cost-effectiveness of upright and lying down positions for women at the start of care in the second stage of labour up to one-year follow-up. The primary health outcome measure for the economic evaluation will be quality-adjusted life-years (QALYs). The results of the cost-effectiveness analysis will be expressed as cost per QALY gained.

Table 1: Summary of the BUMPES economic evaluation

Summary	Description
Health Outcome	Maternal Quality Adjusted Life Years (QALYs)
Cost	Delivery procedure costs, original hospital admissions, readmissions, health care visits (for mother and babies)
Timeframe	1 year (12 months) follow-up after birth
Data	Approx. 1,500 women (750 women in each arm)
Data collection	Data collection booklet and maternal questionnaire at one year after birth
Analysis	Intention to treat analysis
Cost-effectiveness results	Cost per QALY gained

3.2 Data collection

Around the time of birth, patient-level data will be extracted from the data collection booklet as well as any higher level of care forms for the woman and/or infant who receive a higher level of care. One year follow-up data will be obtained by questionnaire completed by all women whose babies are alive. The questionnaire contains questions on general health and well-being, with specific questions related to any urinary and bowel problems. The questionnaire also collects health care resource use for both mother and infant. There are no further follow-ups in the trial.

3.3 Health care resource use data

Tables 2 and 3 detail the specific resource use identified in the BUMPES study, from second stage of labour to hospital discharge (Table 2) and at one-year follow-up (Table 3). Resource use will be collected for both mothers and infants. Note there are no intervention costs for the trial since the trial is of position during labour, which does not have any resources associated to implementation. The resource use included in these tables have been carefully examined by the BUMPES team and revised iteratively. The resource use shaded in grey in Table 2 will not be used for purposes of the economic evaluation as they are already incorporated as part of procedure costs associated to mode of delivery. The economic evaluation will be conducted from a NHS health service perspective and therefore only direct costs to NHS providers will be included. Data on primary and community care visits were not collected alongside the study. We did not want the questionnaire to be too arduous for the woman to complete and we were concerned that these visits, which tend to be less frequent than secondary care visits, would be subject to extensive recall bias. It was also agreed that hospital care would be the main cost driver. However, given that some women in the study may have had symptoms of incontinence for which they may have visited their General Practitioner (GP) and received treatment, we will use section three of the one year-questionnaire which asks about the health of the women to ascertain the proportion that would have been likely to have seen their GP. Data on the proportions of women seeing their GP with specific urinary and faecal incontinence issues will be obtained from research already published in this field by one of the co-investigators of the BUMPES trial (Christine MacArthur).

Table 2: Resource use and unit cost measurement from second stage of labour to hospital discharge (all costs to be valued in pounds sterling, 2014 prices)

Resource use variable	Cost implications	Source of unit cost	Cost valuation/comments	Section of data collection booklet
Maternal details after study entry:				
Epidural technique (epidural/combined spinal or epidural)	Cost of drugs	BNF	Requires looking at pump readings before and afterwards (caveat: missing pump readings)	1.12 & 2.1
Fetal blood sampling	Cost of sampling	NHS	May be different between the arms	2.3
Fetal scalp electrode	Cost of clip	NHS	May be different between the arms	2.4
Drugs for hypotension	Cost of drug (note that no drug recorded)	BNF	May be different between the arms	2.6 & 2.7
Mode of birth	Spontaneous vaginal delivery/assisted delivery/c-section	Reference costs	-	3.3
Primary indication for assisted birth	Cost of assisted by category	NA	No differential staffing so no need to cost	3.4
Anaesthesia required for instrumental birth or c-section (this is in addition to routine epidural pain relief)	Cost of drug	NA	No need to cost – cost will be captured already in reference costs for instrumental births or C-sections	3.5
Active management of third stage labour	Cost of staffing	NA	No differential staffing so no need to cost	3.6
Episiotomy and perineal tear (not counted if woman underwent a c-section)	Cost of episiotomy	Reference costs	Whether the tear was sutured or not is only what is required for costing purposes. Second degree tears will be sutured in the labour ward, whereas suturing of third degree tears will be performed in theatre.	3.7, 3.8, 3.9, 3.10
Manual removal of the placenta	Cost of staff and equipment	Schroeder L, Birthplace costing	£689.32 (2009 cost) -In theatre – needs to be costed separately if a SVD as it will include additional staff, obstetrician, anaesthetist, midwife, and HCA. Does not require costing if	3.11

			woman has had a C-section	
Post-partum haemorrhage requiring transfusion	Cost of PPH & transfusion	Previous NPEU research	-	3.12
Woman admitted to a higher level of care (HDU, ICU) and duration of stay	High dependency care	Reference costs	-	3.14
Infant details:				
Cord blood sampling	Cost of sampling	TBD	Needs to be costed because could represent differences between the arms	3.19
Meconium stained liquor	Additional staff or procedures involved	NA	No differential staffing so no need to cost	3.20
Neonatal resuscitation required at delivery	Resuscitation at birth	Schroeder L, Birthplace costing	£747.77 (2009 cost)	3.21
Infants destination after birth and duration of stay	Higher level neonatal hospitalisation	Reference costs	-	3.24

Table 3: Resource use and cost data collection at one year for the woman and infant

Resource use variable	Resource use identified	Source	Comments
Mother details:			
Hospital admission (reason and duration)	Cost of admission multiplied by duration	Reference costs	Will be the most representative costing figure – by classification of reason for admission or ward stay
Operation undergone	Cost of operation	Reference costs	-
Outpatient clinic attended and number of times: *Perineal care clinic; Gynaecological; Surgical Other*	Cost of clinic attended	Reference costs	Note, need to check data entered as one (first) visit is costed differently to subsequent visits
Infant details:			
Hospital admission (reason and duration)	Cost of admission multiplied by duration	PSSRU	-
Operation undergone	Cost of operation	Reference costs	-
Outpatient clinic attended and number of times: *Orthopaedic; Paediatric Hearing; Eye; Dermatology Other*	Cost of clinic attended	PSSRU	-

3.4 Unit cost data collection

As can be seen in Table 2, where necessary, we have captured items in disaggregated units where we believe the resource use is intervention-related and that a more detailed costing approach will be required. We have in some cases used costing data derived from other studies, whereby clinical experts (clinicians/midwives) document the staffing, medications and equipment, used in the treatment of haemorrhage for example. In these cases, clinical experts were sent a micro-costing sheet to complete with their own resource components. This has comprehensively captured all resource components that might be used.

Unit costs related to health care professionals and services will be derived from national data sources (NHS reference costs or Personal Social Services Research Unit (PSSRU) costs) (Table 3). [48, 51] Reference costs are the average unit cost to the NHS of providing secondary healthcare to NHS patients whereas PSSRU provides salaries for a range of health care professionals.

3.5 Maternal quality of life

There is a lack of quality of life measurement scales specifically relevant for use in the maternal and postnatal context. [62, 74] In addition, the possible impact on quality of life on the infant is also of importance but there is no methodological consensus in the literature about how to combine mother/infant utilities data in practice. Using the QALY concept in a paediatric population is

controversial and more research is needed before a framework can be recommended. [75] Therefore, our QALY analysis will only include maternal quality of life.

Maternal quality of life will be derived from the EQ-5D and SF-12 instruments collected in the one-year questionnaire. [42, 44] In pregnant women, the most frequently cited quality of life tool has been the SF-36 (the 36-item version of the SF-12). [76] Similarly to the EQ-5D, SF-12 data can be converted into utilities using the validated SF-6D algorithm. [77] Previous generic research by Petrou and Hockley has provided evidence that the SF-6D is an empirically valid and efficient alternative multi-attribute utility measure compared to the EQ-5D. [78] In particular, they showed that the SF-6D is more efficient than the EQ-5D at detecting differences in self-reported health status, and differences in illness, disability or infirmity and medication use. However, since the EQ-5D is the recommended outcome measure for economic evaluations by National Institute for Health Care Excellence (NICE), we will report the EQ-5D as our main outcome measure in the economic evaluation. We will use information from the SF-12 as a secondary outcome. [58]

Since we did not measure maternal quality of life at the start of randomisation, we will identify relevant studies reporting quality of life about the short-term quality of life implications of the mode of delivery and subsequent complications using a literature search. Evidence from reviews in the area suggests that there are not many studies reporting the relevant information we require. [62, 74, 75] Such estimates will be used for the baseline values for each woman in the QALY calculation.

3.6 Analytical methods

The economic evaluation will take the form of a within-trial analysis using patient-level data. In line with the main statistical analysis plan, women contributing data will be analysed using intention-to-treat analysis.

NHS volumes of resource use will be multiplied by the corresponding unit cost to estimate the cost per women for each particular category. The total cost per women will be estimated adding the cost of each category up that allows the calculation of mean cost per women for each trial arm. Recent evidence suggests that both parametric and non-parametric methods accurately estimate the true standard errors even when data are highly skewed and moderate to large (n>50) sample sizes. [48] Hence, mean differences and associated uncertainty for particular categories of resource use and costs between the two positions during the late stage of labour will be estimated using parametric methods.

Utilities associated to a particular health state from the EQ-5D instrument, will be estimated using the UK value set. [43] To derive the QALY profile for each woman in the trial between baseline and one year follow-up we will use a linear straight-line interpolation between assessments in the base case. Other assumptions about connecting the two points (e.g. quality of life changed at midpoint between assessment points) will be evaluated in a sensitivity analysis. [79] We acknowledge that the choice of base case will likely pick up the longer term wellbeing effects that are still evident at 12 months. However it is the severe and persistent forms of urinary and faecal incontinence, and the impact on health related quality of life, that are evident at one year that is of primary importance to the BUMPES trial. We will also estimate the QALY profile for each woman using SF-6D utilities in a sensitivity analysis to evaluate the robustness of the base case QALY results. Mean differences and associated uncertainty in utilities between the intervention groups will be assessed using parametric methods.

A descriptive analysis will provide information about how serious is the presence of missing data in resource use, costs and utilities at one-year follow-up. The decision to impute or not missing data and what exactly to impute will be based on current guidance. [55, 80] If imputation techniques need to be implemented, we will use multiple imputation with chained equation methods and will attempt to impute all components in the economic evaluation. [54] However, this may not be possible due to the

amount of missing data and type of model used and at minimum costs and QALYs will be included in the imputation model. We will combine the statistics of interest (e.g. means and standard errors in each group) using appropriate Rubin rules. [56]

Uncertainty around the cost per QALY gained will be expressed calculating 95% confidence interval around the incremental cost-effectiveness ratio (if appropriate) and using cost-effectiveness acceptability curves (CEACs). [57] We will also present the results of the cost-effectiveness analysis using the net benefit statistics. [81] A full parametric approach will be used to derive ICER's confidence intervals and CEACs. [82] We may implement a bootstrap method to estimate pairs of mean costs and QALYs for each intervention to present uncertainty around cost-effectiveness results using the cost-effectiveness plane. [83]

We will discuss with the clinical team whether cost-effectiveness is likely to vary for a particular subgroup(s) of women and will derive cost-effectiveness results for such subgroups. [59] The subgroup analysis will follow the same methods as the primary analysis.