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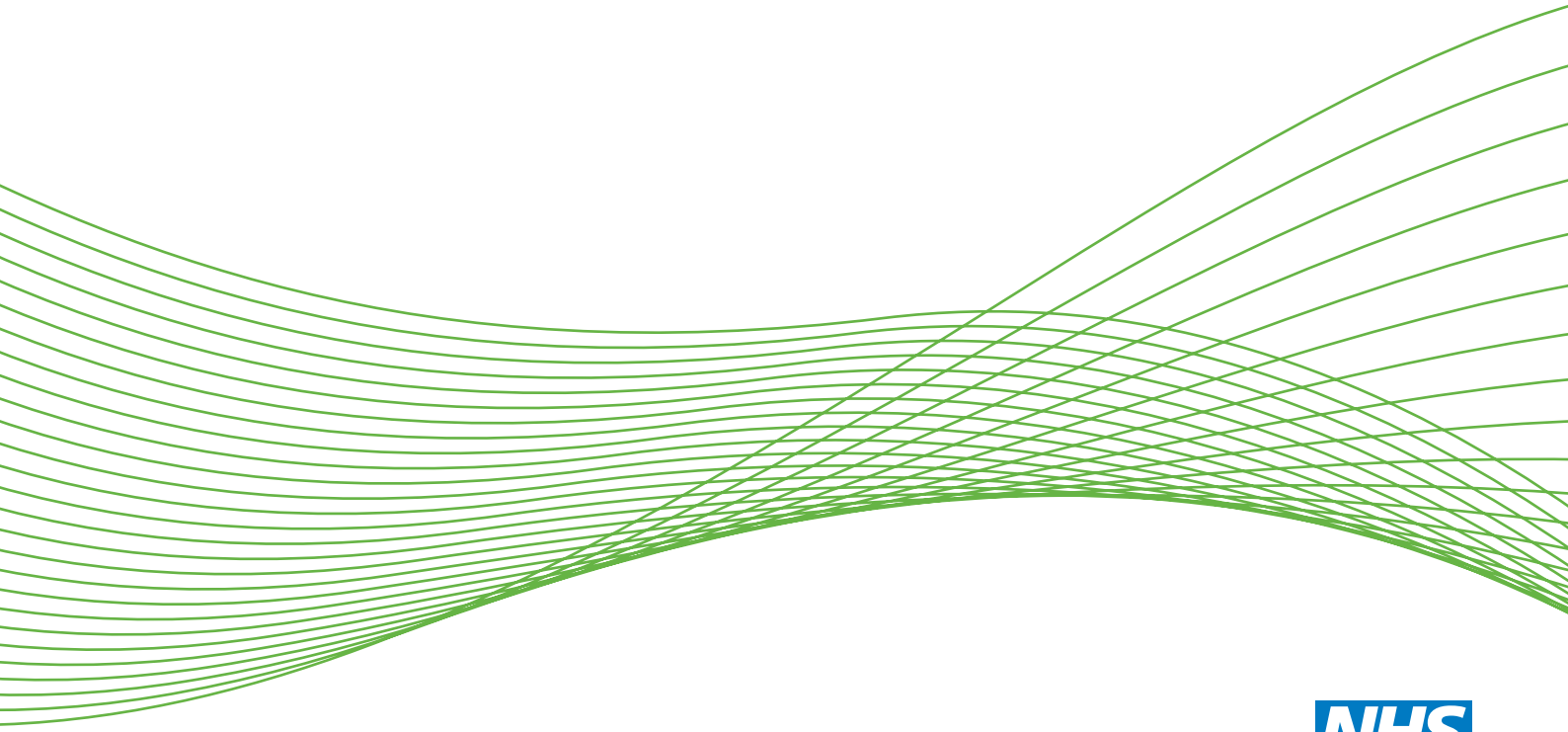

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A multicentre, randomised controlled trial of position during the late stages of labour in nulliparous women with an epidural: clinical effectiveness and an economic evaluation (BUMPES)

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Abstract

A multicentre, randomised controlled trial of position during the late stages of labour in nulliparous women with an epidural: clinical effectiveness and an economic evaluation (BUMPES)

Debra Bick,[1] Annette Briley,[2] Peter Brocklehurst,[3]* Pollyanna Hardy,[4] Edmund Juszczak,[4] Lynn Lynch,[5] Christine MacArthur,[6] Phillip Moore,[7] Mary Nolan,[8] Oliver Rivero-Arias,[4] Julia Sanders,[5] Andrew Shennan[9] and Matt Wilson[10] on behalf of the Epidural and Position Trial Collaborative Group

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Background: Epidural analgesia leads to increased risk of instrumental vaginal delivery (IVD). There is debate about whether or not posture in second-stage labour influences the incidence of spontaneous vaginal birth (SVB).

Objectives: In nulliparous women with epidural analgesia, does a policy of adopting an 'upright position' throughout second-stage labour increase the incidence of SVB compared with a policy of adopting a 'lying-down' position?

Design: Two-arm randomised controlled trial.

Setting: Maternity units in England and Wales.

Participants: Nulliparous women aged ≥ 16 years, at ≥ 37 weeks' gestation with singleton cephalic presentation and intended SVB, in second-stage labour with an epidural providing effective pain relief.

Interventions: (1) Upright position to maintain the pelvis in as vertical a plane as possible; and (2) lying-down position to maintain the pelvis in as horizontal a plane as possible.

Main outcome measures: The primary outcome measure was incidence of SVB. Secondary outcomes included augmentation, interventions to maintain blood pressure, duration of labour, episiotomy, genital tract trauma, post-partum haemorrhage, maternal satisfaction, neonatal metabolic acidosis, 5-minute Apgar score of < 4, resuscitation at birth and admission to neonatal unit. At 1 year for (1) women: urinary

or faecal incontinence, dyspareunia and health-related quality of life; (2) for infants: major morbidity. A cost–consequences analysis with a time horizon of 1 year after the birth from a NHS perspective.

Results: Between October 2010 and January 2014, 3236 women were randomised from 41 centres in England and Wales. There was a statistically significant difference in the incidence of SVB between groups, with 35.2% of women achieving a SVB in the upright group, compared with 41.1% in the lying-down group (adjusted risk ratio 0.86, 95% confidence interval 0.78 to 0.94). There was no evidence of differences in most of the secondary maternal or neonatal outcomes, or in long-term outcomes at the 12-month follow-up. No significant overall cost differences were observed between upright and lying-down positions for mothers or their babies.

Limitations: Measurement of adherence was challenging in this unmasked trial, and adherence could be influenced by midwives' beliefs about the allocated positions. If adherence was poor, this would have diluted the difference between the two groups.

Conclusions: There is clear evidence of the benefit of adopting a lying-down position in second-stage labour in nulliparous women with epidural analgesia, with no apparent disadvantages in either short- or long-term outcomes for mother or baby, and this is cost neutral for the NHS.

Future work: Questions remain about whether or not other positions could increase the incidence of SVB further in this group of women. The results also raise questions about the role of maternal position in second-stage labour in women without an epidural.

Trial registration: Current Controlled Trials ISRCTN35706297.

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List of abbreviations

BMI	body mass index
BP	blood pressure
CI	confidence interval
CIG	Clinical Investigators Group
CLRN	Comprehensive Local Research Network
CONSORT	Consolidated Standards of Reporting Trials
DCB	data collection booklet
DMC	Data Monitoring Committee
EQ-5D-3L	EuroQol-5 Dimensions, three-level version
GCP	good clinical practice
GMR	geometric mean ratio
HLC	higher level of care
HRQoL	health-related quality of life
HTA	Health Technology Assessment
ICER	incremental cost-effectiveness ratio
IMD	Index of Multiple Deprivation
IVD	instrumental vaginal delivery
MD	mean difference
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
QALY	quality-adjusted life-year
R&D	research and development
RCT	randomised controlled trial
REC	Research Ethics Committee
RR	risk ratio
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SE	standard error
SF-12	Short Form questionnaire-12 items
SF-6D	Short Form questionnaire-6 Dimensions
SVB	spontaneous vaginal birth
SWAT	study within a trial
TSC	Trial Steering Committee
UCL	University College London

Plain English summary

The BUMPES study aimed to find out whether or not women having their first babies who have an epidural and give birth in an upright position (kneeling, sitting in a chair or upright in bed), rather than lying down (on their side), are more likely to have a vaginal birth and less likely to need forceps or ventouse.

Between October 2010 and January 2014, 3236 women took part in the study at 41 maternity units in England and Wales. Just over one-third (35.2%) of the women allocated to the 'upright' group had a spontaneous vaginal birth, compared with 41.1% in the 'lying-down' group. Outcomes for the health of the woman and baby (such as whether or not the baby needed special care or the woman had problems with incontinence) were no different between the two groups, either in the short term (just after the birth) or up to 1 year later.

The study offers clear evidence that women having their first baby and who have epidural pain relief in labour are more likely to have a straightforward vaginal birth if they adopt a lying-down position in the late stages of labour when their baby is ready to be born. There are no apparent disadvantages of lying down for either the woman or her baby in the short or long term.

Scientific summary

Background

As the most effective form of pain relief in labour, epidural analgesia is chosen by up to 30% of women in the UK each year, and this proportion has remained relatively stable since 1990. Epidural analgesia leads to an increased risk of instrumental vaginal delivery (IVD); however, this evidence comes mostly from trials using epidural techniques that caused dense neuraxial blockade. 'Low-dose epidurals', which use low-dose local anaesthetic in combination with opioids, result in a lower risk of IVD; however, using this method, the rate of IVD is still higher than that in women with no epidural. Although low-dose epidurals preserve motor function, allowing greater mobility throughout labour and enabling women to adopt upright positions, there is debate about whether or not an upright posture in the second stage of labour increases the incidence of spontaneous vaginal birth (SVB).

A Cochrane review of position in the second stage of labour in women *without* epidurals showed a reduction in IVD in the upright group (Gupta JK, Hofmeyr GJ, Shehmar M. Position in the second stage of labour for women without epidural anaesthesia. *Cochrane Database Syst Rev* 2012;**5**:CD002006). A Cochrane review of position in the second stage of labour for women with epidural analgesia was published in 2013 (Kemp E, Kingswood CJ, Kibuka M, Thornton JG. Position in the second stage of labour for women with epidural anaesthesia. *Cochrane Database Syst Rev* 2013;**1**:CD008070), after the BUMPES trial was started. This review included trials which compared upright with recumbent positions. The incidence of SVB reported in the five included trials, comprising 879 women in total, was 1.02 [95% confidence interval (CI) 0.81 to 1.28]. The authors concluded that there was no clear evidence about whether or not position in the second stage of labour made a difference to outcomes.

Objectives

To evaluate whether or not, in nulliparous women who choose low-dose epidural analgesia, a policy of adopting an 'upright position' throughout the second stage of labour is associated with an increase in the incidence of SVB compared with a policy of adopting a 'lying-down' position.

Design

A two-arm randomised controlled trial.

Setting

Maternity units in England and Wales.

Participants

Women admitted to a participating labour ward who fulfilled all of the following criteria were eligible to be recruited and randomised into the trial:

- aged ≥ 16 years
- ≥ 37 weeks' gestation

- nulliparous (no previous delivery $\geq 24^{+0}$ weeks' gestation)
- singleton cephalic presentation
- intended SVB
- in the second stage of labour
- with a low-dose epidural in situ during the first stage of labour, providing effective pain relief
- able to understand printed documentation produced in English
- able to give written answers in English.

Exclusion criteria

Women who did not fulfil all of the inclusion criteria were not included in the study.

Interventions

Women were allocated to a policy of (1) an upright maternal position that would maintain the pelvis in as vertical a plane as possible during the second stage of labour, with the intention of continuing this until the birth (this could include walking, standing, sitting out of bed, supported kneeling or completely upright in an obstetric bed for as much of the second stage as possible); or (2) a lying-down maternal position (left or right lateral, to prevent aortocaval compression), which would maintain the pelvis in as horizontal a plane as possible during the second stage of labour, with the intention of continuing this until the birth.

Randomisation

Participants were randomised to the allocated intervention (allocation ratio 1 : 1) using a secure web-based central randomisation service. No stratification by clinical characteristics was undertaken, although there was stratification by centre.

Main outcome measures

Primary outcome measure

The primary outcome measure was the incidence of SVB.

Secondary short-term outcomes

- Instrumental vaginal delivery (forceps and ventouse).
- Caesarean section.
- Augmentation of labour.
- Major interventions to maintain blood pressure (e.g. vasopressors).
- Hypotension (systolic blood pressure of < 100 mmHg prior to delivery).
- Application of fetal scalp electrode.
- Fetal blood sampling.
- Total doses of epidural local anaesthetic and opioids administered after randomisation.
- Duration of active second stage of labour.
- Total duration of second stage of labour.
- Additional anaesthesia used for operative delivery.
- Active management of the third stage of labour.
- Episiotomy.
- Pain during delivery.
- Genital tract trauma (location and severity).
- Manual removal of the placenta.
- Primary post-partum haemorrhage necessitating blood transfusion.

- Duration of maternal inpatient stay after delivery.
- Satisfaction with experience of birth.
- Cord artery pH of < 7.05 in the second stage of labour (this is 2 standard deviations below the mean) with base deficit of ≥ 12 mmol/l (this is the threshold above which the risks of neurological damage increase).
- Presence of meconium-stained liquor.
- Apgar score of < 4 at 5 minutes.
- Resuscitation at birth.
- Skin-to-skin contact within the first hour of birth.
- Initiation of breastfeeding within the first hour of birth.
- Duration of infant inpatient stay.
- Admission to neonatal unit and duration of stay.

At 1 year

- Urinary incontinence.
- Faecal incontinence.
- Other bowel problems.
- Dyspareunia.
- General physical and psychological health.
- Major infant morbidity, for example gross neurodevelopmental delay, including cerebral palsy (if a diagnosis has been made).
- Hospital admissions.

Economic evaluation

A cost–consequences analysis with a time horizon of a 1-year follow-up and a NHS perspective was conducted alongside BUMPES.

Data collection schedule

Information at trial entry was collected from hospital notes and entered onto specifically designed study data collection booklets. The attending midwife recorded data about what position the woman was in during the second stage of labour 'for the majority of the time in the last 15 minutes', if this position had changed from the allocated position and the reasons for this. We collected clinical outcome information on the birth as well as neonatal outcomes and hospital inpatient stay data. As soon as possible after the birth, the woman was asked to complete a one-page questionnaire asking about her satisfaction with her birth experience. Women with surviving infants were followed up at 1 year with a self-administered questionnaire asking about specific health problems, their general health, the well-being of their infant's health and their use of NHS health-care resources.

Sample size and analysis

Assuming a rate for the primary outcome of SVB of 55% in the control group [derived from data published from the Comparative Obstetric Mobile Epidural Trial (COMET), which was a randomised trial that compared conventional epidural analgesia with low-dose epidural analgesia in nulliparous women in labour], a sample size of 3000 women (1500 in each arm) would have 90% power to detect a clinically significant (absolute) difference of 6% in the SVB rate between the two policies (with 95% CIs).

A detailed statistical analysis plan was developed and approved by the Trial Steering Committee prior to analysis of the trial data. For the primary analysis, participants were analysed in the groups into which they were randomly allocated, regardless of position recorded at any time during the second stage of labour. In order to take account of the number of comparisons, 95% CIs are presented for the primary outcome and 99% CIs for all other outcomes.

To examine whether or not the effect of the policy of position during the second stage of labour was consistent across specific subgroups, the following prespecified subgroup analyses were undertaken:

- gestational age (37^{+0} to 38^{+6} weeks; 39^{+0} to 40^{+6} weeks; and $\geq 41^{+0}$ weeks)
- maternal age ($\leq$ 24 years, 25–29 years, 30–34 years and $\geq$ 35 years)
- augmentation with oxytocin (Syntocinon®; Novartis Pharmaceuticals UK Ltd, Frimley/Camberley, UK) in the first stage of labour (yes/no)
- Index of Multiple Deprivation (population-based quintiles 1–5).

Results

Between October 2010 and January 2014, 3236 women were randomised to the BUMPES trial from 41 participating centres in England and Wales.

A total of 143 women (4.4%) were excluded from the analysis of the primary outcome. Data collection booklets were available for 100% of women recruited and analysed. Follow-up at 1 year was achieved for 61% of women.

Baseline characteristics were similar between the two arms of the trial.

There was a clear difference in the incidence of the primary outcome, SVB, between the groups, with 35.2% of women achieving SVB in the upright group, compared with 41.1% in the lying-down group (adjusted relative risk 0.86, 95% CI 0.78 to 0.94). This represents a 5.9% absolute risk increase in the chance of SVB in the lying-down group.

There was no evidence of a difference in most of the secondary maternal outcomes after study entry and during the second stage of labour. There was a significant difference in the duration of the active second stage of labour, which was shorter in the lying-down group (geometric mean ratio 1.08 minutes, 99% CI 1.01 to 1.15 minutes). Other secondary maternal outcomes, such as IVD and caesarean section, suggested an increased risk associated with the upright position, but these differences were not statistically significant at the 1% level. For example, the incidence of episiotomy was higher in the upright group than in the lying-down group (although the difference was not significant at the 1% level). There were no statistically significant differences in the risk of perineal trauma, although there appeared to be a slightly higher incidence of obstetric anal sphincter injury in the upright group (6.7%) than in the lying-down group (5.3%), but again this difference was not statistically significant at the 1% level.

Maternal satisfaction in labour was similar between the two groups.

Infant outcomes were extremely good throughout, with very few babies having a low Apgar score at 5 minutes or evidence of metabolic acidosis. Overall, about 12% of babies required resuscitation at birth.

The prespecified subgroup analyses showed no evidence of heterogeneity between any of the prespecified subgroups for the primary outcome of SVB.

There was no evidence of any differences between the groups in relation to the incidence or severity of urinary incontinence, faecal incontinence, constipation, haemorrhoids or dyspareunia, or general

well-being. Similarly, there was no evidence of a difference in the incidence of diagnosed cerebral palsy or severe neurodevelopmental delay in any of the infants at 1 year.

Cost-effectiveness analysis

Women randomised to the lying-down position consumed significantly fewer NHS resources than those randomised to an upright position during the original hospital stay [mean cost difference of £59 (95% CI £6 to £111) favouring the lying-down position]. This result was driven by more SVBs in the lying-down arm. At the 12-month follow-up, there were no significant differences in the overall costs incurred by mothers or their babies between the upright and lying-down groups. The significantly higher costs incurred by the women in the upright group were offset by the slightly, but non-significantly, higher costs incurred during follow-up by the women in the lying-down group.

Conclusions

There is clear evidence of a benefit of adopting a lying-down (lateral) position in the second stage of labour in nulliparous women with epidural analgesia, with no apparent disadvantages in relation to either short- or long-term outcomes for either mother or baby, and this is cost neutral for the NHS.

Like all pragmatic trials, the study had limitations. With an intervention such as this, masking is impossible, so the results may have been influenced by the women's and the midwives' perceptions of the different positions in their ability to achieve a SVB. Given that existing National Institute for Health and Care Excellence guidance recommends that women with an epidural should be encouraged to adopt whatever upright position they find comfortable, we might expect the trial results to suggest an improvement in SVB with an upright position if midwives' and women's behaviour was altered in these positions because of a firm belief that these were preferable. The findings that the lying-down position increased the chances of achieving a SVB suggest that this potential bias was either absent or minimal in its impact, or that the likelihood of the lying-down position leading to a SVB may be even greater.

We can only speculate about the mechanism by which a lying-down position increases the chance of a SVB. We have no direct measurements of the density of the epidural block in the two positions or of the level of the block. It is possible that women in the upright position acquired a more dense block around the birth canal because of the effect of gravity on the epidural drugs, which could have made expulsive efforts more difficult; however, the similarity of drug doses used in each group would suggest that this is unlikely. Women in the upright group, who may have been sitting, may have restricted the pelvic outlet because of the position on the coccyx or because of lower genital tract oedema and venous obstruction causing swelling of the soft tissues obstructing the pelvic outlet. In addition, it is possible that, in the lying-down group, easing of pressure of the fetal head on the pelvis improved uterine blood flow and therefore improved uterine activity. This would suggest a difference in the risk of operative delivery associated with failure to progress; however, the distribution of indications for operative delivery appeared to be the same in both groups. In addition, there was little difference in the use of oxytocin because of delay in labour progress after trial entry.

The response rate to the 1-year follow-up was 61%. Therefore, there is a possibility that the follow-up results are less than robust because of non-response bias. There were, however, no apparent differences in the response rates or characteristics of the two randomised groups, suggesting that there were minimal biases in the comparison of the two groups.

The lack of an impact of the risk of SVB on longer-term outcomes such as faecal incontinence is of interest. The observation that IVD is associated with increased risks of faecal incontinence is robust; however, in the BUMPES trial, the differences between the randomised groups of women in their risk of

SVB and IVD were relatively small, so, although there are associations between different modes of birth and long-term outcomes, these are likely to be diluted in a trial in which the differences in actual mode of birth are relatively modest (a 6% absolute difference in the risk of SVB). This is likely to explain the lack of an observed difference in long-term outcomes.

Trial registration

This trial is registered as ISRCTN35706297.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Chapter 1 Introduction

Scientific background

As the most effective form of pain relief in labour, epidural analgesia is chosen by up to 30% of women in the UK each year,[1] and this proportion has remained relatively stable over the last decade.[2] The uptake is greater in nulliparous women, with up to 40% of women having an epidural in large obstetric sites.[3] However, a systematic review of 23 randomised controlled trials (RCTs) that compared epidural analgesia with non-regional or no analgesia in labour found that epidural analgesia was associated with an increased risk of instrumental vaginal delivery (IVD) [risk ratio (RR) 1.42, 95% confidence interval (CI) 1.28 to 1.57].[4]

The trials that made the most contribution to the evidence base were conducted with epidural techniques that caused dense neuraxial blockade. Significant peripheral motor blockade, which can accompany conventional high-dose local anaesthetic epidural analgesia, inhibits mobility or the adoption of upright positions in labour. 'Low-dose epidurals', which use low-dose local anaesthetic in combination with opioids (usually fentanyl), were introduced in the early 1990s and are now in widespread use in the UK. This approach has been shown to result in a lower risk of IVD;[5] however, the rate of IVD is still higher than that in women with no epidural.[6]

Reducing the rate of IVD and increasing the spontaneous vaginal birth (SVB) rate would reduce short- and long-term morbidity for women by reducing the risk of perineal trauma and the effects of surgical repair. The incidence of perineal pain, dyspareunia and incontinence following IVD could also be reduced.[7–12] Although mobile epidurals preserve motor function (allowing greater mobility throughout labour) and can enable women to adopt upright positions, there is debate about whether or not an upright posture in the second stage of labour increases the SVB rate.

It is worth noting that the terms 'ambulation' and 'mobilisation' are often used interchangeably in the literature about epidural techniques that maintain motor function in the lower limbs. As the posture a woman adopts in labour is in part dependent on the motor power she retains, and this can be compromised by the peripheral motor blockade that accompanies effective epidural pain relief, it is clearly important to draw a distinction between *mobilisation*, the ability to move one's legs, change position or move around the bed normally, and *ambulation*, which refers to the act of walking during labour. The ability to adopt upright postures in labour requires that women retain the capacity to mobilise, and some of these women will be able to ambulate.

A systematic review of the impact on mode of delivery of ambulation or upright positions in the first stage of labour (before full dilatation of the cervix) among women with epidurals found no significant difference between IVD (RR 1.16, 95% CI 0.93 to 1.44) and caesarean section (RR 0.91, 95% CI 0.70 to 1.19).[13] The second stage of labour may represent a period during which the adoption of an upright posture could exert the greatest influence and affect delivery mode by facilitating descent of the fetal head. A Cochrane review of position in the second stage of labour in women *without* epidurals found a reduction in IVD rate in the upright group (19 trials; RR 0.78, 95% CI 0.68 to 0.90).[14]

Effectiveness of an upright position in the second stage of labour for women with epidurals

A Cochrane review of position in the second stage of labour among women with epidural analgesia was published in 2013,[15] after the BUMPES trial started. This review included trials that compared upright

positions with recumbent positions. The RR of SVB reported in the five included trials, including 879 women, was 1.02 (95% CI 0.81 to 1.28). There was clinical heterogeneity between the trials in relation to the eligibility criteria (some included multiparous women whereas others were restricted to nulliparous women) and in the nature of the interventions. In the upright group, for example, some women were actively encouraged to walk, and others were supported in a sitting position. In the recumbent group, some trials had allocated women to a sitting position and others to a lateral position. The authors concluded that there was no clear evidence about whether or not position in the second stage of labour made a difference to outcomes.[15]

Effects on short- and longer-term maternal morbidity

An intervention that increases the rate of SVB by reducing the rate of IVD or caesarean section would also be expected to have an effect on short- and longer-term maternal morbidity. Faecal incontinence is clearly documented as being associated with forceps,[11,16] including ongoing symptoms in women who only ever have one forceps delivery.[17] There may also be an increased risk of urinary incontinence, although this may be more closely associated with a longer second stage of labour;[18,19] however, women who have a caesarean section have a lower risk of symptoms.[20,21] Other bowel problems such as haemorrhoids[19,22,23] and constipation[24] are more common after IVD, as are perineal pain and dyspareunia.[24,25] Caesarean section has many adverse sequelae, but, with the exception of faecal incontinence, most of these symptoms are less likely to occur in association with this delivery mode. It is therefore important to investigate positive impacts as well as any possible negative impacts of upright positions in the second stage of labour on maternal health outcomes.

There is increasing interest in obtaining maternity service users' views of satisfaction with their experience of birth, as an indicator of the quality of their care and to inform organisational and policy changes.[26] Satisfaction is poorly defined and measured, although it is generally agreed that it is a multidimensional concept.[27,28] In a systematic review of factors influencing women's satisfaction with birth, with a focus on the role of pain and pain relief, four factors (caregiver support, participation in decision-making, personal expectations and caregiver–patient relationship) were identified as important influences.[28] As position in the second stage of labour could influence a woman's perceptions of the support she receives, her feelings of control and her expectations and experiences of labour and birth, satisfaction is an important consideration. The impact of negative consequences of the position adopted in the second stage of labour on these perspectives should also be identified.

Policy and practice at the time the trial commenced

Up to 30% of women in the UK use epidural analgesia for pain relief at some point in labour,[1] with wide variation in the rate of epidural use between units. In a 1997 survey of UK units regarding epidural analgesia for labour, the epidural rate, including 'low-dose' epidurals, ranged from 0% to 85%, with an average rate of 24%. Of the 190 units that replied to the survey, 45 (24%) offered 'low-dose epidurals'.[29] There is variation in the epidural technique employed to provide pain relief in labour and hospital policies governing maternal ambulation with an epidural in situ. A UK survey was conducted via the Obstetric Anaesthetists' Association in 2008 to characterise national epidural practice and policy, with a response rate from lead clinicians of 80%.[30] It found that 95% of respondent units employed various epidural techniques consistent with the adoption of a range of upright positions, including ambulation, and that less than 50% of women actually did ambulate. Findings from the BUMPES trial are therefore widely generalisable to the majority of the nulliparous population that chooses epidural pain relief. With regard to reported hospital policies, 34% permitted maternal ambulation with low-dose epidural analgesia in situ.[30] Of those units that did not permit ambulation, 37% cited lack of evidence of a beneficial effect as a reason for this policy. This reluctance may reflect the current uncertainty in this field and that in general midwives have less experience of enabling women with epidurals to ambulate in second-stage labour rather than being in bed.

Rationale for a trial comparing upright with lying-down position

The National Institute for Health and Care Excellence (NICE) guidelines on intrapartum care published in 2007[31] (with no change in the update published in 2014) noted that there is 'no effect of mobilisation following epidural analgesia on any maternal or neonatal outcomes', and recommended that 'women with regional analgesia should be encouraged to move and adopt whatever upright positions they find comfortable throughout labour' (section 1.5.7, p. 22). This guidance is likely to lead to an increase in the use of upright positions, hence the need to compare upright positions with 'lying-down' positions rather than with usual care, given that usual care will increasingly include women assuming an upright position. Good-quality evidence is needed on whether or not upright positions in the second stage of labour in women with epidural analgesia have any beneficial effect on delivery mode and other important outcomes. It is crucial that the policies for the upright and comparison groups are clearly defined and monitored to ensure separation of the two approaches and to provide robust evidence about whether or not adopting an upright position does improve outcomes for women and their babies.

Chapter 2 Methods

Aim of the BUMPES trial

This was a multicentre RCT in which the primary objective was to evaluate whether or not, in nulliparous women who choose low-dose epidural analgesia, a policy of adopting an upright position throughout the second stage of labour is associated with an increase in the incidence of SVB, compared with a policy of adopting a lying-down position.

This objective was supported and supplemented by the following secondary objectives:

- to evaluate whether or not there are differences between the two policies in important clinical outcomes for women and babies around the time of birth and 1 year post partum
- to evaluate the cost-effectiveness of the two policies for position during second-stage labour from a NHS perspective
- to measure women's satisfaction with, and experience of, labour and delivery.

Trial design

The BUMPES study was a pragmatic, multicentre, individually randomised controlled trial that had a target recruitment of 3000 nulliparous women who had a low-dose epidural in situ. It was a two-arm parallel-group trial with one arm allocated to adopting an upright position during the second stage of labour and one arm allocated to adopting a lying-down position during the second stage of labour (*Figure 1*).

Participant eligibility

The following inclusion criteria were applied throughout participant recruitment.

Inclusion criteria

Women admitted to a participating labour ward who fulfilled all of the following criteria were eligible to be randomised into the trial:

- aged ≥ 16 years of age
- ≥ 37 weeks' gestation
- nulliparous (no previous delivery ≥ 24^{+0} weeks' gestation)
- singleton cephalic presentation
- intended SVB
- in the second stage of labour
- with a low-dose epidural in situ during the first stage of labour, providing effective pain relief
- able to understand printed documentation produced in English
- able to give written answers in English.

Exclusion criteria

Women who did not fulfil all of the inclusion criteria were not included in the study.

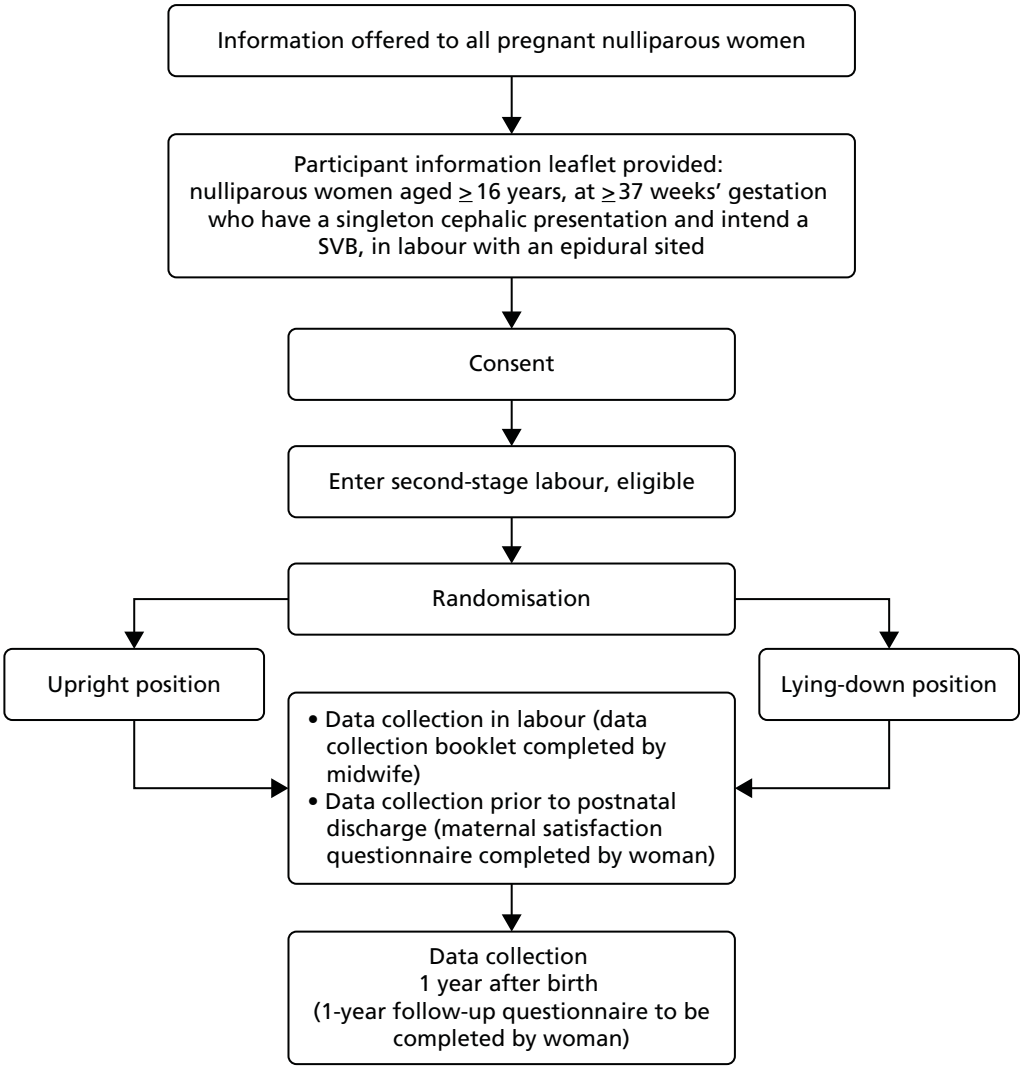

FIGURE 1 Flow chart of participant recruitment.

Sample population

All women who met the inclusion criteria were considered potentially eligible to participate in the study.

Study setting

Trial recruitment was undertaken in the labour wards of participating NHS maternity hospitals.

Information for women and obtaining informed consent

Information about the trial was provided to all nulliparous women during the antenatal period, after their booking appointment. This process was individualised for each participating centre depending on their routine practice to maximise the number of women offered information well in advance of labour. For example, in some sites, women were provided with information about the trial at their routine anomaly scan appointment (18–22 weeks). All women had the opportunity to ask questions of their midwives or obstetricians at the hospital, or they could contact the trial office. When a woman in a participating centre had an effective epidural established during the first stage of labour, she could then be offered a participant

information leaflet on the study. If, after reading this and having the opportunity to ask questions, she was willing to take part in the study, then informed consent was taken. The participant information made it clear that women were free to withdraw from the trial at any time for any reason without prejudice to their future care, and with no obligation to a give a reason for the withdrawal. Written informed consent was obtained by a health professional (e.g. midwife, obstetrician or anaesthetist) with delegated authority from the principal investigator at each site. Consent comprised a dated signature from the woman and a dated signature of the person who obtained informed consent. A copy of the signed informed consent document was given to the woman. In addition, one copy was retained in the woman's medical notes, one was retained in the study site file and one was sent to the Trial Co-ordinating Centre.

Interventions

Women were allocated to a policy of either upright maternal position (intervention group) or lying-down maternal position (control group).

Intervention group

Women were allocated to a policy of *upright maternal position that would maintain the pelvis in as vertical a plane as possible* during the second stage of labour, with the intention of continuing this until the birth. Women allocated to the 'upright' group were encouraged by their midwife to adopt positions that allowed for as upright a posture as possible. This could include walking, standing, sitting out of bed, supported kneeling or completely upright in an obstetric bed (*Figure 2*) for as much of the second stage as possible.

FIGURE 2 Possible positions for women randomised to the upright maternal position. (a) Seated; (b) supported kneeling; (c) seated with extended legs; and (d) completely upright.

Control group

Women were allocated to a policy of a *lying-down maternal position that would maintain the pelvis in as horizontal a plane as possible* during the second stage of labour, with the intention of continuing this until the birth. Women allocated to the 'lying-down' group were encouraged to adopt a lying-down position that would mean lateral positions or lying down in bed for as much of the second stage of labour as possible. The bed could be tilted at up to a maximum of 30 degrees from horizontal (*Figure 3*).

Monitoring of adherence to allocation

In the second stage of labour, women with an effective epidural anaesthetic frequently have no desire to push. After confirmation of the second stage of labour, women were entered into the study. Midwives were encouraged to manage the second stage in two phases: a period of passive second-stage labour, allowing time for descent of the fetal head, followed by an active phase of expulsive pushing.

Training emphasised to the midwives the importance of supporting the woman in her allocated position, especially for the passive stage (which could last up to 2 hours). Positions were recorded on the trial worksheet at 15-minute intervals using a tick box, and midwives recorded 'reason for change' if the woman was moved out of her allocated position. As a pragmatic study, it was agreed that there would be expected reasons for changing position, for example fetal distress, fetal blood sampling or maternal discomfort, or to help improve pushing in the active second stage of labour. It was emphasised that midwives were required to record this information.

Randomisation

Participants were randomised to the allocated intervention (allocation ratio 1 : 1) using a web-based central service. To confirm eligibility, investigators were required to confirm the woman's age and gestational age, that this was the woman's first birth, that the fetus was a singleton with cephalic presentation and that an effective epidural was in situ, as well as obtaining signed consent. The randomisation software used random permuted blocks of sizes 2, 4, 6, 8 and 10, selected according to the proportions specified by Pascal's triangle (1 : 4 : 6 : 8 : 10) to ensure that the staff recruiting women to the trial could not reliably predict the next allocation. Because of the large numbers of women recruited in each centre, no stratification by clinical characteristics was planned, although there was stratification by centre. The procedures for

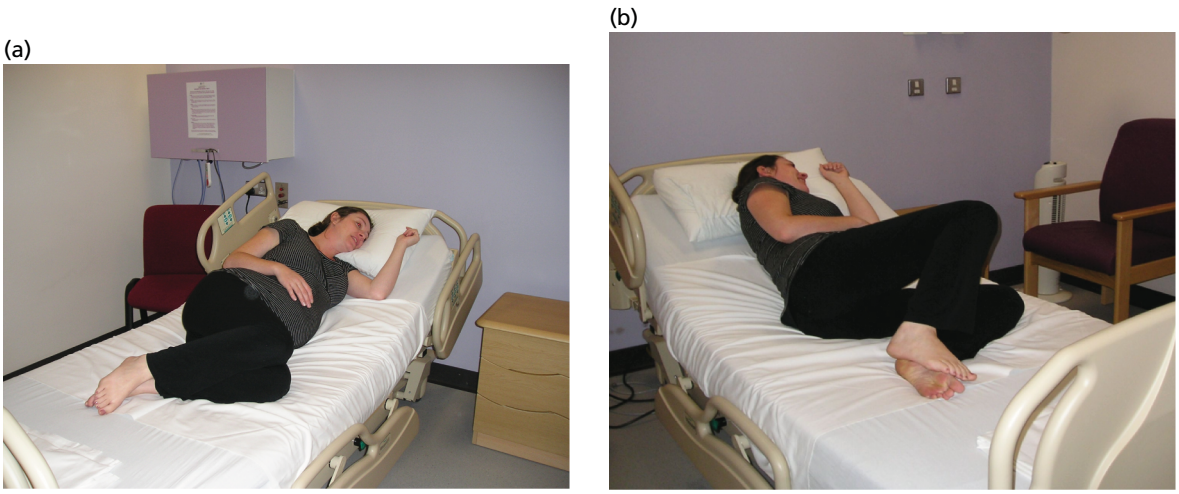

FIGURE 3 Possible positions for women randomised to the lying-down maternal position. (a) From in front; and (b) from behind. Note: a truly supine position (i.e. flat on the back) should not be used during labour because of the risk of aortocaval compression from the gravid uterus causing maternal hypotension.

randomisation were fully documented, tested prior to the start of the trial, and monitored by the randomisation centre during the trial.

Outcome measures

Primary outcome measure

The primary outcome measure was the incidence of SVB.

Secondary outcomes

The following secondary outcomes were collected.

Mode of delivery

- Instrumental delivery (forceps and ventouse)
  - and primary indication.
- Caesarean section
  - and primary indication.

Outcomes from randomisation until delivery

- Augmentation of labour.
- Major interventions to maintain blood pressure (e.g. vasopressors).
- Hypotension (systolic blood pressure of < 100 mmHg prior to delivery).
- Application of fetal scalp electrode.
- Fetal blood sampling.
- Total doses of epidural local anaesthetic and opioids administered after randomisation.
- Duration of active second stage of labour.
- Total duration of second stage of labour.
- Additional anaesthesia used for operative delivery.

Immediate post-delivery outcomes

- Active management of the third stage of labour.
- Episiotomy.
- Pain during delivery.
- Genital tract trauma (location and severity).
- Manual removal of the placenta.
- Primary post-partum haemorrhage requiring blood transfusion.

Postnatal period: woman

- Duration of inpatient stay after delivery.
- Satisfaction with experience of birth.

Postnatal period: infant

- Cord artery pH of < 7.05 in second stage of labour [this is 2 standard deviations (SDs) below the mean] with a base deficit of ≥ 12 mmol/l (this is the threshold above which the risks of neurological damage increase).

- Presence of meconium-stained liquor.
- Apgar score of < 4 at 5 minutes.
- Resuscitation at birth.
- Skin-to-skin contact within the first hour of birth.
- Initiation of breastfeeding within the first hour of birth.
- Duration of inpatient stay.
- Admission to neonatal unit and duration of stay.

One year after birth: woman

- Urinary incontinence.
- Faecal incontinence.
- Other bowel problems.
- Dyspareunia.
- General physical and psychological health.

One year after birth: infant

- Major morbidity, for example gross neurodevelopmental delay, including cerebral palsy (if a diagnosis has been made).
- Hospital admissions.

Data collection schedule

Information at trial entry, including eligibility and maternal characteristics, was collected from hospital notes onto the specifically designed data collection booklet (DCB) (see *Appendix 1*). The position to which the woman was allocated was recorded on the DCB in two places – once in the eligibility section and again on the worksheet used to record the woman's actual positions. As soon as possible after the woman was randomised, the attending midwife encouraged her into the allocated position and started recording on the DCB what position the woman was in 'for the majority of the time in the last 15 minutes', and if this position had changed from the allocated position and, if so, the reasons for this. Information on drugs taken after study entry and during labour was also recorded, as was other clinical information about the labour. The DCB also allowed for the collection of clinical outcome information on the delivery, as well as on neonatal outcomes and hospital stay.

If either the woman or the infant received a higher level of care (HLC), the relevant HLC form (see *Appendices 2* and *3*) was completed by the attending midwife.

As soon as possible after delivery, the woman was asked to complete a one-page questionnaire asking about her satisfaction with her birth experience, as well as asking her to provide an overview of what position she was in most of the time after study entry (see *Appendix 4*).

Women with surviving infants were followed up at 1 year with a self-administered questionnaire asking about their general health and well-being, with specific questions relating to any urinary and bowel problems. This questionnaire also requested information on the use of health services for themselves or their child (see *Appendix 5*). Prior to contact, mortality status and place of residence of both the woman and her infant were checked using NHS summary care records. Only women whose infants resided at the same address were contacted.

An overview of the time points at which trial data were collected is presented in *Table 1*.

TABLE 1 Summary of data collection schedule

Data collection instrument	Time point			Person completing the data collection instrument
	During labour	After delivery	12 months	
Woman and infant DCB	✗	✗		Completed by the attending midwife during labour and immediately after birth For all participating women and infants
HLC form: woman		✗		Completed by the attending midwife during the woman's admission and/or immediately after discharge from hospital; checked by the local principal investigator Only completed for women receiving a HLC following delivery
HLC form: infant		✗		Completed by the attending midwife during the infant's admission and/or immediately after discharge from hospital; checked by the local principal investigator Only completed for infants receiving a HLC following birth
Maternal satisfaction form		✗		Completed by the woman as soon as possible after delivery For all participating women
Follow-up questionnaire			✗	Postal questionnaire completed by the woman For all women whose babies were alive and both the woman and baby were resident at the same address

Sample size

The proposed sample size was 3000 women. At the time of writing the funding application, the assumed rate of the primary outcome of SVB in the control group was 55%. This was derived from data published from the Comparative Obstetric Mobile Epidural Trial (COMET) reflecting SVB rates in nulliparous women with a mobile epidural in the second stage of labour.[5] A total sample size of 3000 women (1500 in each arm) would have 90% power to detect a clinically significant (absolute) difference of 6% in the SVB rate between the two policies (with a 95% CI). The cost of implementing this technology is low; therefore, even modest differences in outcome are likely to be cost-effective. Detecting the smallest and most clinically relevant effect size possible was therefore desirable. A 6% absolute risk difference, which equates to a 10% RR reduction (approximately), was well within the uncertainty of the existing evidence (despite the existing trials' heterogeneity) and was considered sufficient to change clinical practice.

The proportion of the upright group achieving a SVB was anticipated to be 61% under the null hypothesis. The test statistic used was the two-sided *z*-test with pooled variance. The significance level of the two-sided test was targeted at 5%. When considering longer-term outcomes, the proposed sample size of 3000 would be sufficient to detect a difference in the prevalence of faecal incontinence of 12% in the control group compared with 8% in the intervention group. The incidence of this outcome has been estimated as 14% among forceps deliveries and 10% among women with a SVB.[11]

On collation of the pilot data for an interim analysis presented to the Data Monitoring Committee (DMC) in 2011, it was recognised that the combined primary outcome event rate was lower than anticipated. As of 6 December 2011, the overall SVB rate for BUMPES (combining upright and lying-down groups) was 33.8% [(95% CI 26.1% to 42.1%) based on 49/145 events]. With a reduction in the control group event rate (from an anticipated 55% to between 30% and 40%), keeping the sample size fixed at 3000 would mean that a RR of between 1.13 and 1.19 would be detectable, equivalent to an absolute risk reduction of 5–6%. Although there was not sufficient power to detect a RR as small as the planned 1.11, the

absolute risk detectable is similar. The Trial Steering Committee (TSC) agreed that changes to the target sample size were therefore unnecessary.

Governance

Ethics arrangements

Favourable ethics approval for the study was granted by the National Research Ethics Service – Oxfordshire Research Ethics Committee (REC) B on 5 January 2010 (reference number 09/H0605/114). Approval was also sought from the Health and Social Care Information Centre (now known as NHS Digital) to establish the status of the mothers and their babies and details of the general practice at which they were registered. This was to ensure that 1-year follow-up questionnaires were not sent if either mother or baby may have died or if the family had changed address. NHS Digital approval was granted on 29 January 2013.

Approval was obtained from the research and development (R&D) departments for all participating hospitals. *Table 2* provides details of the substantial amendments to the protocol approved by the REC. The R&D office of each participating hospital was notified of all amendments after REC approval was received. The REC were notified of all serious adverse events (SAEs) and progress reports were submitted annually.

The trial was registered with the International Standard Randomised Controlled Trial Register under the reference number 35706297, and was adopted into the National Institute for Health Research (NIHR) portfolio under reference 8375.

TABLE 2 Research Ethics Committee amendments

Amendment	Date	Description of main items in the request for approval (including version of protocol if revised)
Substantial amendment 1	9 June 2010	Protocol version 2 (1 March 2010) Key changes to the protocol were clarification on defining the term 'nulliparous', rewording the data collection section and updating the photographs of maternal positions. The PIL, consent form and antenatal leaflet were also updated
Substantial amendment 2	13 August 2010	Submission of the maternal satisfaction questionnaire for approval
Non-substantial amendment 1	4 August 2010	Administrative updates to the version numbers on the PIL and consent forms
Non-substantial amendment 2	23 September 2010	Administrative update to the antenatal leaflet
Substantial amendment 3	7 March 2011	Protocol version 3 (1 December 2010) The majority of changes to the protocol were typographical or were made to increase clarity. The term 'mobile epidural' was replaced by 'low-dose epidural' throughout the document for consistency and to conform with clinical terminology. The secondary outcomes: 'application of fetal scalp clip' and 'fetal blood sampling' were added in order to assess concern over potential fetal distress Recruitment posters were also designed to encourage midwives to recruit women to BUMPES
Substantial amendment 4	25 July 2011	Protocol version 4 (20 July 2011) Transfer of study sponsorship from the NPEU, University of Oxford to UCL. All study documents updated to reflect changes. The follow-up questionnaire entitled 'You and Your First Child's Health at One Year' and a study poster were also submitted for approval

TABLE 2 Research Ethics Committee amendments (*continued*)

Amendment	Date	Description of main items in the request for approval (including version of protocol if revised)
Substantial amendment 5	24 November 2011	With study sponsorship and co-ordination being transferred from the NPEU to UCL, a letter was designed that notified women of the intention to also transfer their data (including name and address details) to UCL
Non-substantial amendment 3	14 February 2012	Contact details updated on the study protocol, PIL, consent form, 1-year follow-up form, maternal satisfaction form and antenatal leaflet
Non-substantial amendment 4	13 March 2012	Updated version number of PIL referenced in consent form
Substantial amendment 6	2 May 2012	Protocol version 5 (2 March 2012) Protocol changes made to reflect the change in contact details of the co-ordinating team, number of participating centres and minor typographical changes. For women with missing consent forms, a re-consent form and a covering letter for this form were also submitted for approval. The photos of the 'lying-down' positions were changed in the PIL and antenatal leaflet to reflect the positions more accurately. A life-size poster to be placed in the antenatal clinics and delivery suites was also submitted for approval
Substantial amendment 7	12 September 2012	A follow-up reminder letter was designed to be sent to recruited women when no response was received following a 1-year follow-up questionnaire being sent out
Substantial amendment 8	7 January 2013	Change of principal investigator at one of the participating centres. Minor amendment raised as substantial in error
Substantial amendment 9	16 April 2013	The 1-year follow-up accompanying letter was designed to be sent with 1-year follow-up questionnaire. As the questionnaire sent out coincided with the infant's first birthday, a gender-neutral birthday card was designed and submitted for approval. Minor changes were also made to the re-consent letter
Non-substantial amendment 5	16 May 2013	Permission to use NIHR 'OK to Ask' promotion with the addition of the BUMPES logo and the words 'Ask your midwife about'. This was used to promote BUMPES locally for International Clinical Trials Day (20 May 2012)
Substantial amendment 10	21 February 2014	The 1-year follow-up accompanying letter content and layout were updated to include details of the online questionnaire. Approval was sought to remind participants to complete questionnaires via text message and/or e-mail. Details regarding a small incentive to complete the 1-year follow-up questionnaire in the form of a £5 shopping voucher were also included in the letter, e-mail and text message sent to women
Substantial amendment 11	14 July 2014	Submission of the nested study protocol to assess the effectiveness on the return rate of the 1-year follow-up postal questionnaires. This was a promise of a monetary incentive (£10 voucher) made at the point of sending the initial follow-up questionnaire or on reminder letters only. One-year follow-up accompanying letters were also updated to include details on incentives
Substantial amendment 12	27 April 2015	Protocol version 6 (27 April 2015) Changes on how adherence to the allocated position would be analysed, minor clarification to the per diem cost calculation and clarification on how the study data would be analysed

NIHR, National Institute for Health Research; NPEU, National Perinatal Epidemiology Unit; PIL, participant information leaflet; UCL, University College London.

Trial governance

Trial Steering Committee

The TSC included an independent chairperson, four other independent professional members (statistician, consultant anaesthetist, health economist, professor of midwifery) and one patient representative. Non-independent members included the chief investigator. Membership of the committee was approved by the NIHR Health Technology Assessment (HTA) programme. The TSC agreed a charter at its first meeting, based on that used by the Medical Research Council Clinical Trials Unit. The TSC met five times.

Data Monitoring Committee

The DMC was established for the trial and met as and when the DMC members requested.[32] The DMC comprised an independent chairperson and three independent members (a statistician, a professor of women's health and a consultant in maternal and fetal medicine). Membership of the committee was approved by the NIHR HTA programme. During the period of recruitment to the trial, interim analyses were supplied, in strict confidence, to the DMC, together with any other analyses the DMC members requested. Meetings of the committee were arranged periodically, as considered appropriate by the chairperson.
In the light of interim data, and other evidence from relevant studies (including updated overviews of the relevant RCTs), the DMC agreed to inform the TSC if, in its view, there was proof beyond reasonable doubt that the data indicated that any part of the protocol under investigation was either clearly indicated or clearly contraindicated, either for all women or for a particular subgroup of trial participants. A decision to inform the TSC would be based on statistical, clinical and ethical considerations.

The TSC and DMC members met jointly on two occasions: once at the beginning of the project before recruitment started, to review and comment on the protocol and data collection instruments, and to agree the TSC and DMC charters, and then again at the end of the project to agree the final analysis and provide feedback to the investigators about interpretation of the findings.

Clinical Investigators Group

The Clinical Investigators Group (CIG) comprised the chief investigator, co-applicants (including a lay member), clinical investigators from selected study sites, trial health economists and the trial statistician.

Appendix 6 lists the membership of the TSC, the DMC and the CIG.

Serious adverse event reporting

Serious adverse events were reported to the University College London (UCL) Trial Co-ordinating Office within 48 hours. The Trial Co-ordinating Office notified the chairperson of the DMC and the REC. All SAEs occurring during the trial observed by the investigator or reported by the participant, whether or not attributed to the trial, were reported on the DCB. SAEs considered to be related to the trial by the investigator were followed up until resolution or until the event was considered stable. The local investigator was asked to provide follow-up information when necessary. All related SAEs that could have resulted in a participant's withdrawal from the trial, or which were present at the end of the trial, were followed up until a satisfactory resolution occurred.

The chief investigator submitted to the REC, once a year throughout the clinical trial, a safety report that included all SAEs.

Data handling, checks, cleaning and processing

All data collection forms (i.e. DCBs, HLC forms, maternal satisfaction and 1-year follow-up forms) and consent forms, once completed and returned to the UCL Comprehensive Clinical Trials Unit (CCTU), were logged as

received and date stamped. Data were double entered at the UCL CCTU using the study database, by independent data clerks. Validation routines checked for missing data and inconsistencies on an ongoing basis. This included screening for out-of-range data, with cross-checks for conflicting data within and between data collection forms using computerised logic-checking screens. Any validation errors on the DCBs and HLC forms were queried and documented. Queries were communicated to the appropriate centres by the trial manager. Errors on the maternal satisfaction questionnaire and the 1-year follow-up form were not queried with the woman.

Cost-effectiveness analysis

An economic evaluation was conducted as part of this trial and is reported in detail in *Chapter 6*.

Patient and public involvement

When the initial investigator group was being assembled to develop the trial, the National Childbirth Trust was approached to suggest a lay member who would be willing to join the group as a co-investigator. Mary Nolan agreed to join the group, and assumed equal membership of the co-investigator group at all planning meetings and trial conduct meetings, and in the drafting of the application, developing the detailed trial protocol and data collection forms, and report and paper writing. Mary took a lead in helping the team to develop participant information leaflets to be used in the antenatal period and at the time of labour, as well as helping to plan dissemination activities and drafting and developing the summary information for the public. During the course of the trial, Mary Nolan left the NCT to take up a position as Professor of Perinatal Education at the University of Worcester, but continued to represent the potential participant's perspective in all aspects of the trial development, conduct and analysis.

Chapter 3 Analysis plan

The statistical analysis plan (SAP) was written and approved before unblinding the data for statistical analysis (see *Appendix 7*). The SAP provided details of the presentation and analysis of the results from the trial. The principles set out in the SAP were not intended to curtail exploratory analysis (e.g. to decide cut-off points for categorisation of continuous variables) or to prohibit accepted practices (e.g. data transformation prior to analysis), but they were intended to establish the rules that were followed, as closely as possible, when analysing and reporting the trial.

Any deviations from the SAP are described and justified in this report.

Patient groups for analysis

Losses to the trial post randomisation were defined as any of the following:

- women for whom a valid consent form was not received
- women for whom consent to use their data was withdrawn
- women not in the second stage of labour when randomised and who did not reach the second stage before delivery
- women not in labour or without an epidural in place at the time of randomisation.

The numbers (with percentages of the randomised population) of post-randomisation exclusions are reported by randomised treatment group, and the reasons summarised.

Women could specify whether or not data collected up to the point of withdrawal could be used. If the response was 'no', then they were counted as post-randomisation exclusions. If the response was 'yes', then they were reported as 'missing' for all subsequent outcomes.

For the primary analysis, participants were analysed in the groups into which they were randomly allocated, that is, comparing the outcomes of all women and infants for women allocated to a policy of an upright position with those of women allocated to a policy of lying down, regardless of position recorded at any time during the second stage of labour. Losses to the trial post randomisation are excluded from all analyses, with the exception of the safety-reporting population, which excluded women for whom a valid consent form was not received and women who withdrew and did not consent to use of their data.

The unit of analysis was the woman for all maternal outcomes and the infant for all infant outcomes.

Descriptive analyses

The flow of participants through each stage of the trial is summarised using a Consolidated Standards of Reporting Trials (CONSORT) diagram (see *Figure 8*). Specifically, for each intervention group we report the numbers of women randomly assigned and women for whom the incorrect allocation was recorded in the eligibility section of the DCB. The number of ineligible women randomised is reported, with reasons for ineligibility. The number of post-randomisation exclusions and women analysed for the primary outcome is also reported. We report numbers for the 1-year follow-up, women lost to follow-up and women who withdrew before 1 year. The total number of eligible women was not collected during the conduct of this study, as it was considered too great a burden for the participating centres and would not be sufficiently reliable.

Numbers (with percentages) for binary and categorical variables and means (and SDs) or medians (with lower and upper quartiles), or geometric means for continuous variables are presented; no tests of statistical significance were performed, nor CIs calculated, for differences between randomised groups on any baseline variable.

The number (with percentages) of losses to follow-up among women selected for the 1-year assessment is reported in the CONSORT flow chart by trial arm, and the reasons reported. Selected demographic and clinical characteristics, the primary outcome and selected short-term outcomes of women and their infants with 1-year data available were compared with those without 1-year data.

Missing data for primary and secondary outcomes, from baseline to the end of follow-up, are summarised for the two trial arms. Not all data were routinely collected by all hospitals; for example body mass index (BMI), cord artery pH and base deficit were sometimes omitted. The DCB allowed midwives to tick 'data not recorded'. These data are summarised by trial arm and reported separately from data missing or unknown. Missing data for the primary outcome were negligible. If any data items were missing on the DCBs, every effort was made to extract these data from the hospital involved.

Primary effectiveness analyses

Outcomes are summarised by trial arm using counts and percentages for categorical variables, means and SDs for normally distributed continuous variables or medians and interquartile ranges for other continuous variables. In addition, geometric means are presented for durations of stages of labour, as these are inherently highly skewed data.

An adjusted analysis was performed on all comparative analyses adjusting for centre (the stratification factor at randomisation) as a random effect. Binary outcomes were analysed using log-binomial regression models and results presented as adjusted RRs with corresponding CIs. If the model did not converge, then log-Poisson regression models with robust variance estimation were used.[33] If the model was still unstable, then the centre was removed and unadjusted RRs presented. Continuous outcomes were analysed using linear regression models and results presented as adjusted differences in means with associated CIs. Unadjusted Hodges–Lehmann[34] median differences (plus CIs) for skewed continuous variables are presented. The estimates are based on a difference between distributions. The Hodges–Lehmann median difference is calculated by forming all possible differences between the first treatment group and the second treatment group, and taking the median of those differences.

In addition, geometric mean ratios (GMRs) are presented for durations of the stages of labour as the distribution of these data is highly skewed. A geometric mean is a measure of central tendency that is based on the product of values (as opposed to an arithmetic mean that sums the values). A ratio of geometric means provides an indication of how large one geometric mean is relative to another.

Comparisons between randomised groups of all primary and secondary outcomes are reported in full for completeness and transparency, that is, there is no selective reporting of outcomes.

In order to take account of the number of comparisons, 95% CIs are presented for the primary outcome and 99% CIs for all other outcomes.

Description of adherence to allocation

As described in *Chapter 2*, *Data collection schedule*, a record was made every 15 minutes of the woman's position 'for the majority of the time since the last assessment', and if this position had changed from the previous assessment the reasons for this change were recorded. Reasons for a change from a woman's allocated position were recorded as free text.

Positions recorded on the DCB were categorised according to whether or not the women were 'lying down', 'upright' or in 'other' positions for each 15-minute interval. For each interval, the categorised position was compared with the position allocated for the woman, and if the allocated position was the same as the categorised position then that 15-minute interval was coded as 'adherent'. All other positions were coded as 'non-adherent'. Some manual coding was required for positions recorded as text. Positions recorded as lithotomy were categorised as 'lying down' as the pelvis was in a horizontal position.

A summary of adherence to allocated position is reported by trial arm for (1) the passive second stage (i.e. before pushing commenced); (2) the active second stage (i.e. pushing); and (3) the whole of the second stage. Summaries of adherence data are calculated as the proportion of 15-minute intervals a woman spends in the position to which she was allocated out of the total number of 15-minute intervals recorded in the passive, active or whole of the second stage of labour. Medians and interquartile ranges are presented owing to the skewed distribution of the data.

Hodges–Lehmann differences in medians with corresponding 95% CIs are presented by randomised group.

There are a variety of reasons why women change from their allocated position. Changing position to allow fetal blood sampling to be performed, to improve effective fetal heart rate monitoring, was considered 'clinically unavoidable'. All reasons for change were reviewed and classified as clinically avoidable or unavoidable in accordance with these criteria. The analysis was performed for adherence by dealing with periods in which changes to a non-allocated position were considered necessary for 'clinically unavoidable reasons' as adherent.

Reasons for change from allocated position were coded by the trial statistician and an independent assessor, and are presented by trial arm using counts and percentages.

The self-completed maternal satisfaction questionnaire included a question asking the woman to record what position she was in for the majority of the time during the passive and active stages of labour with possible responses being 'lying down', 'upright', 'other' and 'can't remember'. These data have been summarised by trial arm using counts and percentages along with 95% CIs for differences in percentages. A qualitative comparison has been made between these results and the results from the DCB data provided by the midwife, to ascertain the extent to which reporting bias may have occurred, if at all.

Additional effectiveness analyses

The primary analysis was adjusted further for the primary outcome (pre-specified in the SAP) to investigate the impact of the following known prognostic factors (in addition to centre): age as a continuous variable, ethnicity, diagnosis of delay and onset of labour (induced vs. spontaneous).

To examine whether or not the effect of policy of position during the second stage of labour was consistent across specific subgroups of women, the following prespecified subgroup analyses were undertaken:

- gestational age (37^{+0} to 38^{+6} weeks; 39^{+0} to 40^{+6} weeks; and $\geq 41^{+0}$ weeks)
- maternal age ($\leq$ 24 years, 25–29 years, 30–34 years and $\geq$ 35 years)
- augmentation with oxytocin (Syntocinon®; Novartis Pharmaceuticals UK Ltd, Frimley/Camberley, UK) in the first stage of labour (yes/no)
- Index of Multiple Deprivation (IMD; population-based quintiles 1–5; derived using the postcode of the woman's last known address based on the Indices of Multiple Deprivation 2010[35] and Ordnance Survey Code-Point Open[36] February 2013).

For the trial primary outcome, results are presented as forest plots showing the RR plus 95% CI for each subgroup,[37] by intervention group, with the *p*-value for the statistical test of interaction.[38] Centre was included as a stratifying factor in the list of subgroup analyses in the original protocol, as we were expecting

to recruit to target using five centres only. Recruitment rates were poor and we expanded the number of recruiting centres to 41. A subgroup analysis on 41 centres was therefore not considered relevant.

A prespecified sensitivity analysis on the 1-year maternal outcomes was carried out on a restricted data set that excluded all women who were pregnant or had another child at the time of completing the follow-up questionnaire.

Statistical software

Stata/SE® for Windows version 13.1 (StataCorp LP, College Station, TX, USA) was used for all analyses.

Reliability

All outcome data, except for maternal satisfaction questionnaire data and 1-year questionnaire data, were recorded in the women's hospital notes. Site-monitoring visits verified a random sample of data collected on the DCBs and HLC forms, by making comparisons with information recorded in hospital notes. Self-administered forms were not verified.

Data relating to the calculation of the process outcomes (i.e. maternal position at 15-minute intervals since study entry) were recorded by the midwife on the DCB only, and the DCB was itself the source documentation and can therefore not be verified directly with any other source. The maternal satisfaction questionnaire aimed to confirm these data with a question asking the women to record what position they were in for the majority of the time during the passive and active stages of labour.

The coding of position data and reasons for a change from allocated position recorded as text were validated by an independent clinician.

Protocol violations and deviations

A protocol violation is a failure to comply fully with the final study protocol as approved by the REC and research department, such as a serious non-compliance with the protocol resulting from error, fraud or misconduct, and results in the exclusion of a patient from the analysis for the study. There were no protocol violations.

A protocol deviation is a departure from the final study protocol as approved by the REC, with minor consequences on the integrity of the data. Protocol deviations are those that resulted in exclusion from the analysis reported in *Chapter 5* (see *Figure 8*). There was only one other protocol deviation, and that was unrecognised at the time of randomisation; the woman had intrathecal analgesia.

Chapter 4 Trial conduct

There were two major challenges during the conduct of the trial: recruitment and monitoring of adherence to the intervention. These are explained below.

Recruitment

Trial recruitment was initially planned to be undertaken in the maternity units of four acute NHS trusts in England and one health board in Wales. The BUMPES study design originally outlined in the trial protocol described a single-centre internal pilot study to assess feasibility, develop teaching materials and field-test trial data collection processes. After 9 months of the pilot phase, it was noted that, although the trial infrastructure and data capture were satisfactory, accrual did not meet projected targets, despite accurate predictions of available participants. At the recommendation of the TSC, the trial was initiated at a second pilot site prior to 'roll-out', in order to establish if these limitations were site specific or reflected broader barriers to recruitment. It was noted that recruitment across the two pilot centres remained unsatisfactory, with an average of 49% of the overall recruitment target being met over the 6 months since the second pilot site opened to recruitment (*Figures 4* and *5*).

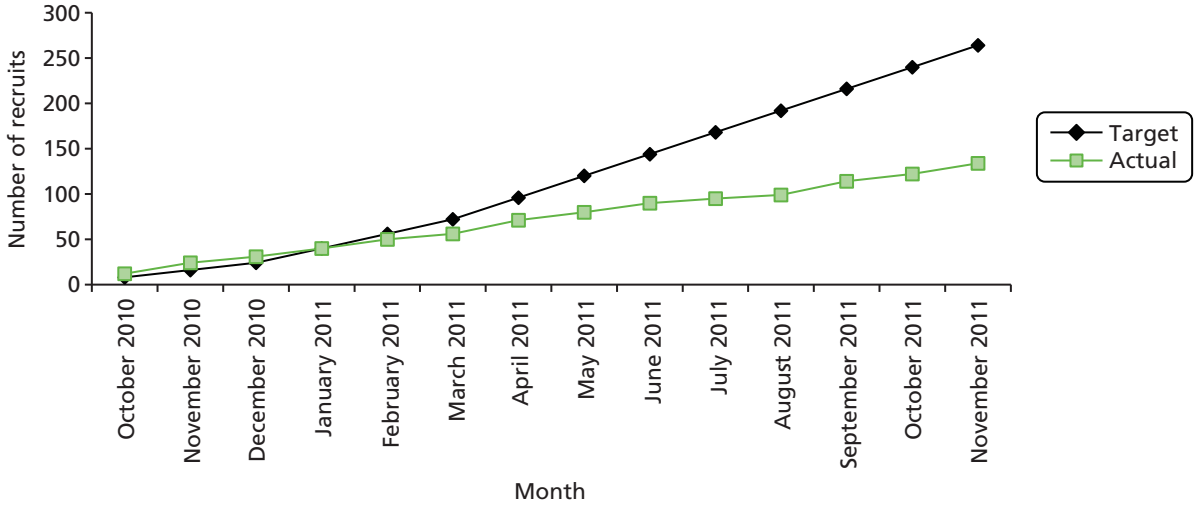

FIGURE 4 Recruitment at first pilot centre.

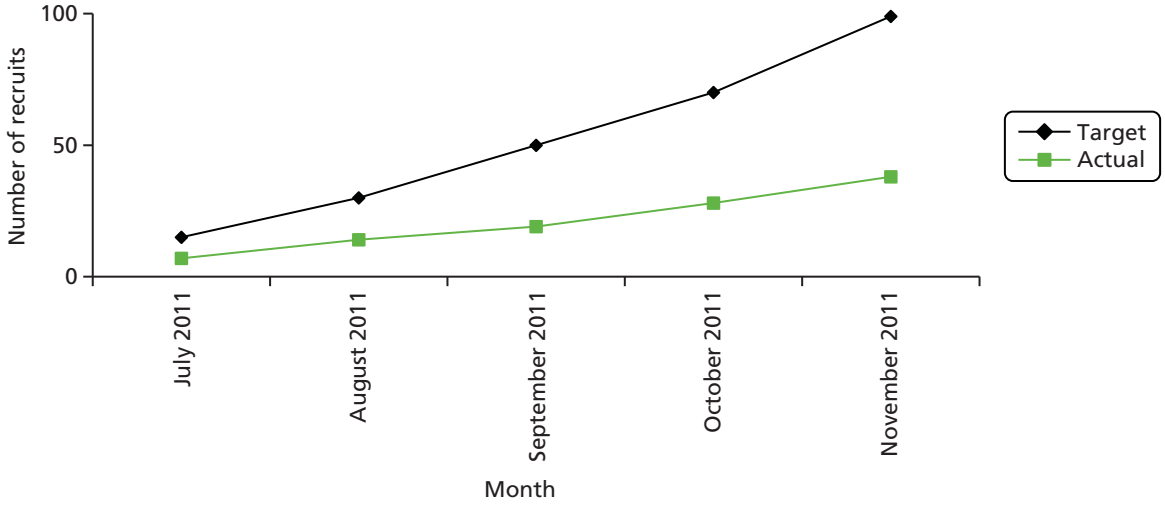

FIGURE 5 Recruitment at second pilot centre.

Challenges to study recruitment

Equipoise

Engagement with clinical midwifery staff for feedback and exploration of obstacles to recruitment was repeatedly sought. Initially this process revealed a lack of equipoise regarding the trial intervention in some individuals. While unsupported by evidence, this was a powerful perceptual obstacle, which may in part have resulted from sources of conflicting information. As described earlier, the NICE Intrapartum Care Guidelines (2007)[31] stated that:

> *Women with regional analgesia should be encouraged to move and adopt whatever upright position they find comfortable throughout labour.*
>
> *NICE Clinical Guidelines, No. 190 (section 1.5.7, p. 22)*[31]

These recommendations acknowledged that current evidence was inadequate and did not favour any specific positions. However, it is possible that misinterpretation of these guidelines could have affected equipoise and accounted for the perception that a particular position confers an advantage in birth outcomes. It may also explain the initial reluctance of midwives on the labour wards to identify with the study.

During the study, when women were approached to participate, they readily agreed. Thus there was nothing to suggest that those women who consented represented a distinct population that could reduce the generalisability of the trial findings. Furthermore, women in labour appeared to have genuine equipoise with respect to the intervention. Continued feedback to midwives and further training emphasised the importance of equipoise in order for the research to generate a definitive answer to the research question.

Clinical issues

Consent

Local R&D departments at participating units insisted that the clinical midwives attending women in labour required good clinical practice (GCP) training in order to take informed consent. The initiation visit allowed these issues to be explored and addressed locally either by arranging GCP training for midwives working on the labour wards or arranging for anaesthetists/research staff to be contacted to take consent. This inevitably led to delays in initiating recruitment and an ongoing barrier to recruitment, as most staff were not GCP trained, and many felt that this was unnecessary.

Competing studies

During the recruitment phase, several hospitals introduced other intrapartum studies, for which consent had been gained in the antenatal period or in early labour. The local staff felt that women could not be recruited to more than one study in the intrapartum period and midwives therefore did not approach these women.

As a consequence of these challenges, a decision was made that participation in the study should be expanded to more centres, in addition to the original five proposed.

Recruitment strategies

During the whole period of recruitment, a number of initiatives were launched to improve recruitment. These included:

- Timing of informed consent. During the pilot phase, it was noted that gaining informed consent in the second stage of labour (from full dilatation of the cervix to birth of the baby) was delaying time to randomisation and therefore study entry. As the second stage of labour is a clinically demanding time on labour wards, this could potentially be a barrier to recruitment. Following approval (REC amendment 4, 25 July 2011), consent could be sought and obtained from potential study participants in the first stage

of labour, once an effective epidural had been administered. Randomisation had to be delayed until the second stage of labour had been confirmed, but this process alleviated the burden of recruitment for the attending midwife.

- To recruit at more sites. Following a proposal from the CIG and agreement from the TSC, there was approval to recruit a further 36 maternity units, which were opened to recruitment over a 24-month period (a total of 41 hospitals). Additional units that had a good track record of participation in health research in pregnancy were approached, along with hospitals that had already expressed an interest in participating. An initiation visit from the research midwife in the BUMPES team was arranged to fully explain the study to lead midwives, anaesthetists and local R&D departments, and also to evaluate their enthusiasm and the level of support that they would offer the study. Following R&D approvals, dates were arranged for the research midwife to attend the maternity units, and provide training to staff and support them during initial recruitment. This usually took 1 full week, covering day and night shifts, and involved small groups of midwives and anaesthetists. A training manual, posters, recruitment packs and randomisation flow charts, as well as 24-hour contact details, were in place for all centres prior to the start of recruitment. Further training was also provided to many units on request to support recruitment.
- Change to funding model. Initially, BUMPES provided funding to appoint a 'BUMPES midwife' at each of the original five maternity units for 2 days per week. Their role was to support training, recruitment, data collection and the day-to-day running of the study. With the involvement of 36 more maternity units, the existing funding model was unsustainable within the trial budget, so this was changed to a 'payment-per-recruit' model (£85) for each of the maternity units. This proposal was approved by both the TSC (9 December 2011) and the NIHR HTA programme, and was in place from January 2012.
- Development of local BUMPES champions and Comprehensive Local Research Network (CLRN) support (England). Given the change in the funding model, and the loss of specific BUMPES midwives, a revised model of local support was designed. This involved the introduction of BUMPES champions. Clinical midwives active on each labour ward shift were identified to promote the study, identify potential recruits, facilitate consent and support randomisation. This ensured that, as much as possible, someone was available who was knowledgeable about the trial and able to support recruiting midwives. This was supported in some units with extra CLRN funding and in others by the payment-per-recruit monies.
- DCBs. Following feedback from the units, the DCBs were redesigned. Staff complained that DCBs were too long and the amount of information requested was too much, so that, on a busy labour ward shift, midwives were put off recruiting or completing the booklets. The DCBs were redesigned into parts 1 and 2. Part 1 was reduced to a single-page A3 worksheet and was the only section that the attending midwife during labour needed to complete. This requested information that could not be collected at a later date, for example visual analogue scale score (pain assessment), the date and time when the woman adopted the allocated position, times and positions every 15 minutes and reasons for change. CLRN and the National Institute for Social and Health Research [(NISCHR) Wales] research staff or staff employed using the BUMPES payment per recruit monies were able to complete part 2 at a later date with information from the maternal and neonatal notes.
- Increasing midwifery ownership. A short article to raise awareness was published in the Royal College of Midwives Journal (2012). This was designed to encourage midwifery ownership of the study and the importance of the results, which could potentially have an impact on future midwifery practice and be beneficial to women. A Collaborators' Study Day for recruiting units was arranged in November 2012 to improve networking, and for sharing ideas and identifying areas of good practice. This was attended by 34 midwives from 18 participating centres and feedback from the day was excellent.
- Promoting BUMPES. Life-sized posters and other promotional items were designed and, when required, received REC approval. This helped to encourage promotion of the study to midwives, women and antenatal educators.
- Recruitment updates and newsletters. Recruitment updates were sent to units monthly. Newsletters were published quarterly and included recruitment targets, the identity of new participating units and answers to frequently asked questions, to help improve awareness and address common errors and queries.

- Incentives. Approved incentives for midwives such as fob watches, notebooks, Post-it® (3M, Cynthiana, KY, USA) notes, mugs, key rings, pens, tape measures, lanyards and lip gels were purchased and given during training sessions. This helped to identify and promote contact details of the study. Occasional gift vouchers were approved and given to support recruitment as well as seasonal gifts, such as Love Hearts (Swizzels Matlow, New Mills, Stockport, UK) for Valentine's Day, Easter eggs, summer rock candy, Halloween-themed sweets and an advent calendar in December.

The combination of marketing the trial more actively and participation of the additional centres resulted in a substantial improvement in recruitment. The project management group continued to monitor recruitment closely throughout the trial. An example of the monitoring data reviewed is shown in *Table 3* and *Figure 6*.

However, the delays inherent in establishing the participation of a greater number of centres resulted in a request to the NIHR HTA programme for a 12-month extension of the trial. This no-cost extension was granted in September 2013.

TABLE 3 Study recruitment details from March 2012 to February 2013

Recruitment	Month, grand totals											
	March 2012	April 2012	May 2012	June 2012	July 2012	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013	February 2013
Monthly targets	25	44	63	75	90	111	114	141	164	176	188	192
Monthly recruitment	14	28	47	59	75	72	68	95	132	126	118	133
Monthly target achieved (%)	56	64	75	79	83	65	60	67	80	72	63	69
Target cumulative total	469	514	569	634	711	800	901	1014	1139	1276	1425	1586
Actual cumulative total	216	244	291	350	425	497	565	660	792	918	1036	1169
Overall percentage of target	46	47	51	55	60	62	63	65	70	72	73	74

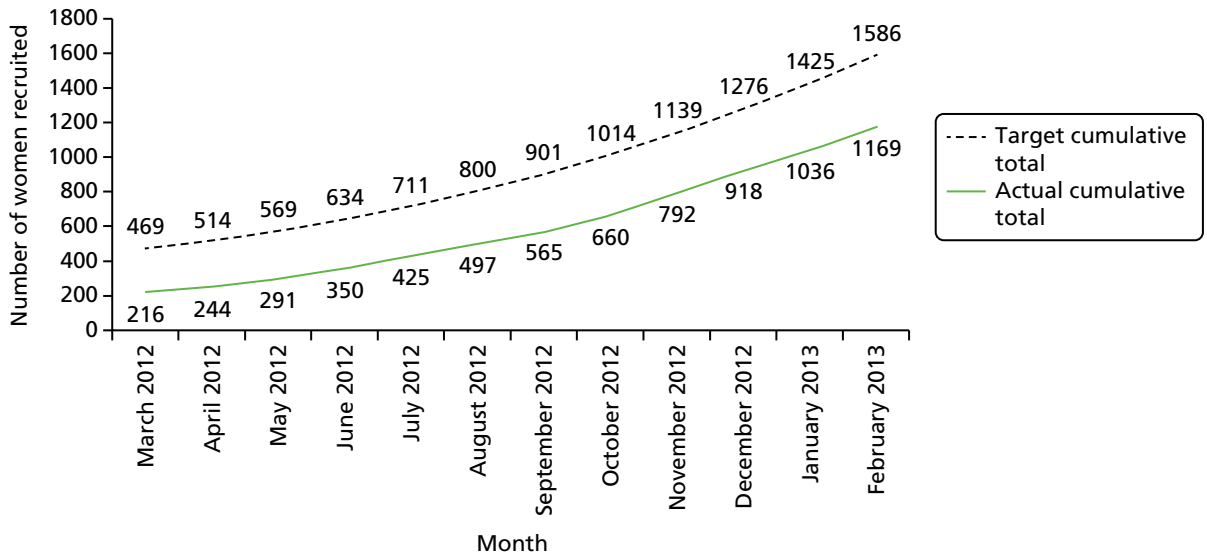

FIGURE 6 Study recruitment details from March 2012 to February 2013.

Chapter 5 Results

Between 4 October 2010 and 31 January 2014, 3236 women were randomised to the BUMPES trial from 41 participating centres (*Figure 7*).

In accordance with the prespecified SAP, 143 women (4.4%) met the criteria to be excluded from the analysis of the primary outcome. The majority of these exclusions were because of missing or incomplete consent forms. For 32 women, exclusion was because they were randomised in error (19 were not in the second stage of labour at the time of randomisation and never reached the second stage of labour, having caesarean section prior to full dilatation of the cervix, and 12 were apparently randomised after delivery). These are detailed in the participant flow diagram (*Figure 8*). DCBs were available for all women recruited and analysed. Follow-up at 1 year was achieved for 61% of women (see *Figure 8*).

Baseline characteristics were similar between the two arms of the trial (*Table 4*). Mean maternal age was 28.4 years (SD 5.6 years). The majority of women in both arms had a gestational age of between 37 and 41 completed weeks, although 7.5% of women were at ≥ 42 weeks. The vast majority of women participating in the trial were of white ethnic origin and mean BMI at booking was just over 25 kg/m^2. Approximately 40% of women had their labour induced, which is higher than might be expected in the general maternity population.[40] However, as recruited women all had epidural analgesia, which is associated with longer and more painful labours, as is induction of labour, this proportion does not appear excessive. Similarly, 50% of women had augmentation with oxytocin during their labour, which is compatible with women requesting epidural analgesia because of a longer labour.[40]

Approximately 80% of women were able to perform a straight leg raise at the time of trial entry, suggesting that these women had reasonable mobility with their epidural analgesia.

There is an apparent disparity between the two groups in the position of the women at the time of trial entry. It appears that there was a higher proportion of women who were lying down in the group allocated to lying down than for women allocated to the upright position. The way these data were requested could have led to misclassification of this variable, in that midwives may have recorded the position of the women at the time of allocation, that is, after they had already assumed the allocated position. As all other characteristics of the women were similar at baseline, it appears very unlikely that this would represent the true position at the time of randomisation; rather, it would be a combination of this plus actual allocation.

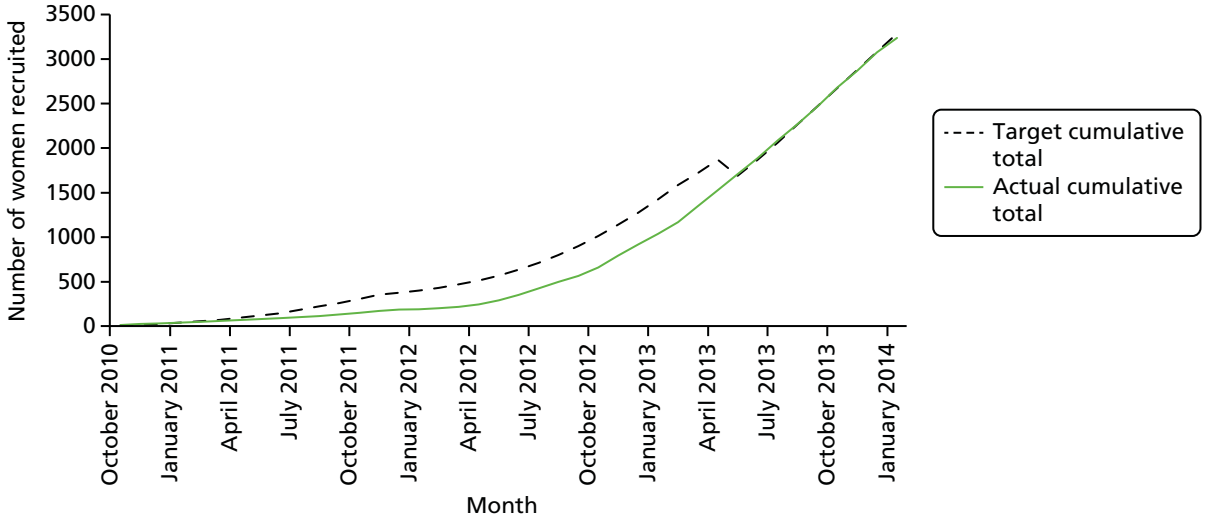

FIGURE 7 BUMPES final recruitment.

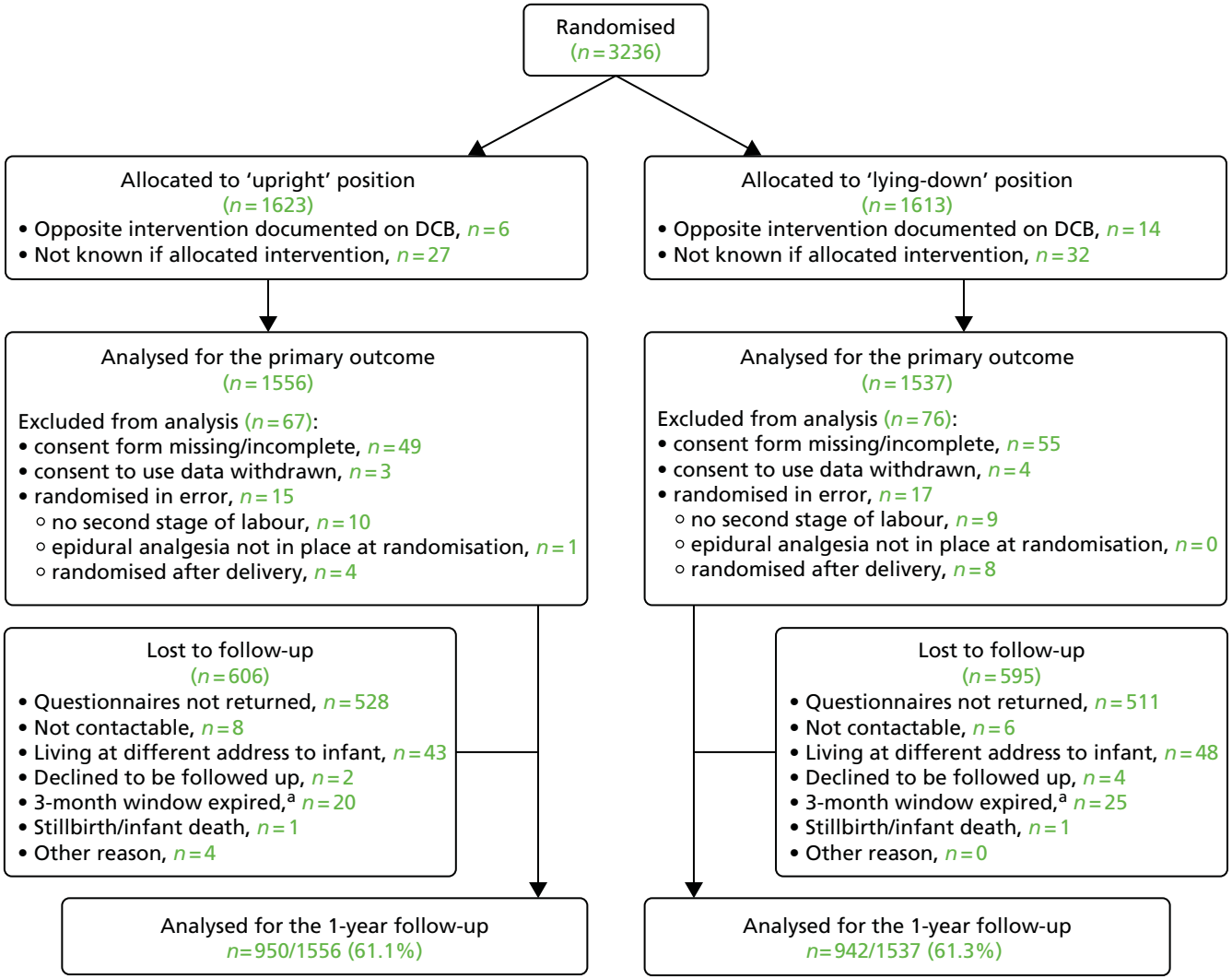

FIGURE 8 Participant flow diagram. a, If not contactable after 15 months since randomisation, then the questionnaire was not sent. Reproduced from The Epidural and Position Trial Collaborative Group.[39] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) license, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: http://creativecommons.org/licenses/by/4.0/.

TABLE 4 Centre recruitment and characteristics of women prior to study entry

Characteristic	Trial arm	
	Upright (*N* = 1556)	Lying down (*N* = 1537)
Centre, *n* (%)		
Birmingham Women's Hospital	116 (7.5)	118 (7.7)
St Thomas' Hospital	237 (15.2)	241 (15.7)
Queen Alexandra Hospital, Portsmouth	43 (2.8)	42 (2.7)
University Hospital of Wales	150 (9.6)	146 (9.5)
Royal United Hospitals Bath	99 (6.4)	101 (6.6)
Bradford Royal Infirmary	58 (3.7)	55 (3.6)
Jessop Wing, Sheffield Teaching Hospital	93 (6.0)	94 (6.1)
Princess of Wales Hospital	22 (1.4)	19 (1.2)
Singleton Hospital, Swansea	19 (1.2)	18 (1.2)
Royal Gwent Hospital, Newport	29 (1.9)	25 (1.6)
Gloucestershire Royal Hospital	26 (1.7)	22 (1.4)
Nevill Hall Hospital	9 (0.6)	10 (0.7)
Frimley Park Hospital	97 (6.2)	96 (6.3)
Sunderland Royal Hospital	21 (1.4)	22 (1.4)
Pinderfields Hospital	36 (2.3)	36 (2.3)
Warrington Hospital	29 (1.9)	29 (1.9)
Tameside Hospital	26 (1.7)	24 (1.6)
Medway Maritime Hospital	15 (1.0)	10 (0.7)
South Tyneside District Hospital	8 (0.5)	7 (0.5)
Queen Mary's Hospital, London	64 (4.1)	62 (4.0)
Queen Charlotte's and Chelsea Hospital	7 (0.5)	11 (0.7)
Queen Elizabeth Hospital	24 (1.5)	21 (1.4)
Great Western Hospital	27 (1.7)	30 (2.0)
Royal Cornwall Hospital	19 (1.2)	20 (1.3)
Bedford Hospital	26 (1.7)	30 (2.0)
University College Hospital, London	18 (1.2)	13 (0.9)
Royal Sussex County Hospital	16 (1.0)	13 (0.9)
North Manchester General Hospital	30 (1.9)	28 (1.8)
New Cross Hospital, Wolverhampton	22 (1.4)	19 (1.2)
James Paget Hospital	21 (1.4)	23 (1.5)
St George's Hospital	32 (2.1)	33 (2.2)
Princess Royal University Hospital	6 (0.4)	2 (0.1)
King's College Hospital, London	39 (2.5)	41 (2.7)
St Mary's Hospital	3 (0.2)	4 (0.3)
Dorset County Hospital	10 (0.6)	10 (0.7)

continued

TABLE 4 Centre recruitment and characteristics of women prior to study entry (*continued*)

Characteristic	Trial arm	
	Upright (*N* = 1556)	Lying down (*N* = 1537)
Kingston Hospital	41 (2.6)	46 (3.0)
Hillingdon Hospital	7 (0.5)	5 (0.3)
Arrowe Park Hospital	7 (0.5)	5 (0.3)
Lewisham Hospital	2 (0.1)	1 (0.1)
Prince Charles Hospital	2 (0.1)	5 (0.3)
Maternal age (years), *n* (%)		
Mean (SD)	28.4 (5.7)	28.4 (5.6)
< 20	111 (7.1)	99 (6.4)
20–24	303 (19.5)	292 (19.0)
25–29	437 (28.1)	463 (30.1)
30–34	488 (31.4)	482 (31.4)
35–39	182 (11.7)	161 (10.5)
≥ 40	34 (2.2)	40 (2.6)
Missing	1	0
Gestational age at entry (weeks)		
Mean (SD)	40.4 (1.2)	40.4 (1.2)
37^{+0} to 39^{+6}, *n* (%)	482 (31.0)	500 (32.6)
40^{+0} to 41^{+6}, *n* (%)	955 (61.5)	921 (60.0)
≥ 42^{+0}, *n* (%)	116 (7.5)	115 (7.5)
Missing	3	1
IMD: quintile, *n* (%)		
First (least deprived)	205 (16.0)	204 (16.0)
Second	182 (14.2)	201 (15.7)
Third	246 (19.2)	235 (18.4)
Fourth	349 (27.2)	345 (27.0)
Fifth (most deprived)	299 (23.3)	294 (23.0)
Wales – not derived	224	217
Postcode missing	51	41
Ethnic group, *n* (%)		
White	1305 (84.5)	1275 (83.5)
Indian	48 (3.1)	57 (3.7)
Pakistani	26 (1.7)	30 (2.0)
Bangladeshi	6 (0.4)	3 (0.2)
Black African	28 (1.8)	30 (2.0)
Black Caribbean	14 (0.9)	11 (0.7)
Any other ethnic group	117 (7.6)	121 (7.9)
Not known/missing	12	10

TABLE 4 Centre recruitment and characteristics of women prior to study entry (*continued*)

Characteristic	Trial arm	
	Upright (*N* = 1556)	Lying down (*N* = 1537)
BMI at booking visit (kg/m^2)		
Mean (SD)	25.5 (5.4)	25.2 (5.3)
Height and/or weight not known	65	60
Woman undergone FGM, *n* (%)	6 (0.4)	1 (0.1)
Missing	6	7
Onset of labour, *n* (%)		
Spontaneous	941 (60.6)	904 (58.9)
Induced	613 (39.5)	632 (41.2)
Missing	2	1
Duration of first stage (minutes)		
Median (IQR)	510 (360–715)	495 (350–705)
Geometric mean	484.9	481.9
Missing	17	10
Diagnosis of pre-eclampsia, *n* (%)	52 (3.4)	52 (3.4)
Missing	5	3
Continuous electronic fetal monitoring, *n* (%)	1485 (95.5)	1470 (95.8)
Missing	1	2
Diagnosis of delay requiring intervention, *n* (%)	796 (51.2)	770 (50.2)
Missing	1	3
Systemic opioids given prior to epidural, *n* (%)	442 (28.4)	435 (28.3)
Pethidine	353 (79.9)	330 (75.9)
Diamorphine	77 (17.4)	88 (20.2)
Remifentanil	3 (0.7)	4 (0.9)
Morphine	0 (0.0)	0 (0.0)
Meptazin	12 (2.7)	17 (3.9)
Missing	1	1
Epidural technique, *n* (%)		
Epidural	1492 (96.0)	1481 (96.4)
Combined spinal epidural	62 (4.0)	55 (3.6)
Missing	2	1
Epidural maintained with PCEA/infusion, *n* (%)	1224 (80.6)	1196 (79.9)
Missing	37	40
Woman's pain score for last contraction		
Median (IQR)	10 (0–30)	10 (0–38)
Missing	162	184

continued

TABLE 4 Centre recruitment and characteristics of women prior to study entry (*continued*)

Characteristic	Trial arm	
	Upright (*N* = 1556)	Lying down (*N* = 1537)
Able to perform straight leg raise, *n* (%)	1162 (78.7)	1152 (80.2)
Missing	79	101
Position prior to study entry, *n* (%)		
Lying down	432 (29.0)	546 (37.7)
Upright	977 (65.6)	832 (57.4)
Lithotomy	5 (0.3)	6 (0.4)
Semi-recumbent	58 (3.9)	53 (3.7)
Other	17 (1.1)	12 (0.8)
Missing	67	88
Time from VE diagnosing second stage to study entry (minutes)		
Median (IQR)	16 (9–30)	16 (8–30)
Apparently randomised before diagnosis of second stage[a]	70	79
Time apparently > 180 minutes[a]	6	7
Missing	7	2
Time from study entry to start of recording positions (minutes)		
Median (IQR)	1 (–2 to 6)	1 (–3 to 7)
Time from study entry to recording position > 15 minutes,[b] *n* (%)	154 (10.1)	150 (9.9)
Time apparently > 15 minutes before study entry[a]	227	218
Missing	30	27
Baby's birth weight (grams)[c]		
Mean (SD)	3500 (450)	3488 (442)
Missing	1	1

FGM, female genital mutilation; IQR, interquartile range; PCEA, patient-controlled epidural analgesia; VE, vaginal examination.
a Values set to missing for calculation of median and interquartile range.
b Values included for calculation of median and interquartile range.
c Measured after study entry but not an outcome.

The time from randomisation to trial entry, and all other durations recorded in the results section, are prone to errors because of time differences recorded in different parts of the labour ward. The time of randomisation is accurate, as this was recorded by the randomisation service. However, all other times will depend on the accuracy of the clocks in the different locations in the labour ward. For example, the clock in the central midwifery station may read a slightly different time from that in the labour room, and these may both be different from the clock in theatre. There were many (relatively minor) problems with derived duration variables in the data set (e.g. negative values), suggesting variation in actual time recorded between different settings.

There was a clear difference in the incidence of the primary outcome, SVB, between the groups, with 35.2% of women achieving a SVB in the upright group compared with 41.1% achieving a SVB in the lying-down group [adjusted RR 0.86, 95% CI 0.78 to 0.94 (*Table 5*)]. This represents a 5.9% absolute risk increase in the chance of a SVB in the lying-down group. The original and subsequently revised sample size estimation aimed to detect a 5–6% absolute risk reduction.

TABLE 5 Primary outcome: SVB

Outcome	Trial arm		
	Upright ($N = 1556$), n (%)	Lying down ($N = 1537$), n (%)	Adjusted[a] RR (95% CI)
SVB	548 (35.2)	632 (41.1)	0.86 (0.78 to 0.94)
Missing	1	0	–

a Adjusted for centre.

As specified in the SAP, the primary outcome analysis was further adjusted for the characteristics age, ethnicity, the diagnosis of delay and the nature of the onset of labour (*Table 6*).

There was no evidence of a difference found for most of the secondary maternal outcomes after study entry and during labour, particularly with respect to epidural drug dosage, use of augmentation, fetal blood sampling or the use of fetal scalp electrodes (*Table 7*). There was a statistically significant difference at the 1% level in the duration of the active second stage of labour with a shorter duration of labour in the lying-down group (GMR 1.08 minutes, 99% CI 1.01 to 1.15 minutes).

Other secondary maternal outcomes, such as IVD and caesarean section, suggested an increased risk associated with the upright position, but again these differences were not statistically significant at the 1% level. For those women undergoing operative delivery (instrumental or caesarean section), the indications appeared to be similar between the two arms of the trial. Just over one-third were reported to be caused by fetal distress and nearly 60% caused by failure to progress.

With respect to genital tract trauma there was a suggestion that there may be an increase in the incidence of episiotomy in the upright group compared with the lying-down group, although this was not significant at the 1% level. There were no statistically significant differences in the risk of perineal trauma, although there appeared to be a higher incidence of obstetric anal sphincter injury in the upright group (6.7%) than in the lying-down group (5.3%), but again this difference was not statistically significant at the 1% level (*Table 8*).

There was no evidence of a difference in maternal satisfaction in labour between the two arms of the trial, although there were interesting findings with respect to women's views about the care they received in labour (*Table 9*). The majority of women 'strongly agreed' or 'agreed' with many of the statements, such as their satisfaction with their overall childbirth experience, that they were treated with respect by all the staff and that they were involved in decision-making during labour. However, in the case of factors such as whether or not their expectations for labour and birth were met, or if they felt in control, the proportions of women who 'strongly agreed' or 'agreed' were lower. Of particular interest in the context of BUMPES is that less than half of women 'strongly agreed' or 'agreed' that they were able to move as much as they wanted. Perhaps not surprisingly, the majority of women were satisfied with their pain relief during labour.

Infant outcomes were extremely good overall, with very few babies having a low Apgar score at 5 minutes or evidence of metabolic acidosis (*Table 10*). There did appear to be more babies with metabolic acidosis in

TABLE 6 Adjusted analysis for the primary outcome

Primary outcome	Adjusted RR (95% CI)
Full model:[a] adjusting for maternal age, ethnicity, diagnosis of delay and onset of labour	0.86 (0.79 to 0.94)

a Model adjusts for centre as a random effect.

TABLE 7 Secondary maternal outcomes after study entry and during labour

Outcome	Trial arm		Adjusted[a] effect measure (99% CI)
	Upright (*N* = 1556)	Lying down (*N* = 1537)	
Epidural drugs[b] administered after study entry, *n* (%)	832 (75.4)	862 (76.7)	–
Missing	453	413	
Total-dose local anaesthetic[b] (mg)			
Bupivacaine	814	849	Median difference 0 (–2 to 0)
Mean (SD)	26.4 (22.2)	26.7 (21.2)	
Median (IQR)	20 (10–31)	20 (12–33)	
Lidocaine	6	8	Median difference 0 (–100 to 180)
Mean (SD)	256.7 (88.0)	205 (99.6)	
Median (IQR)	200 (200–360)	200 (180–250)	
Ropivicaine	2	1	Median difference 0 (–23 to 23)
Mean (SD)	75 (31.8)	75	
Median (IQR)	75 (53–98)	75 (75–75)	
Total-dose opioids[b]			
Fentanyl (μg)	809	840	Median difference 0 (–4 to 0)
Mean (SD)	49.4 (39.0)	51.6 (41.6)	
Median (IQR)	40 (20–60)	40 (22–64)	
Diamorphine (mg)	4	1	Median difference 0 (0 to 0)
Mean (SD)	3.0 (0.0)	3.0	
Median (IQR)	3 (3–3)	3 (3–3)	
Hypotension (systolic BP of < 100 mmHg), *n* (%)	42 (2.7)	49 (3.2)	RR 0.85 (0.50 to 1.44)
Missing	3	4	
Vasopressors to increase blood pressure, *n* (%)	13 (0.8)	12 (0.8)	RR 1.07 (0.39 to 2.99)
Missing	3	2	
Syntocinon for augmentation, *n* (%)	172 (11.1)	163 (10.6)	RR 1.04 (0.80 to 1.35)
Missing	3	2	
Fetal blood sampling performed, *n* (%)	90 (5.8)	72 (4.7)	RR 1.17 (0.82 to 1.68)
Missing	4	3	
Fetal scalp electrode applied, *n* (%)	94 (6.1)	85 (5.6)	RR 1.09 (0.76 to 1.57)
Missing	6	11	
Duration of active second stage[c] (minutes)			
Geometric mean	80.9	75.0	GMR 1.08 (1.01 to 1.15)
Median (IQR)	94 (56–133)	88 (51–126)	Median difference 6 (1 to 11)
Missing	14	12	
Total duration of second stage[d] (minutes)			
Geometric mean	130.5	125.1	GMR 1.04 (0.98 to 1.10)
Median (IQR)	149 (100–197)	141 (95–188)	Median difference 7 (0 to 13)
Missing	6	0	

BP, blood pressure; IQR, interquartile range.
a Adjusted for centre.
b Includes 'top-up' and/or patient-controlled epidural anaesthesia.
c Defined as the time from when pushing commenced until birth.
d Defined as the time from study entry until birth.

TABLE 8 Secondary maternal outcomes at and immediately post delivery

Outcome	Trial arm		Adjusted[a] effect measure (99% CI)
	Upright (*N* = 1556)	Lying down (*N* = 1537)	
Mode of delivery, *n* (%)			
IVD[b]	849 (54.6)	778 (50.6)	RR 1.08 (0.99 to 1.18)
Forceps	578 (37.2)	503 (32.7)	
Ventouse	271 (17.4)	275 (17.9)	
Caesarean section[c]	158 (10.2)	127 (8.3)	RR 1.23 (0.92 to 1.64)
Category[d] of caesarean section			
1	54 (34.2)	33 (26.0)	
2	95 (60.1)	81 (63.8)	
3	9 (5.7)	13 (10.2)	
Missing	1	0	
Primary indication for assisted (non-spontaneous) delivery, *n* (%)			
Instrumental			
Fetal distress	338 (39.9)	304 (39.1)	
Failure to progress	504 (59.4)	468 (60.2)	
Other	6 (0.7)	5 (0.6)	
Missing	1	1	
Caesarean section			
Fetal distress	39 (24.7)	32 (25.2)	
Failure to progress	118 (74.7)	94 (74.0)	
Other	1 (0.6)	1 (0.8)	
Anaesthesia required for instrumental/caesarean section delivery,[e] *n* (%)	587 (58.5)	515 (57.4)	RR 1.03 (0.95 to 1.12)
Technique used[f]			
Local infiltration	65 (11.1)	94 (18.3)	
Pudendal block	16 (2.7)	16 (3.1)	
High-dose epidural top-up	439 (74.8)	342 (66.4)	
Spinal anaesthesia	68 (11.6)	72 (14.0)	
General anaesthesia	11 (1.9)	6 (1.2)	
Missing	4	7	
Active management of third stage, *n* (%)	1450 (98.0)	1432 (98.2)	RR 1.00 (0.91 to 1.10)
Missing	76	78	
Genital tract trauma, *n* (%)			
Episiotomy performed	914 (58.8)	838 (54.6)	RR 1.07 (0.99 to 1.16)
Missing	1	1	
Perineal tear evident, including perineal tear with episiotomy	759 (48.9)	785 (51.1)	RR 0.95 (0.87 to 1.04)
Missing	4	1	

continued

TABLE 8 Secondary maternal outcomes at and immediately post delivery (*continued*)

Outcome	Trial arm		Adjusted[a] effect measure (99% CI)
	Upright (*N* = 1556)	Lying down (*N* = 1537)	
Severity,[g] *n* (%)			
1	90 (11.9)	96 (12.2)	
2	563 (74.4)	608 (77.5)	
3a	49 (6.5)	53 (6.8)	
3b	33 (4.4)	17 (2.2)	
3c	16 (2.1)	7 (0.9)	
4	6 (0.8)	4 (0.5)	
Missing	2	0	
Obstetric anal sphincter injury[h]	104 (6.7)	81 (5.3)	RR 1.27 (0.88 to 1.84)
Perineum sutured, *n* (%)	1284 (82.6)	1248 (81.4)	RR 1.02 (0.92 to 1.12)
Missing	2	3	
Anterior tear evident and sutured, *n* (%)	102 (6.6)	107 (7.0)	RR 0.95 (0.67 to 1.33)
Missing	7	4	
Manual removal of the placenta performed, *n* (%)	99 (6.5)	101 (6.7)	RR 0.97 (0.69 to 1.38)
Missing	28	35	
Post-partum haemorrhage requiring blood transfusion, *n* (%)	63 (4.1)	52 (3.4)	RR 1.20 (0.75 to 1.93)
Units transfused,[i] mean (SD)	2.6 (1.5)	2.2 (1.0)	MD –0.34 (–0.94 to 0.27)
Missing	1	1	
Woman's pain score for birth			
Median (IQR)	15 (0–50)	10 (0–50)	Median difference[j] 0 (0 to 0)
Missing	345	347	
Length of inpatient stay after delivery (hours)			
Median (IQR)	38.7 (24.9–59.7)	37.5 (24.2–56.5)	Median difference[j] –1.2 (–3.2 to 0.7)
Missing	48	34	

IQR, interquartile range; MD, mean difference.
a Adjusted for centre.
b Compared with no IVD.
c Compared with no caesarean section.
d Royal College of Obstetricians and Gynaecologists classifications: (1) immediate threat to life of woman or fetus; (2) threat of maternal or fetal compromise; (3) no threat of compromise but needs early delivery.
e Anaesthesia additional to the routine epidural pain relief given in labour.
f Categories are not mutually exclusive.
g Degree of severity according to NICE intrapartum guidelines:[31] (1) injury to skin only; (2) injury to perineal muscles but not anal sphincter; (3) injury to perineum involving anal sphincter complex [(i) < 50% of external anal sphincter thickness torn; (ii) > 50% of external anal sphincter thickness torn; and (iii) internal anal sphincter torn]; and (4) injury to perineum involving anal sphincter complex and anal epithelium.
h Severity grades 3 and 4.
i In women who had blood transfused.
j Not adjusted for centre.

TABLE 9 Maternal satisfaction

Outcome	Trial arm		RR[a,b] (99% CI)
	Upright ($N = 1556$), n (%)	Lying down ($N = 1537$), n (%)	
Number of questionnaires returned	1208 (77.6)	1165 (75.8)	–
Satisfied with overall childbirth experience			0.97 (0.92 to 1.01)
Strongly agree	553 (47.2)	539 (47.1)	
Agree	410 (35.0)	434 (37.9)	
Neutral	114 (9.7)	100 (8.7)	
Disagree	65 (5.6)	40 (3.5)	
Strongly disagree	30 (2.6)	31 (2.7)	
Missing	36	21	
Treated with respect by all staff			1.01 (0.99 to 1.02)
Strongly agree	968 (82.0)	937 (81.3)	
Agree	178 (15.1)	176 (15.3)	
Neutral	19 (1.6)	20 (1.7)	
Disagree	7 (0.6)	11 (1.0)	
Strongly disagree	8 (0.7)	8 (0.7)	
Missing	28	13	
Involved in making decisions			0.99 (0.96 to 1.02)
Strongly agree	824 (69.9)	788 (68.5)	
Agree	278 (23.6)	299 (26.0)	
Neutral	56 (4.8)	45 (3.9)	
Disagree	11 (0.9)	10 (0.9)	
Strongly disagree	10 (0.9)	9 (0.8)	
Missing	29	14	
Expectations for labour and birth were met			1.00 (0.93 to 1.08)
Strongly agree	444 (38.0)	437 (38.2)	
Agree	359 (30.7)	346 (30.2)	
Neutral	209 (17.9)	207 (18.1)	
Disagree	118 (10.1)	113 (9.9)	
Strongly disagree	40 (3.4)	41 (3.6)	
Missing	38	21	
Felt safe at all times			1.01 (0.98 to 1.04)
Strongly agree	793 (67.4)	773 (67.2)	
Agree	312 (26.5)	299 (26.0)	
Neutral	39 (3.3)	51 (4.4)	
Disagree	24 (2.0)	16 (1.4)	
Strongly disagree	9 (0.8)	11 (1.0)	
Missing	31	15	
Good communication from staff			1.01 (0.99 to 1.03)
Strongly agree	913 (77.3)	864 (75.3)	
Agree	222 (18.8)	230 (20.0)	
Neutral	30 (2.5)	33 (2.9)	
Disagree	9 (0.8)	10 (0.9)	

continued

TABLE 9 Maternal satisfaction (*continued*)

Outcome	Trial arm		RR[a,b] (99% CI)
	Upright (*N* = 1556), *n* (%)	Lying down (*N* = 1537), *n* (%)	
Strongly disagree	7 (0.6)	11 (1.0)	
Missing	27	17	
Felt in control			1.01 (0.94 to 1.08)
Strongly agree	428 (36.4)	426 (37.2)	
Agree	396 (33.6)	368 (32.1)	
Neutral	223 (19.0)	232 (20.2)	
Disagree	105 (8.9)	93 (8.1)	
Strongly disagree	25 (2.1)	27 (2.4)	
Missing	31	19	
Able to move as much as wanted			0.95 (0.85 to 1.06)
Strongly agree	283 (24.5)	310 (27.2)	
Agree	285 (24.7)	279 (24.5)	
Neutral	239 (20.7)	236 (20.7)	
Disagree	253 (21.9)	228 (20.0)	
Strongly disagree	95 (8.2)	86 (7.6)	
Missing	53	26	
Satisfied with position before pushing			1.03 (0.99 to 1.07)
Strongly agree	590 (50.3)	566 (49.4)	
Agree	460 (39.2)	430 (37.5)	
Neutral	83 (7.1)	83 (7.2)	
Disagree	29 (2.5)	52 (4.5)	
Strongly disagree	12 (1.0)	15 (1.3)	
Missing	34	19	
Satisfied with position while pushing			1.02 (0.98 to 1.06)
Strongly agree	613 (52.2)	570 (49.8)	
Agree	425 (36.2)	422 (36.9)	
Neutral	94 (8.0)	91 (8.0)	
Disagree	29 (2.5)	48 (4.2)	
Strongly disagree	13 (1.1)	14 (1.2)	
Missing	34	20	
Satisfied with labour pain relief			1.00 (0.97 to 1.03)
Strongly agree	791 (67.2)	774 (67.4)	
Agree	300 (25.5)	288 (25.1)	
Neutral	60 (5.1)	51 (4.4)	
Disagree	14 (1.2)	23 (2.0)	
Strongly disagree	12 (1.0)	13 (1.1)	
Missing	31	16	

a Unadjusted RRs presented as adjusted models did not converge.
b Strongly agree/agree vs. strongly disagree/disagree/neutral.

TABLE 10 Infant outcomes

Outcome	Trial arm		
	Upright ($N = 1556$)	Lying down ($N = 1537$)	Adjusted[a] effect measure (99% CI)
Apgar score of < 4 at 5 minutes, *n* (%)	2 (0.1)	3 (0.2)	RR 0.66 (0.06 to 6.88)
Missing	5	7	
Metabolic acidosis,[b] *n* (%)	6 (0.4)	17 (1.2)	RR 0.35 (0.10 to 1.18)
pH and/or base deficit not done[c]	531 (35.5)	597 (40.4)	
Missing	61	60	
Meconium-stained liquor at delivery, *n* (%)	347 (22.4)	341 (22.2)	RR 1.01 (0.85 to 1.19)
Missing	6	4	
Resuscitation at birth, *n* (%)	206 (13.3)	180 (11.7)	RR 1.13 (0.89 to 1.45)
Missing	1	2	
Method[d]			
Facial oxygen	122 (59.5)	94 (52.2)	
Suction	75 (36.6)	74 (41.1)	
Bag and mask ventilation	82 (40.0)	82 (45.6)	
Intubation	6 (2.9)	8 (4.4)	
Complex resuscitation	4 (2.0)	1 (0.6)	
Missing	1	0	
Skin-to-skin contact in first hour after birth, *n* (%)	1165 (77.1)	1163 (78.4)	RR 0.98 (0.94 to 1.03)[e]
Missing	45	53	
Breastfeeding initiated in first hour after birth, *n* (%)	780 (51.3)	781 (52.1)	RR 0.98 (0.90 to 1.07)
Missing	36	38	
Length of inpatient hospital stay (hours) from birth			
Median (IQR)	38.7 (24.8–59.7)	37.5 (24.2–56.9)	Median difference[f] –1.1 (–3.1 to 0.8)
Missing	51	38	
Admission to HLC,[g] *n* (%)	108 (7.0)	96 (6.3)	RR 1.11 (0.79 to 1.56)
Missing	1	1	
Length of stay in HLC[h] (days)			
Total	71	63	
Median (IQR)	2 (1–4)	3 (1–6)	Median difference[f] 1 (0 to 2)
Missing	4	5	

IQR, interquartile range.
a Adjusted for centre.
b Defined as cord-artery pH of < 7.05 with base deficit of ≥ 12 mmol/l.
c Included in denominator.
d Categories are not mutually exclusive.
e Unadjusted model presented as adjusted model did not converge.
f Not adjusted for centre.
g Includes transitional care.
h Excludes transitional care.

the lying-down group than in the upright group, but this difference was not statistically significant at the 1% level. Of interest, of the 23 babies with metabolic acidosis, 10 (six in the lying-down group and four in the upright group) were born in apparently normal condition with normal Apgar scores and with no evidence that they required resuscitation at the time of birth. Only eight of these babies received any HLC (six in the lying-down group and two in the upright group).

Overall, about 12% of babies required resuscitation at birth. This figure was slightly higher in the upright group than in the lying-down group, but this difference was not statistically significant at the 1% level. There was also a suggestion that babies in the upright group may have required more intensive resuscitation at birth, but again the numbers were very small and this difference was not statistically significant. There was no evidence of a difference in the proportions of babies with skin-to-skin contact in the first hour after birth, or in the proportions of babies who were breastfed in the first hour after birth. Median length of stay in hospital was approximately 38 hours for each group, and approximately 7% of babies were admitted for HLC (which included transitional care, special care or intensive care).

The data on adherence to the intervention are presented in *Table 11* and *Figure 9*.

The prespecified subgroup analyses are presented as forest plots in *Figure 10* and *Table 12*. There is no evidence of heterogeneity between any of the prespecified subgroups for the primary outcome of SVB.

TABLE 11 Adherence (proportion of time spent in allocated position)

Outcome	Trial arm		Median difference (95% CI)
	Upright ($n = 1556$)	Lying down ($n = 1537$)	
During the passive second stage,[a] median (IQR)	1.0 (1.0–1.0)	1.0 (0.67–1.0)	0 (0 to 0)
Missing: no passive time periods recorded	320	314	
Missing: time from study entry to start of recording positions at > 15 minutes	227	217	
Missing: pushing or birth dates/times not recorded	13	10	
Missing: position times not recorded	50	36	
During the active second stage,[b] median (IQR)	0.88 (0.60–1.0)	0.75 (0.38–1.0)	0 (0 to 0)
Missing: no active time periods recorded	11	19	
Missing: time from study entry to start of recording positions at > 15 minutes	227	217	
Missing: pushing or birth dates/times not recorded	13	10	
Missing: position times not recorded	50	36	
During the whole second stage,[c] median (IQR)	0.88 (0.67–1.0)	0.78 (0.50–1.0)	0 (0–0)
Missing: time from study entry to start of recording positions at > 15 minutes	227	217	
Missing: birth dates/times not recorded	1	0	
Missing: position times not recorded	54	36	

TABLE 11 Adherence (proportion of time spent in allocated position) (*continued*)

Outcome	Trial arm		Median difference (95% CI)
	Upright ($n = 1556$)	Lying down ($n = 1537$)	
Reason for change from allocated position, *n* (%)			
Passive stage	201	343	–
Clinical	94 (50.0)	78 (24.5)	
Non-clinical	77 (41.1)	218 (68.3)	
Clinical and non-clinical	17 (9.0)	23 (7.2)	
Missing	13	24	
Active stage	699	981	
Clinical	416 (60.6)	298 (31.1)	
Non-clinical	136 (19.8)	368 (38.5)	
Clinical and non-clinical	135 (19.7)	291 (30.4)	
Missing	12	24	
Whole of second stage	788	1082	
Clinical	435 (56.6)	306 (28.9)	
Non-clinical	164 (21.3)	419 (39.5)	
Clinical and non-clinical	170 (22.1)	335 (31.6)	
Missing	19	22	
Maternal reported adherence, *n* (%)			
Passive stage			
Mostly lying down	226 (21.6)	752 (72.3)	
Mostly upright	794 (75.8)	242 (23.3)	
Other	24 (2.3)	35 (3.4)	
Cannot remember	3 (0.3)	11 (1.1)	
Missing	161	125	
Form not completed	348	372	
Active stage			
Mostly lying down	202 (19.7)	652 (63.7)	
Mostly upright	745 (72.5)	281 (27.4)	
Other	78 (7.6)	75 (7.3)	
Cannot remember	3 (0.3)	16 (1.6)	
Missing	180	141	
Form not completed	348	372	

a Defined as the time from study entry to when pushing commenced.
b Defined as the time from when pushing commenced until birth.
c Defined as the time from study entry until birth.

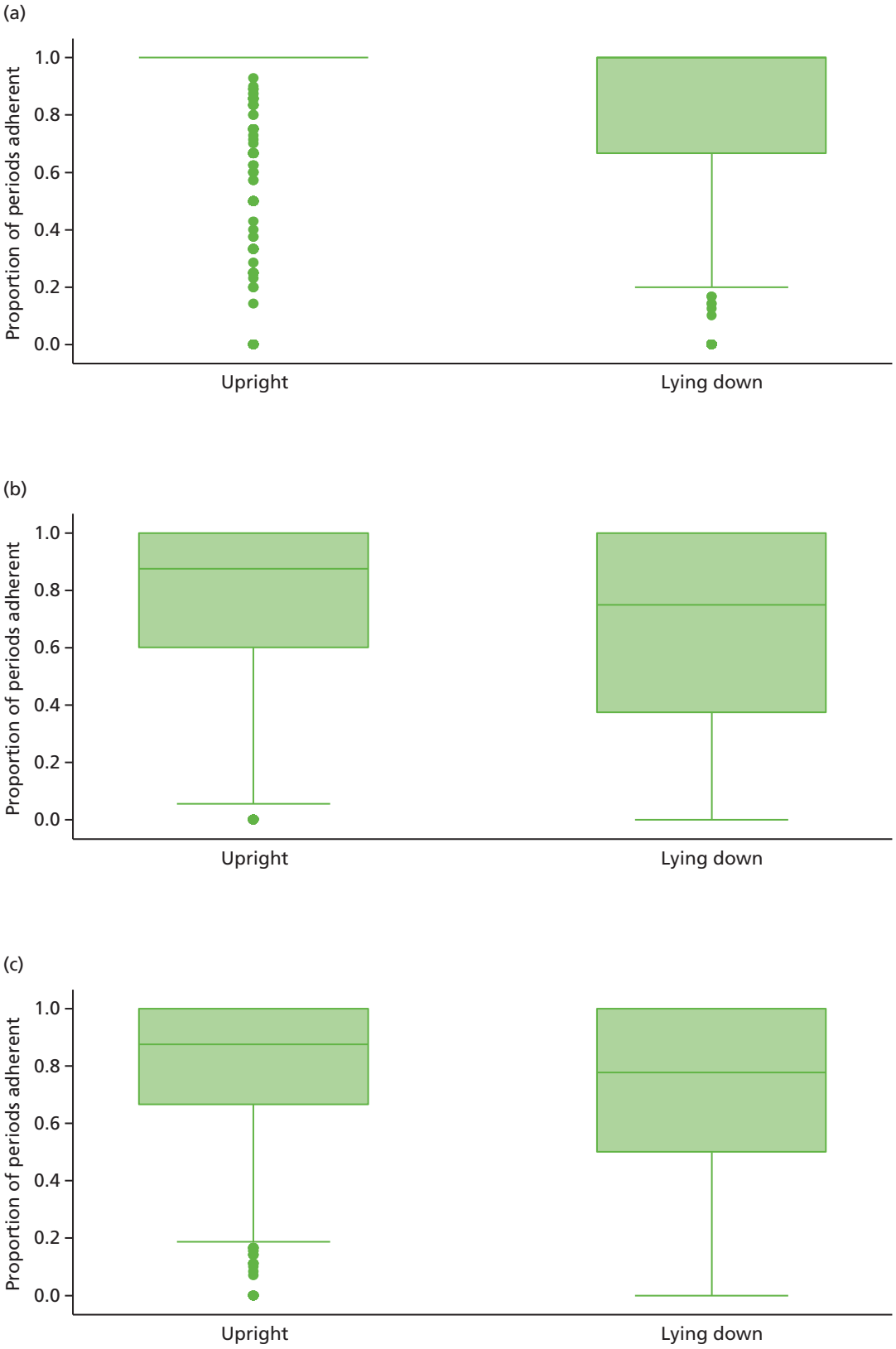

FIGURE 9 Box and whisker plots of adherence (proportion of time spent in allocated position). (a) Passive stage; (b) active stage; and (c) whole of second stage. Reproduced from The Epidural and Position Trial Collaborative Group.[39] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) license, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: http://creativecommons.org/licenses/by/4.0/.

	Upright *Number of events/total number (%)*		Lying down *Number of events/total number (%)*		Adjusted[a] RR (95% CI)	Interaction *p*-value
Gestational age (weeks)						
37^{+0} to 38^{+6}	76/198	(38.4)	97/211	(46.0)	0.85 (0.67 to 1.07)	0.84
39^{+0} to 40^{+6}	278/774	(35.9)	320/745	(43.0)	0.84 (0.74 to 0.95)	
≥41^{+0}	193/581	(33.2)	215/580	(37.1)	0.89 (0.76 to 1.04)	
Maternal age (years)						
<25	199/414	(48.1)	210/391	(53.7)	0.89 (0.78 to 1.02)	0.75
25–29	155/437	(35.5)	188/463	(40.6)	0.87 (0.74 to 1.03)	
30–34	141/488	(28.9)	178/482	(36.9)	0.79 (0.66 to 0.94)	
≥35	53/216	(24.5)	56/201	(27.9)	0.88 (0.64 to 1.21)	
Oxytocin in first stage[b]						
Yes	221/683	(32.4)	255/649	(39.3)	0.82 (0.71 to 0.95)	0.42
No	327/872	(37.5)	376/885	(42.5)	0.89 (0.79 to 0.99)	
IMD: quintile						
First (least deprived)	59/205	(28.8)	74/204	(36.3)	0.81 (0.61 to 1.07)	0.19
Second	66/182	(36.3)	76/201	(37.8)	0.96 (0.74 to 1.26)	
Third	78/246	(31.7)	96/235	(40.9)	0.78 (0.61 to 0.99)	
Fourth	113/349	(32.4)	155/345	(44.9)	0.72 (0.60 to 0.87)	
Fifth (most deprived)	135/299	(45.2)	134/294	(45.6)	0.97 (0.81 to 1.15)	

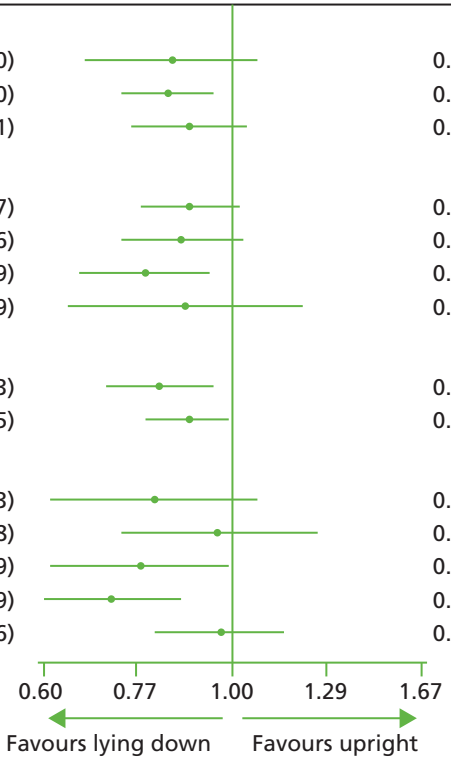

FIGURE 10 Subgroup analyses for SVB (forest plot). a, All models adjusted for centre as a random effect; and b, diagnosis of delay prior to study entry requiring oxytocin. Reproduced from The Epidural and Position Trial Collaborative Group.[39] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) license, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: http://creativecommons.org/licenses/by/4.0/.

TABLE 12 Subgroup analyses for SVB

Factor	Trial arm			
	Upright ($N = 1556$), *n* (%)	Lying down ($N = 1537$), *n* (%)	Adjusted[a] RR (95% CI)	Interaction *p*-value
Gestational age (weeks)				
37^{+0} to 38^{+6}	76/198 (38.4)	97/211 (46.0)	0.85 (0.67 to 1.07)	0.839
39^{+0} to 40^{+6}	278/774 (35.9)	320/745 (43.0)	0.84 (0.74 to 0.95)	
$\geq 41^{+0}$	193/581 (33.2)	215/580 (37.1)	0.89 (0.76 to 1.04)	
Maternal age (years)				
< 25	199/414 (48.1)	210/391 (53.7)	0.89 (0.78 to 1.02)	0.747
25–29	155/437 (35.5)	188/463 (40.6)	0.87 (0.74 to 1.03)	
30–34	141/488 (28.9)	178/482 (36.9)	0.79 (0.66 to 0.94)	
≥ 35	53/216 (24.5)	56/201 (27.9)	0.88 (0.64 to 1.21)	
Oxytocin in the first stage[b]				
Yes	221/683 (32.4)	255/649 (39.3)	0.82 (0.71 to 0.95)	0.417
No	327/872 (37.5)	376/885 (42.5)	0.89 (0.79 to 0.99)	
IMD: quintile				
First (least deprived)	59/205 (28.8)	74/204 (36.3)	0.81 (0.61 to 1.07)	0.187
Second	66/182 (36.3)	76/201 (37.8)	0.96 (0.74 to 1.26)	
Third	78/246 (31.7)	96/235 (40.9)	0.78 (0.61 to 0.99)	
Fourth	113/349 (32.4)	155/345 (44.9)	0.72 (0.60 to 0.87)	
Fifth (most deprived)	135/299 (45.2)	134/294 (45.6)	0.97 (0.81 to 1.15)	

a All models adjusted for centre as a random effect.
b Diagnosis of delay prior to study entry requiring oxytocin.

Responses to postal questionnaires at 1 year after the birth were received from 61% of women. The characteristics of women who did and did not respond to the questionnaire are detailed in *Table 13*. Responders were more likely to be slightly older and live in less deprived areas, and to be white. They were also less likely to have had a SVB, and more likely to have had an instrumental delivery. There were no differences between responders and non-responders in the risk of caesarean section or the onset of labour (spontaneous or induced), or in the incidence of neonatal resuscitation or for their babies to be admitted to a HLC.

Table 14 list the secondary maternal outcomes up to 1 year after birth in women who responded to the questionnaires. There was no evidence of any differences between the groups in relation to the incidence or severity of urinary incontinence, faecal incontinence, constipation, haemorrhoids or dyspareunia. Similarly, there was no evidence of a difference in the incidence of diagnosed cerebral palsy or severe neurodevelopmental delay in any of the infants at 1 year (see *Table 15*).

The prespecified sensitivity analysis, which excluded women who had another birth or were pregnant at the time of the 1-year follow-up, demonstrates no change in the conclusions of the study (see *Table 16*).

There were a number of adverse events reported during the course of the trial. The majority of these did not appear to be related to the intervention (*Table 17*).

TABLE 13 Generalisability of women followed up

Characteristic	1-year follow-up		
	Received ($N = 1892$)	Not received ($N = 1201$)	p-value
Maternal age (years)			
Mean (SD)	29.7 (5.2)	26.5 (5.7)	$p < 0.001$[a]
Missing	0	1	
Gestational age at entry (weeks)			
Mean (SD)	40.4 (1.2)	40.3 (1.2)	$p = 0.048$[a]
Missing	1	3	
IMD: quintile, *n* (%)			$p < 0.001$[b]
First (least deprived)	279 (17.6)	130 (13.3)	
Second	259 (16.4)	124 (12.7)	
Third	318 (20.1)	163 (16.7)	
Fourth	431 (27.2)	263 (26.9)	
Fifth (most deprived)	295 (18.7)	298 (30.5)	
Wales: not derived	265	176	
Postcode missing	45	47	
Ethnic group, *n* (%)			$p < 0.001$[b]
White	1624 (86.5)	956 (80.1)	
Indian	58 (3.1)	47 (3.9)	
Pakistani	22 (1.2)	34 (2.9)	
Bangladeshi	3 (0.2)	6 (0.5)	
Black African	30 (1.6)	28 (2.4)	
Black Caribbean	11 (0.6)	14 (1.2)	
Any other ethnic group	129 (6.9)	109 (9.1)	
Not known/missing	15	7	
BMI at booking visit (kg/m^2)			
Mean (SD)	25.2 (5.2)	25.6 (5.6)	$p = 0.030$[a]
Height and/or weight not known, *n*	70	55	
Onset of labour, *n* (%)			
Spontaneous	1121 (59.3)	724 (60.3)	$p = 0.573$[b]
Induced	769 (40.7)	476 (39.7)	
Missing	2	1	
Diagnosis of delay requiring intervention, *n* (%)	985 (52.1)	581 (48.4)	$p = 0.043$[b]
Missing	3	1	
SVB, *n* (%)	677 (35.8)	503 (41.9)	$p = 0.001$[b]
Missing	0	1	
IVD,[c] *n* (%)	1040 (55.0)	587 (48.9)	$p = 0.001$[b]
Missing	0	1	

continued

TABLE 13 Generalisability of women followed up (*continued*)

Characteristic	1-year follow-up		*p*-value
	Received (*N* = 1892)	Not received (*N* = 1201)	
Caesarean section,[d] *n* (%)	175 (9.3)	110 (9.2)	$p = 0.94$[b]
Missing	0	1	
Episiotomy performed, *n* (%)	1120 (59.2)	632 (52.7)	$p < 0.001$[b]
Missing	1	1	
Obstetric anal sphincter injury,[e] *n* (%)	116 (6.1)	69 (5.8)	$p = 0.675$[b]
Missing	2	5	
Perineum sutured, *n* (%)	1585 (83.9)	947 (79.1)	$p = 0.001$[b]
Missing	2	3	
Resuscitation at birth, *n* (%)	241 (12.8)	145 (12.1)	$p = 0.584$[b]
Missing	2	1	
Breastfeeding initiated in the first hour after birth, *n* (%)	994 (53.8)	567 (48.4)	$p = 0.004$[b]
Missing	45	29	
Infant admission to HLC,[f] *n* (%)	121 (6.4)	83 (6.9)	$p = 0.572$[b]
Missing	1	1	

a *t*-test preformed.
b Chi-squared test performed.
c Compared with no IVD.
d Compared with no caesarean section.
e Severity grades 3 and 4.
f Includes transitional care.

TABLE 14 Secondary maternal outcomes up to 1 year

Outcome	Trial arm		Adjusted[a] effect measure (99% CI)
	Upright (*N* = 950)	Lying down (*N* = 942)	
Urinary incontinence, *n* (%)			
Leaking in the first 3 months	462 (48.8)	461 (49.2)	RR 0.99 (0.88 to 1.12)
Missing	4	4	
ICIQ-UI score[b] over the past 4 weeks			
Median (IQR)	0 (0–4)	0 (0–4)	Median difference[f] 0 (0 to 0)
Missing, *n*	39	34	
Faecal incontinence, *n* (%)			
No bowel control and/or soiling			
In the first 3 months	108 (11.5)	132 (14.2)	RR 0.81 (0.59 to 1.11)
Missing	7	9	
In the past 4 weeks	32 (3.4)	27 (2.9)	RR 1.18 (0.61 to 2.28)
Missing	10	8	

TABLE 14 Secondary maternal outcomes up to 1 year (*continued*)

Outcome	Trial arm		Adjusted[a] effect measure (99% CI)
	Upright ($N = 950$)	Lying down ($N = 942$)	
No bowel control and/or soiling and/or feel need to go, *n* (%)			
In the first 3 months	215 (22.8)	251 (26.9)	RR 0.85 (0.69 to 1.05)
Missing	8	8	
In the past 4 weeks	113 (12.1)	102 (10.9)	RR 1.10 (0.79 to 1.53)
Missing	12	10	
No bowel control at times,[c] *n* (%)			
Never	829 (87.9)	806 (86.1)	
In the first 3 months	83 (8.8)	103 (11.0)	
In the past 4 weeks	13 (1.4)	19 (2.0)	
At any other time	29 (3.1)	20 (2.1)	
Missing	7	5	
Soiling from back passage on underwear,[c] *n* (%)			
Never	836 (88.6)	838 (89.5)	
In the first 3 months	70 (7.4)	75 (8.0)	
In the past 4 weeks	24 (2.5)	14 (1.5)	
At any other time	24 (2.5)	22 (2.4)	
Missing	6	6	
Feel need to go and have to go immediately,[c] *n* (%)			
Never	640 (67.9)	616 (65.8)	RR 0.85 (0.67 to 1.08)
In the first 3 months	173 (18.4)	202 (21.6)	
In the past 4 weeks	98 (10.4)	90 (9.6)	RR 1.08 (0.76 to 1.55)
At any other time	77 (8.2)	82 (8.8)	
Missing	8	6	
Constipation,[c] *n* (%)			
Never	367 (38.9)	406 (43.2)	RR 1.12 (0.96 to 1.29)
In the first 3 months	395 (41.8)	353 (37.6)	
In the past 4 weeks	94 (10.0)	107 (11.4)	RR 0.87 (0.62 to 1.23)
At any other time	140 (14.8)	154 (16.4)	
Missing	6	2	
Haemorrhoids,[c] *n* (%)			
Never	495 (52.4)	518 (55.1)	RR 1.03 (0.87 to 1.23)
In the first 3 months	308 (32.6)	297 (31.6)	
In the past 4 weeks	108 (11.4)	116 (12.3)	RR 0.93 (0.67 to 1.28)
At any other time	108 (11.4)	115 (12.2)	
Missing	6	2	

continued

TABLE 14 Secondary maternal outcomes up to 1 year (*continued*)

Outcome	Trial arm		Adjusted[a] effect measure (99% CI)
	Upright (*N* = 950)	Lying down (*N* = 942)	
Dyspareunia,[c,d] *n* (%)			
Never	366 (40.7)	363 (40.6)	RR 0.95 (0.82 to 1.10)
In the first 3 months	364 (40.5)	381 (42.6)	
In the past 4 weeks	80 (8.9)	79 (8.8)	RR 1.01 (0.68 to 1.49)
At any other time	160 (17.8)	151 (16.9)	
Missing	5	2	
Not applicable (not had sexual intercourse since the birth)	46	45	

ICIQ-UI, International Consultation on Continence Modular Questionnaire – Urinary Incontinence; IQR, interquartile range.
a Adjusted for centre.
b Scored on a scale of 0 to 21, with a high score indicating worse problems.
c Woman could tick more than one option, so percentages may total > 100%.
d Excludes women who have not had sexual intercourse.
Adapted from The Epidural and Position Trial Collaborative Group.[39]

TABLE 15 One-year infant outcomes

Outcome	Trial arm		Adjusted[a] RR (99% CI)
	Upright (*N* = 950), *n* (%)	Lying down (*N* = 942), *n* (%)	
Major morbidity[b]	1 (0.11)	4 (0.42)	0.25 (0.01 to 4.40)

a Adjusted for centre.
b For example gross neurodevelopmental delay, including cerebral palsy (if a diagnosis has been made).

TABLE 16 Sensitivity analysis: 1-year maternal outcomes, excluding women who had another child/were pregnant at the time of assessment

Outcome	Trial arm		Adjusted[a] effect measure (99% CI)
	Upright (*N* = 950)	Lying down (*N* = 942)	
Women who have had another baby, *n* (%)	6 (0.6)	4 (0.4)	
Missing	6	14	
Women pregnant at time of completing questionnaire, *n* (%)	61 (6.5)	72 (7.8)	
Missing	9	20	
Denominator excluding women who were pregnant/had another baby	883	866	
Urinary incontinence, *n* (%)			
Leaking in the first 3 months	432 (49.2)	426 (49.4)	RR 0.99 (0.88 to 1.13)
Missing	4	4	

TABLE 16 Sensitivity analysis: 1-year maternal outcomes, excluding women who had another child/were pregnant at the time of assessment (*continued*)

Outcome	Trial arm		Adjusted[a] effect measure (99% CI)
	Upright (*N* = 950)	Lying down (*N* = 942)	
ICIQ-UI score[b] over the past 4 weeks			
Median (IQR)	0 (0–4)	0 (0–4)	Median difference 0 (0 to 0)
Missing	38	30	
Faecal incontinence			
No bowel control and/or soiling			
In the first 3 months	101 (11.5)	122 (14.2)	RR 0.81 (0.59 to 1.12)
Missing	7	9	
In the past 4 weeks	28 (3.2)	27 (3.2)	RR 1.02 (0.51 to 2.02)
Missing	10	8	
No bowel control and/or soiling and/or feel the need to go			
In the first 3 months	203 (23.2)	235 (27.4)	RR 0.85 (0.68 to 1.05)
Missing	8	7	
In the past 4 weeks	106 (12.2)	93 (10.9)	RR 1.12 (0.79 to 1.58)
Missing	12	9	
Feel need to go and have to go immediately[c]			
In the first 3 months	161 (18.4)	191 (22.2)	RR 0.83 (0.65 to 1.06)
In the past 4 weeks	92 (10.5)	81 (9.4)	RR 1.12 (0.77 to 1.62)
Missing	8	5	
Constipation,[c] *n* (%)			
In the first 3 months	368 (42.0)	328 (38.0)	RR 1.11 (0.95 to 1.29)
In the past 4 weeks	82 (9.4)	90 (10.4)	RR 0.90 (0.62 to 1.30)
Missing	6	2	
Haemorrhoids,[c] *n* (%)			
In the first 3 months	291 (33.2)	278 (32.2)	RR 1.03 (0.86 to 1.23)
In the past 4 weeks	100 (11.4)	102 (11.8)	RR 0.97 (0.69 to 1.36)
Missing	6	2	
Dyspareunia,[c,d] *n* (%)			
In the first 3 months	339 (40.7)	351 (42.9)	RR 0.95 (0.82 to 1.10)
In the past 4 weeks	75 (9.0)	78 (9.5)	RR 0.95 (0.64 to 1.41)
Missing	5	2	
Not applicable (not had sexual intercourse since the birth)	45	45	

ICIQ-UI, International Consultation on Continence Modular Questionnaire – Urinary Incontinence; IQR, interquartile range.
a Adjusted for centre.
b Scored on a scale of 0 to 21, a high score indicating worse problems.
c Woman could tick more than one option so percentages may total.
d Excludes women who have not had sexual intercourse.

TABLE 17 Adverse events

Adverse event	Trial arm	
	Upright (*N* = 1556)	Lying down (*N* = 1537)
Woman, *n*		
Dizziness	29	21
Post-partum haemorrhage	1	1
Seizure	0	2
Other	3	3
Baby, *n*		
Stillbirth	1	0
Birth trauma	1	0
Other	2	0

Chapter 6 Economic evaluation

In this chapter we present the results of the economic evaluation conducted alongside the BUMPES trial. A within-trial cost–consequences analysis with a time horizon of a 1-year follow-up and a NHS perspective was conducted. The aim of this analysis was to inform about health-care utilisation and costs for the treatment pathways followed by mothers and their babies from trial entry up to 1 year after birth. In addition to the consequences of the different positions during the late stages of labour in women with an epidural presented in previous chapters, we also report maternal health-related quality of life (HRQoL) at 1 year after birth. Details of each component of the economic analysis are provided in this chapter.

Methods

A health economics analysis plan was developed to guide the health economics team during the development of the economic evaluation (see *Appendix 8*). Overall, the team followed this analysis plan during the conduct of the economic evaluation, but there was one deviation from the plan that affected the final presentation of results of the economic analysis. The original analysis plan stated quality-adjusted life-years (QALYs) as the primary health outcome measure and used a cost–utility analysis to present the results of the economic evaluation. However, quality-of-life data at randomisation were not collected owing to the intrinsic difficulties in collecting this information during labour. In addition, it was not planned to collect data during the early postnatal period as part of the trial. As a result, the calculation of a QALY profile for the trial duration could not be derived. The next alternative could have been to conduct a cost-effectiveness analysis using the primary outcome in the trial or another clinical end point to present the results of the economic analysis. However, given that this was, to our knowledge, the first economic evaluation of position during labour, the results of such an analysis would have been difficult to interpret by decision-makers in the absence of a willingness to pay for health gains for the selected outcome. Therefore, we decided to conduct a cost–consequences evaluation as the primary analysis for the economic evaluation. In a cost–consequences analysis, the different components of costs and benefits of the interventions under evaluation are presented in a disaggregated manner without an attempt to estimate a summary measure [e.g. incremental cost-effectiveness ratio (ICER)].[41] As a secondary outcome of the economic analysis we conducted a cost-effectiveness analysis using the number of additional cases of SVB as the outcome measure. The latter analysis was included as a benchmark for future economic evaluations studies in obstetrics.

Health outcome measures

Health outcomes for women and their babies before discharge and at the 1-year follow-up were evaluated as potential consequences to include in the economic evaluation. *Chapter 5* reported a number of secondary maternal, neonatal and longer-term outcomes in addition to the primary outcome in the trial. Most of these outcomes led to health-care service utilisation, which was accounted for in our analysis, and only a selection of maternal and infant outcomes were therefore included in the cost–consequences analysis. For women, we selected the incidence of SVB, maternal satisfaction with labour as reported immediately after the birth and urinary and faecal incontinence at 1 year's follow-up. An Apgar score of < 4 at 5 minutes and major morbidity at 1 year's follow-up were the consequences selected for infants. When reporting the results of difference in estimates between upright and lying-down positions for any of these outcomes, we refer to the appropriate tables in *Chapter 5* rather than replicating the tables here.

In addition to the above consequences, maternal HRQoL information using the EuroQol-5 Dimensions, three-level version (EQ-5D-3L) and the Short Form questionnaire-12 items (SF-12) instruments was collected at the 1-year follow-up. The EQ-5D-3L is an increasingly widely used multiattribute generic instrument for measuring HRQoL in cost–utility analyses.[42] It has two components: a descriptive system covering five

dimensions (mobility, self-care, usual activity, pain/discomfort and anxiety/depression), each of which has three levels (no problem, some problems and extreme problems), and a 'feeling thermometer' using a visual analogue scale. The 243 health states of the EQ-5D-3L can be converted into preference-based utility values using a value set obtained from a British general population sample.[43] The SF-12 is a generic HRQoL instrument derived from its longer counterpart, the Short Form questionnaire-36 items (SF-36),[44] designed to measure general health functioning. The SF-12 items measure physical or emotional limitations, physical functioning, pain, general health, vitality, social functioning and mental health problems. The number of levels in each SF-12 question varies depending on the version used, and in this study the SF-12 version 2 was administered. Health states from the SF-12 instrument can be converted into preference-based utilities using the Short Form questionnaire-6 Dimensions (SF-6D) algorithm, which was used in this study.[45]

NHS health-care resource use

Detailed information about secondary care usage was collected and included resources consumed during the late stages of labour to hospital discharge, and during the first 12 months after birth as reported at the 1-year follow-up. *Chapter 5* reported some data about health-care usage that we also present in this chapter with additional information. Data from trial entry up to postnatal hospital discharge were collected from hospital records and included in the DCB (see *Appendix 1*). A postal questionnaire was used to collect secondary care information at the 1-year follow-up, and this was sent by the trial management team, which also dealt with reminders and appropriate double-data entry and data cleaning. Information was collected for women and their babies. The different items of resource use collected for each category of secondary care health service are summarised in *Table 18*.

No intervention-specific costs were assigned to either upright or lying-down position as neither was associated with the use of any additional resources . Given that all randomised women already had epidural analgesia and that any remaining medication after the birth was considered to be waste, epidural-specific costs were excluded from the cost analysis. In addition, any top-up epidural drugs costs in both arms were excluded from the cost analysis as there was no evidence of a difference between groups (see *Table 7*).

TABLE 18 Categories of resource use and associated unit costs used in the cost analysis (expressed in 2013/14 UK £)

Resource use item	Unit cost (£)	Source	Notes
Maternal			
Birth related			
Augmentation (oxytocin)	1	BNF 2015[46]	Oxytocin, injection, price for 10 units/ml, 1-ml ampoule
Fetal blood sampling	28	John Radcliffe Hospital Women's Centre (Oxford)	Obtained from hospital finance department
Fetal scalp electrode	5	Schroeder *et al.*[47]	
Hypotension medication	10	BNF 2015[46]	Injection, phenylephrine hydrochloride 10 mg/ml (1%), 1-ml ampoule = £9.91
Mode of birth			
Vaginal delivery	1462	*NHS Reference Costs 2013–14*[48]	Normal delivery with a complication score of 0 (HRG data)
Assisted delivery	1860	*NHS Reference Costs 2013–14*[48]	Assisted delivery with a complication score of 0 (HRG data)
Caesarean section delivery	3674	*NHS Reference Costs 2013–14*[48]	Emergency caesarean section

TABLE 18 Categories of resource use and associated unit costs used in the cost analysis (expressed in 2013/14 UK £) (*continued*)

Resource use item	Unit cost (£)	Source	Notes
Episiotomy	27	Schroeder *et al.*[47]	
Perineal tear			
First- and second-degree tears	23	Schroeder *et al.*[47]	
Third- and fourth-degree tears	64	Schroeder *et al.*[47]	
Manual removal of the placenta	74	Schroeder *et al.*[47]	
Post-partum haemorrhage	154	Eddama *et al.*[49]	
Blood transfusion	157	Schroeder *et al.*[47]	Per blood pack
HLC admissions			
Level of care (per day)			
Level 0	643	*NHS Reference Costs 2013–14*[48]	
Level 1	890	*NHS Reference Costs 2013–14*[48]	
Level 2	1266	*NHS Reference Costs 2013–14*[48]	
Level 3	1449	*NHS Reference Costs 2013–14*[48]	
Investigations			
MRI	139	*NHS Reference Costs 2013–14*[48]	
CT	80	*NHS Reference Costs 2013–14*[48]	
Radiography	48	*NHS Reference Costs 2013–14*[48]	
Transfer to another hospital	435	Schroeder *et al.*[47]	
Outpatient visits			
Perineal care clinic	13	*NHS Reference Costs 2013–14*[48]	
Gynaecological	13	*NHS Reference Costs 2013–14*[48]	
Surgical	11	*NHS Reference Costs 2013–14*[48]	
Other	127	–	Average cost of outpatient visits
Hospital visits			
Hospital inpatient (per day)	757	*NHS Reference Costs 2013–14*[48]	Average cost of regular day or night admissions
Postnatal ward stay (per day)	103	Schroeder *et al.*[47]	
Infant			
Birth related			
Cord blood sampling	0.05	Schroeder *et al.*[47]	
HLC admissions			
Level of care (per day)			
Special care	41	*NHS Reference Costs 2013–14*[48]	
High dependency	839	*NHS Reference Costs 2013–14*[48]	
Intensive care	1118	*NHS Reference Costs 2013–14*[48]	

continued

TABLE 18 Categories of resource use and associated unit costs used in the cost analysis (expressed in 2013/14 UK £) (*continued*)

Resource use item	Unit cost (£)	Source	Notes
Investigations			
Radiography	85	*NHS Reference Costs 2013–14*[48]	
CT scans	37	*NHS Reference Costs 2013–14*[48]	
MRI	48	*NHS Reference Costs 2013–14*[48]	
Transfer to another hospital	1259	*NHS Reference Costs 2013–14*[48]	Neonatal critical care, transportation
Neonatal death	696	Schroeder *et al.*[47]	
Outpatient visits			
Orthopaedic	148	*NHS Reference Costs 2013–14*[48]	
Paediatric	289	*NHS Reference Costs 2013–14*[48]	
Hearing	138	*NHS Reference Costs 2013–14*[48]	
Eye	115	*NHS Reference Costs 2013–14*[48]	
Dermatology	144	*NHS Reference Costs 2013–14*[48]	
Other	167	–	Average cost of outpatient
Hospital visits			
Hospital inpatient (per day)	886	*NHS Reference Costs 2013–14*[48]	Paediatric high-dependency ward

CT, computerised tomography; HRG, Healthcare Resource Group; MRI, magnetic resonance imaging.

At the study design stage, there was a general concern about including primary care and community care visits as part of the data collection because these tend to be frequent and poorly recalled by new mothers compared with secondary care visits.[50] It was agreed that hospital care constituted the main cost driver for this population and the target source data to collect in the study. Therefore, primary care and community care visit data were not collected. However, urinary and faecal incontinence are important outcomes following birth and may be related to the mode of delivery, and can have long-lasting effects on HRQoL and additional visits to primary care.[17,21] Therefore, it was decided that, if necessary, primary care visits related to these adverse events would be estimated using recent data from the literature if significant differences between treatment arms were observed. Nevertheless, this was not the case (see *Table 14*), and such visits were not incorporated as part of the categories of resource use in the cost analysis and are presented as part of the health outcomes in the cost–consequences analysis. We also assumed that any costs for specific surgeries were reflected in the length of stay and the unit cost attached to the admission. Therefore, we did not conduct a micro-costing approach for the maternal and infant surgeries performed in different time periods.

Unit cost data collection

Sources and associated estimates of unit costs for the different categories of resource use are presented in *Table 18*. Unit costs were mainly extracted from national sources, including the Personal Social Services Research Unit[51] and the *NHS Reference Costs 2013–14*,[48] and from a recent published cost-effectiveness analysis of alternative planned places of birth in woman at low risk of complications.[47] The unit cost of undertaking fetal blood sampling for the assessment of metabolic acidosis was not available in any of the sources consulted and was provided by the finance department of a large obstetric unit in Oxford. All costs were expressed in 2013/14 pounds sterling inflated to this base using the Hospital and Community Health Service Inflation Index[52] where appropriate.

Statistical analysis

Volumes of categories of resource use were multiplied by the corresponding unit cost to estimate the cost per woman or baby in a particular category. This was then averaged across each trial arm to obtain a mean cost per woman or baby of a particular category. We estimated health-care resource use deriving mean estimates and SDs either across all women and their babies in an arm of the trial or only for those consuming the resource category. The latter analysis using standard descriptive statistics was expected to provide information about potential outliers influencing the estimation of mean resource use and costs for a particular category of resource use in each arm of the trial. Categories of resource use and associated costs are presented separately for women and their babies, but the estimation of summary costs for a particular resource use category (e.g. total costs at 12-month follow-up) was calculated adding information from the pair. Health-care resource use between treatment arms was compared using RRs for binomial variables and mean differences for continuous covariates. Costs were compared using mean differences between treatment arms. Recent evidence suggests that both parametric and non-parametric methods accurately estimate the true standard errors (SEs) of means, even when data are highly skewed, and moderate to large ($n > 50$) sample sizes for continuous variables.[53] Hence, mean resource use and cost differences and associated uncertainty for particular categories of resource use and costs between the two positions during the late stage of labour were estimated using parametric methods. In line with the statistical analysis of the primary outcome, differences between treatment arms were adjusted using a random intercept binomial (for RRs) or linear (for mean differences) model using hospital centre as a random effect. In order to be consistent with the original SAP, a 95% significance level was defined to determine significant differences in health-care resource use for the primary outcome (SVB) whereas a 99% significance level was used for the other categories of resource use. A 95% significance level was used to compare main categories of costs between treatment arms.

Mean differences and associated uncertainty in EQ-5D-3L and SF-6D utilities between the treatment arms were assessed using parametric methods and adjusted using a random intercept linear model for hospital centre.

The number of missing data for secondary care resource use up to hospital discharge was very low in each treatment arm (< 1%), and we present the health-care resource use and costs during this period using a complete-case analysis. The proportion of missing data on both resource use and HRQoL was higher at the 1-year follow-up. In this case, resource use was presented using a complete-case analysis, but in the case of maternal quality-of-life scores and costs we implemented a multiple imputation framework with chained equation.[54] Current guidance on handling missing data in cost-effectiveness analysis was followed to inform such analysis.[55] Only missing utility scores (for both EQ-5D-3L index and SF-6D utilities) and individual cost items were imputed and the distribution of responses for both instruments was reported for data available. We constructed an imputation model that included covariates with complete data on trial entry characteristics (maternal age, gestational age at entry, BMI and baby's birth weight), HRQoL variables (EQ-5D-3L and SF-6D scores), and all individual categories of cost variables. We used prediction mean-matching, estimated 50 different imputations, and the imputation model was implemented separately by trial allocation. Mean estimates and estimates of SE were combined between imputed data sets using Rubin's rule[56] and adjusted using a random intercept linear model for hospital centre.

Mean differences in the total costs at 12 months' follow-up and the number of additional cases of SVB between treatment arms were combined into the ICER to determine cost-effectiveness as a secondary outcome in the economic evaluation. The lying-down position was used as the comparator in the ICER calculation. Uncertainty around the ICER was evaluated parametrically using 95% CIs.[57] The five parameters needed (difference in costs, SE of difference in costs, difference in effects, SE of difference in effects and correlations of differences in costs and effects) to estimate parametrically the uncertainty around the ICER were obtained from the multiple imputation analysis.

The statistical analysis was conducted in Stata/SE for Windows version 13.1.

Results

Clinical consequences

In *Chapter 5* we reported that there were significantly fewer SVBs in the upright group (see *Table 5*) and that we found no evidence of differences between the two intervention groups in maternal satisfaction (see *Table 9*), maternal urinary and faecal incontinence (see *Table 14*), frequency of Apgar score of < 4 at 5 minutes (see *Table 10*) or major morbidity (see *Table 15*).

NHS health-care resource use

Tables 19 and *20* present the maternal and infant health-care resource use from trial entry to postnatal hospital discharge for the birth-related, HLC admissions and hospital length of stay categories of resource use. In line with reporting of the primary outcome in *Chapter 5*, the only statistically significant difference observed between trial arms was the higher number of SVBs in the lying-down arm. The number of infants in whom cord blood was sampled was slightly higher in the upright group than in the lying-down group, yielding a statistically significant RR (99% CI) of 1.012 (1.010 to 1.013). No other significant differences were detected.

TABLE 19 Maternal health-care resource use from trial entry to hospital discharge

Health-care resource use	Trial arm: Upright (*N* = 1556)	Trial arm: Lying down (*N* = 1537)	RR/MD (99% CI)[a]
Delivery-related, *n* (%)			
Augmentation (oxytocin)	172 (11.08)	163 (10.62)	1.04 (0.80 to 1.35)
Missing	3	2	
Fetal blood sampling	90 (5.80)	72 (4.69)	1.17 (0.82 to 1.68)
Missing	4	3	
Fetal scalp electrode	94 (6.06)	85 (5.57)	1.09 (0.76 to 1.57)
Missing	6	11	
Hypotension medication	13 (0.84)	12 (0.78)	1.07 (0.39 to 2.99)
Missing	3	2	
Mode of birth			
SVB	548 (35.24)	632 (41.12)	0.86 (0.78 to 0.94)*
IVD	849 (54.60)	778 (50.62)	1.08 (0.98 to 1.18)
Caesarean section	158 (10.16)	127 (8.26)	1.23 (0.92 to 1.64)
Missing	1	0	
Episiotomy	914 (58.78)	838 (54.56)	1.08 (0.99 to 1.16)
Missing	1	1	
Perineal tear	760 (48.97)	785 (51.11)	0.95 (0.87 to 1.04)
First- or second-degree tear	654 (42.19)	704 (45.83)	
Third- or fourth-degree tear	104 (6.71)	81 (5.27)	
Missing	6	1	
Manual removal of the placenta	99 (6.48)	101 (6.72)	0.97 (0.69 to 1.38)
Missing	28	35	

TABLE 19 Maternal health-care resource use from trial entry to hospital discharge (*continued*)

Health-care resource use	Trial arm: Upright (*N* = 1556)	Trial arm: Lying down (*N* = 1537)	RR/MD (99% CI)[a]
Post-partum haemorrhage with blood transfusion	63 (4.05)	52 (3.39)	1.20 (0.75 to 1.92)
Missing	1	1	
HLC admissions			
Level of care (days), mean (SD)			
Level 0	0.035 (0.339)	0.025 (0.320)	0.010 (–0.020 to 0.040)
Level 1	0.041 (0.222)	0.029 (0.201)	0.011 (–0.007 to 0.031)
Level 2	0.021 (0.202)	0.023 (0.191)	–0.002 (–0.020 to 0.016)
Level 3	0.005 (0.076)	0.001 (0.036)	0.003 (–0.002 to 0.009)
Missing	3	2	
Surgery performed	7 (0.45)	4 (0.26)	
Missing	3	2	
Transfer to another hospital	2 (0.13)	0 (0.00)	
Missing	3	2	
Investigations, mean (SD)			
Radiography	0.0032 (0.0671)	0.0039 (0.0721)	–0.0007 (–0.007 to 0.006)
CT	0.0013 (0.0359)	0.0007 (0.0255)	0.0006 (–0.002 to 0.005)
MRI	0 (0)	0.0007 (0.0255)	–0.0007 (–0.002 to 0.001)
Missing	3	2	
Hospital length of stay, mean (SD)			
Length of stay (days)	2.73 (2.28)	2.74 (2.94)	–0.003 (–0.242 to 0.243)
Missing	5	5	

*$p < 0.05$.
CT, computerised tomography; MD, mean difference; MRI, magnetic resonance imaging.
a Adjusted for centre. 95% CI used for primary outcome (SVB).

A breakdown of health-care resources consumed at 12-month follow-up for women and their babies for outpatient and hospital visits is presented in *Table 21* using a complete-case analysis. No significant differences for any of the categories between treatment groups were observed.

Similar information to that in *Tables 19–20* is presented in *Tables 22* and *23*, but only for women and their babies consuming the health-care resource use. The results from such analysis confirmed the presence of a few individuals (as indicated by the range) consuming more of some resource use categories than the remaining participants (e.g. one infant admitted for intensive care for 31 days in the upright position or women having more than 30 visits as an outpatient in both groups). However, the impact of these outliers was minimal when averaging across all participants, given the low number of participants consuming any of these resources.

TABLE 20 Infant health-care resource use from trial entry to hospital discharge [values represent frequencies (percentages) unless stated otherwise]

Health-care resource use	Trial arm: Upright ($N = 1556$)	Trial arm: Lying down ($N = 1537$)	RR/MD (99% CI)[a]
Birth-related, *n* (%)			
Cord blood sampling	1025 (66.21)	940 (61.56)	1.012 (1.010 to 1.013)*
Missing	8	10	
Resuscitation	206 (13.24)	180 (11.71)	1.32 (0.89 to 1.44)
Facial oxygen	122 (7.85)	94 (6.12)	
Suction	75 (4.83)	74 (4.82)	
Bag and mask ventilation	82 (5.28)	82 (5.34)	
Intubation	6 (0.39)	8 (0.52)	
Complex resuscitation	4 (0.26)	1 (0.07)	
Missing	2	2	
HLC admissions			
Level of care (in days), mean (SD)			
Special care	0.10 (0.65)	0.14 (1.16)	–0.042 (–0.127 to 0.046)
Missing	13	7	
High dependency	0.02 (0.17)	0.03 (0.33)	–0.010 (–0.035 to 0.015)
Missing	9	4	
Intensive care	0.04 (0.83)	0.03 (0.32)	0.017 (–0.041 to 0.076)
Missing	9	3	
Surgery performed, *n* (%)	2 (0.13)	3 (0.20)	
Missing	9	4	
Transfer to another hospital, *n* (%)	2 (0.13)	4 (0.26)	
Missing	9	3	
Neonatal death, *n* (%)	0	0	
Missing	33	29	
Investigations, mean (SD)			
Radiography	0.02 (0.21)	0.04 (0.49)	–0.015 (–0.050 to 0.197)
Missing	11	7	
CT	0 (0)	0.002 (0.447)	–0.002 (–0.005 to 0.001)
Missing	10	6	
MRI	0.0020 (0.0440)	0.0007 (0.0256)	0.0013 (–0.002 to 0.005)
Missing	10	6	
Hospital length of stay, mean (SD)			
Length of stay (days)	3 (1.93)	3.07 (3.15)	–0.067 (–0.308 to 0.174)
Missing	6	5	

*$p < 0.01$.
CT, computerised tomography; MD, mean difference; MRI, magnetic resonance imaging.
a Adjusted for centre.

TABLE 21 Breakdown of health-care resource use at 1 year over the last 12 months for mothers and their infants

	Trial arm										
	Upright ($N = 1556$)					Lying down ($N = 1537$)					
Resource use category	*n*	Missing	Min.	Max.	Mean (SD)	*n*	Missing	Min.	Max.	Mean (SD)	MD (99% CI)[a]
Maternal											
Outpatient visits											
Perineal care clinic	941	615	0	10	0.140 (0.781)	936	601	0	10	0.109 (0.711)	0.030 (–0.059 to 0.118)
Gynaecological	925	631	0	8	0.144 (0.590)	931	606	0	10	0.179 (0.815)	–0.035 (–0.120 to 0.050)
Surgical	944	612	0	6	0.035 (0.322)	936	601	0	5	0.049 (0.346)	–0.014 (–0.054 to 0.025)
Other	927	629	0	50	0.514 (2.371)	920	617	0	35	0.414 (1.814)	0.099 (–0.154 to 0.715)
Hospital visits											
Hospital inpatient (days)	935	621	0	28	0.198 (1.328)	927	610	0	24	0.201 (1.257)	–0.003 (–0.120 to 0.115)
Number of operations	950	606	0	2	0.036 (0.202)	942	595	0	2	0.050 (0.232)	–0.014 (–0.040 to 0.012)
Infant											
Outpatient visits											
Orthopaedic	943	613	0	20	0.060 (0.760)	935	602	0	10	0.056 (0.466)	0.005 (–0.070 to 0.080)
Paediatric	923	633	0	8	0.250 (0.745)	912	625	0	20	0.279 (1.077)	–0.027 (–0.138 to 0.084)
Hearing	942	614	0	4	0.037 (0.272)	937	600	0	10	0.043 (0.411)	–0.006 (–0.047 to 0.036)
Eye	935	621	0	3	0.042 (0.248)	932	605	0	3	0.062 (0.305)	–0.021 (–0.054 to 0.013)
Dermatology	944	612	0	6	0.039 (0.328)	938	599	0	5	0.036 (0.282)	0.003 (–0.033 to 0.039)
Other	930	626	0	10	0.206 (0.855)	924	613	0	22	0.297 (1.378)	–0.090 (–0.225 to 0.048)
Hospital visits											
Hospital inpatient (days)	928	628	0	21	0.374 (1.441)	919	618	0	45	0.491 (2.245)	–0.123 (–0.344 to 0.103)
Number of operations	950	606	0	2	0.015 (0.129)	942	595	0	1	0.023 (0.151)	–0.009 (–0.025 to 0.008)

Max., maximum; MD, mean difference; min., minimum.
a Adjusted for centre.

TABLE 22 Maternal and infant health-care resource use for HLC admissions from trial entry to hospital discharge for women consuming the resource use category

Health-care resource use	Trial arm									
	Upright					Lying down				
	n	Mean (SD)	Min.	Max.	Width of IQR	*n*	Mean (SD)	Min.	Max.	Width of IQR
Mothers admitted to HLC										
Level of care (days)										
Level 0	28	1.928 (1.676)	1	8	1	17	2.235 (2.137)	1	8	2
Level 1	56	1.125 (0.384)	1	3	0	38	1.184 (0.512)	1	3	0
Level 2	23	1.391 (0.941)	1	4	0	26	1.346 (0.629)	1	3	1
Level 3	6	1.667 (0.408)	1	2	0	2	1 (0)	1	1	0
Surgery performed	7	–	–	–	–	4	–	–	–	–
Transfer to another hospital	2	–	–	–	–	0	–	–	–	–
Investigations										
Radiography	4	1.2 (0.5)	1	2	1	5	1.2 (0.447)	1	2	1
CT	2	1 (0)	1	1	0	1	1	1	1	0
MRI	–	–	–	–	–	1	1	1	1	0
Infants admitted to HLC										
Level of care (days)										
Special care	58	2.66 (2.15)	1	11	3	53	4.08 (4.78)	1	30	13
High dependency	15	1.53 (0.92)	1	3	2	14	2.71 (2.27)	1	9	8
Intensive care	17	3.88 (7.16)	1	31	2	14	2.79 (1.89)	1	7	6
Surgery performed	2	–	–	–	–	3	–	–	–	–
Transfer to another hospital	4	–	–	–	–	2	–	–	–	–
Neonatal death	0	–	–	–	–	0	–	–	–	–
Investigations										
Radiography	26	1.35 (0.85)	1	5	0	21	2.76 (3.27)	1	13	9
CT	–	–	–	–	–	3	1 (0)	1	1	0
MRI	3	1 (0)	1	1	0	1	1	1	1	0

CT, computerised tomography; IQR, interquartile range; max., maximum; min., minimum; MRI, magnetic resonance imaging.

NHS costs

Patterns of missing data for summary cost categories using a complete-case analysis are presented in *Figures 11* and *12*. It was evident from the plots that in each trial arm the number of missing data from trial entry to hospital discharge was low following a primarily monotonic missing data pattern. A larger number of missing data out of the overall data available was observed at the 12-month follow-up. The charts showed the potential cost information available (indicated by the grey area) to inform the multiple imputation model. The frequency of missing information in each trial arm and for all categories of health-care resource use are reported in *Tables 19–21*.

TABLE 23 Breakdown of health-care resource use at 1 year over the last 12 months for mothers and their infants consuming the resource use category

	Trial arm									
	Upright					Lying down				
Health-care resource use	*n*	Min.	Max.	Width of IQR	Mean (SD)	*n*	Min.	Max.	Width of IQR	Mean (SD)
Maternal										
Outpatient visits										
Perineal care clinic	55	1	10	2	2.4 (2.257)	38	1	10	2	2.684 (2.384)
Gynaecological	75	1	8	1	1.773 (1.192)	80	1	10	1	2.088 (1.943)
Surgical	16	1	6	2	2.063 (1.436)	26	1	5	1	1.770 (1.142)
Other	135	1	50	3	3.526 (5.303)	113	1	35	2	3.372 (4.117)
Hospital visits										
Hospital inpatient (days)	49	1	28	2	3.776 (4.534)	48	1	24	4	3.875 (4.072)
Number of operations	31	1	2	0	1.097 (0.301)	44	1	2	0	1.068 (0.255)
Infant										
Outpatient visits										
Orthopaedic	21	1	20	1	2.714 (4.429)	24	1	10	24	2.167 (2.014)
Paediatric	130	1	8	1	1.777 (1.109)	118	1	20	1	2.153 (2.229)
Hearing	23	1	4	0	1.522 (0.898)	23	1	10	14	1.739 (2.027)
Eye	30	1	3	1	1.3 (0.535)	43	1	3	1	1.349 (0.529)
Dermatology	19	1	6	1	1.947 (1.311)	21	1	5	1	1.619 (1.024)
Other	84	1	10	2	2.286 (1.834)	87	1	22	3	3.149 (3.360)
Hospital visits										
Hospital inpatient (days)	102	1	21	4	3.402 (2.943)	113	1	45	4	3.991 (5.218)
Number of operations	13	1	2	0	1.077 (0.277)	22	1	1	0	1 (0)

IQR, interquartile range; max., maximum; min., minimum.

Table 24 reports the results of the cost analysis using multiple imputation over the study period for mothers and their babies. A statistically significant mean cost difference (95% CI) of £59 (£6 to £111) between trial arms favouring the lying-down policy was detected in the delivery-related cost category. This translated into a statistically significant mean difference (95% CI) of £78 (£13 to £143) from trial entry to hospital discharge per delivery favouring the lying-down strategy. A significant mean cost difference (95% CI) of £0.002 (£0.001 to £0.004) favouring the lying-down position was observed for the birth-related cost category. This difference disappeared when adding the cost of HLC admissions to the total cost for infants from trial entry to hospital discharge. A summary of the overall costs from trial entry to 12-month follow-up for women and their infants using multiple imputation is also shown at the end of *Table 24*. The mean (SE) total cost per woman/infant pair at 12-month follow-up (adding all categories of costs) was estimated to be £3207 (£73) and £3252 (£81) in the upright and lying-down positions, respectively, a non-significant mean cost difference (95% CI) of –£42 (–£254 to £169) favouring the upright position.

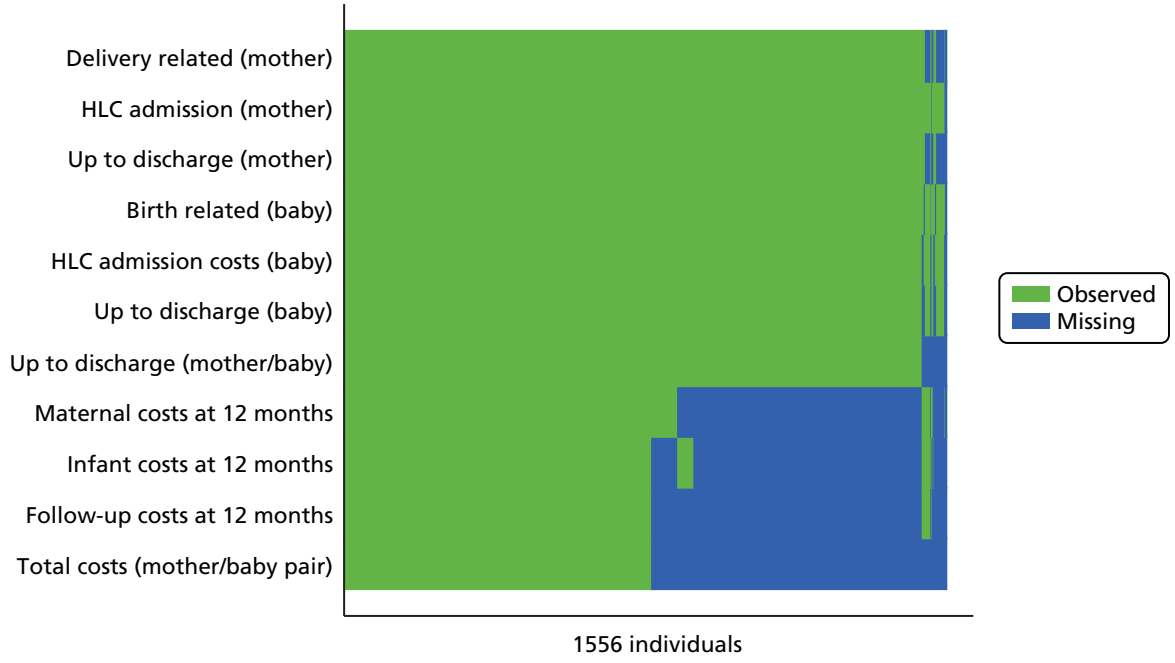

FIGURE 11 Pattern of missing data for main categories of costs for the upright group. Blue shading represents missing data for one or more individuals (horizontal axis) for a particular cost variable (vertical axis); green shading represents observed data.

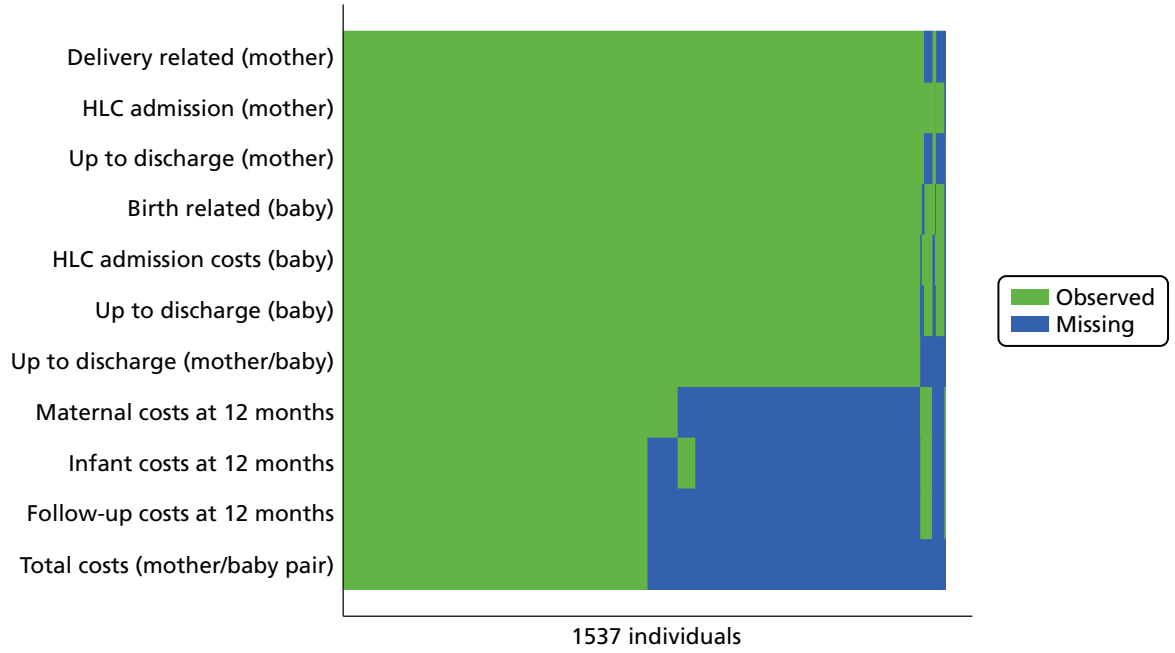

FIGURE 12 Pattern of missing data for main categories of costs for the lying-down group. Blue shading represents missing data for one or more individuals (horizontal axis) for a particular cost variable (vertical axis); green shading represents observed data.

TABLE 24 Cost analysis (2013/14 UK £) of maternal health-care resource use over the study period using multiple imputation

	Trial arm		
	Upright ($N = 1556$)	Lying down ($N = 1537$)	
Cost category	Mean (SE)	Mean (SE)	MD (95% CI)[a]
Maternal			
From trial entry discharge			
Total delivery related	2283 (19)	2225 (19)	59 (6 to 111)*
Total cost HLC admissions	92 (12)	73 (11)	20 (–11 to 51)
Total cost per delivery	2375 (24)	2298 (23)	78 (13 to 143)*
Follow-up costs			
Total outpatient visits	104 (11)	94 (9)	10 (–17 to 37)
Hospital admissions	159 (35)	159 (30)	0.09 (–96 to 97)
Total cost per delivery	263 (37)	252 (33)	13 (–84 to 109)
Infant			
From trial entry to discharge			
Total birth related	0.033 (0.001)	0.031 (0.001)	0.002 (0.001 to 0.004)*
Total cost HLC admissions	108 (28)	114 (22)	–6 (–76 to 64)
Total cost per baby	108 (28)	114 (22)	–6 (76 to 63)
Follow-up costs			
Total outpatient visits	129 (9)	153 (13)	–23 (–54 to 8)
Hospital admissions	333 (0)	434 (56)	–102 (–238 to 34)
Total cost per baby	462 (42)	587 (68)	–123 (–273 to 34)
Total 12-month follow-up costs	725 (58)	839 (71)	–113 (–293 to 66)
Total costs per woman/baby pair	3207 (73)	3252 (81)	–42 (–254) to 169)

*$p < 0.05$.
MD, mean difference.
a Adjusted for centre.

Maternal health-related quality of life at 12-month follow-up

Summary EQ-5D-3L and SF-6D scores at 12-month follow-up for each trial arm using a multiple imputation analysis is reported in *Table 25*. Quality-of-life scores were very similar (almost identical) between trial arms for both instruments and therefore no significant mean differences were detected.

TABLE 25 Maternal HRQoL using EQ-5D-3L and SF-6D scores at 12-month follow-up using multiple imputation

HRQoL instrument	*n*	Mean	SE	*n*	Mean	SE	MD (95% CI)[a]
EQ-5D-3L score	1556	0.919	0.005	1537	0.922	0.004	–0.003 (–0.016 to 0.011)
SF-6D score	1556	0.802	0.004	1537	0.805	0.004	–0.004 (–0.015 to 0.006)

MD, mean difference.
a Adjusted for centre.

The distribution of responses of available data for both instruments is reported in detail in *Tables 26* and *27*, respectively. It is clear that, using both instruments, the majority of women participating in BUMPES reported a good quality of life at 1 year post delivery.

Cost-effectiveness analysis as a secondary outcome in the economic evaluation

A summary of cost-effectiveness results comparing upright with lying-down positions during the second stage of labour is shown in *Table 28*. The ICER (95% CI) was estimated to be £722 (–£2968 to £6358) per additional case of SVB.

TABLE 26 Distribution of EQ-5D-3L responses across the dimensions for available data at 12-month follow-up

	Trial arm	
EQ-5D-3L dimension	Upright (*N* = 1556), *n* (%)	Lying down (*N* = 1537), *n* (%)
Mobility		
No problems	809 (94.5)	811 (95.6)
Some problems	46 (5.4)	37 (4.4)
Confined to bed	1 (0.1)	0 (0.0)
Missing	700	689
Self-care		
No problems	850 (99.1)	845 (99.7)
Some problems	6 (0.7)	3 (0.4)
Unable to wash or dress	1 (0.1)	0 (0.0)
Missing	699	689
Usual activities		
No problems	798 (93.3)	787 (92.7)
Some problems	56 (6.6)	61 (7.2)
Unable to perform activities	1 (0.1)	1 (0.1)
Missing	701	688
Pain/discomfort		
No pain	687 (80.4)	669 (79.1)
Moderate pain	161 (18.9)	171 (20.2)
Extreme pain	6 (0.7)	6 (0.7)
Missing	702	691
Anxiety/depression		
Not anxious or depressed	702 (82.0)	708 (83.5)
Moderately anxious or depressed	140 (16.4)	133 (15.7)
Extremely anxious or depressed	14 (1.6)	7 (0.8)
Missing	700	689

TABLE 27 Distribution of SF-12 responses across the dimensions for available data at 12-month follow-up

SF-12 dimension	Trial arm	
	Upright ($N = 1556$), n (%)	Lying down ($N = 1537$), n (%)
General health		
Excellent	172 (18.2)	168 (17.9)
Very good	465 (49.2)	473 (50.5)
Good	261 (27.6)	259 (27.6)
Fair	38 (4.0)	36 (3.8)
Poor	10 (1.1)	1 (0.1)
Missing	610	600
Moderate activities		
Yes, limited a lot	24 (2.5)	21 (2.2)
Yes, limited a little	76 (8.0)	79 (8.4)
No, not limited at all	848 (89.5)	837 (89.3)
Missing	608	600
Climbing several flights of stairs		
Yes, limited a lot	28 (3.0)	24 (2.6)
Yes, limited a little	119 (12.7)	120 (13.0)
No, not limited at all	792 (84.4)	782 (84.5)
Missing	617	611
Accomplished less than would like (physical health)		
All of the time	10 (1.1)	4 (0.4)
Most of the time	28 (3.0)	25 (2.7)
Some of the time	64 (6.8)	69 (7.4)
A little of the time	152 (16.1)	146 (15.6)
None of the time	690 (73.1)	693 (74.0)
Missing	612	600
Limited in the kind of work/activities (physical health)		
All of the time	8 (0.9)	5 (0.5)
Most of the time	20 (2.1)	12 (1.3)
Some of the time	44 (4.7)	52 (5.6)
A little of the time	130 (13.8)	109 (11.7)
None of the time	741 (78.6)	754 (80.9)
Missing	613	605
Accomplished less than would like (emotional health)		
All of the time	8 (0.9)	2 (0.2)
Most of the time	26 (2.8)	21 (2.2)
Some of the time	88 (9.3)	79 (8.4)
A little of the time	184 (19.5)	179 (19.1)
None of the time	638 (67.6)	658 (70.1)
Missing	612	598

continued

TABLE 27 Distribution of SF-12 responses across the dimensions for available data at 12-month follow-up (*continued*)

SF-12 dimension	Trial arm	
	Upright ($N = 1556$), *n* (%)	Lying down ($N = 1537$), *n* (%)
Less careful than usual (emotional health)		
All of the time	6 (0.6)	2 (0.2)
Most of the time	17 (1.8)	15 (1.6)
Some of the time	70 (7.4)	56 (6.0)
A little of the time	153 (16.3)	152 (16.3)
None of the time	695 (73.9)	709 (75.9)
Missing	615	603
Pain interfering with normal work		
Not at all	719 (76.2)	706 (75.1)
A little bit	165 (17.5)	186 (19.8)
Moderately	35 (3.7)	26 (2.8)
Quite a bit	21 (2.2)	18 (1.9)
Extremely	4 (0.4)	4 (0.4)
Missing	612	597
Felt calm and peaceful		
All of the time	81 (8.6)	87 (9.3)
Most of the time	510 (54.0)	490 (52.1)
Some of the time	240 (25.4)	244 (26.0)
A little of the time	86 (9.1)	103 (11.0)
None of the time	27 (2.9)	16 (1.7)
Missing	612	597
Have a lot of energy		
All of the time	47 (5.0)	46 (4.9)
Most of the time	432 (45.7)	440 (46.9)
Some of the time	310 (32.8)	302 (32.2)
A little of the time	109 (11.5)	115 (12.3)
None of the time	47 (5.0)	35 (3.7)
Missing	611	599
Felt downhearted and low		
All of the time	10 (1.1)	9 (1.0)
Most of the time	35 (3.7)	36 (3.8)
Some of the time	174 (18.5)	180 (19.2)
A little of the time	346 (36.8)	341 (36.4)
None of the time	376 (40.0)	372 (39.7)
Missing	615	599
Physical/emotional health interfered with social activities		
All of the time	7 (0.7)	5 (0.5)
Most of the time	26 (2.8)	21 (2.2)
Some of the time	105 (11.1)	102 (10.9)
A little of the time	173 (18.3)	186 (19.9)
None of the time	636 (67.2)	623 (66.5)
Missing	609	600

TABLE 28 Summary of cost-effectiveness results comparing upright with lying-down position during the second stage of labour

Position during labour	Total cost (2013/14 UK £)	Incremental costs	Proportion of SVBs	Incremental effect (additional cases of SVB)	ICER
	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (95% CI)
Lying down	3252 (81)	–	0.411 (0.012)	–	–
Upright	3207 (73)	–42 (108)	0.352 (0.012)	–0.06 (0.02)	722 (–2968 to 6358)

Discussion

This chapter has described in detail the methods and results of the economic evaluation conducted as part of the BUMPES trial. We have implemented a robust methodology based on more recent guidance to present these results.[58]

Our results suggested that women randomised to the lying-down position consumed significantly fewer resources than those randomised to an upright policy during the original hospital stay. Such results were driven by more SVBs in the lying-down treatment arm. Infants incurred similar costs in both arms of the trial during this time. At the 12-month follow-up, no significant overall cost differences were observed between upright and lying-down positions for mothers or their babies. The significantly higher costs incurred from trial entry to discharge by women in the upright group were offset by the slightly, but non-significantly, higher costs incurred during follow-up by the babies of women in the lying-down arm. A possible explanation is that SVB was associated with higher follow-up costs than instrumental delivery or caesarean section. However, additional analysis assessing follow-up costs by mode of delivery between the trial groups suggested that this was not the case (data available from the corresponding author). No evidence of differences was found for the other secondary maternal outcomes, neonatal clinical outcomes or maternal HRQoL. Therefore, the results of the cost–consequences analysis provided robust evidence clearly in favour of lying down, at no risk to women or their babies, and at no extra cost to the NHS.

Future studies can use the results of our cost-effectiveness analysis using the cost per additional case of SVB as an outcome measure as the benchmark for future comparisons in the area. However, we recommend that such comparisons are used with caution owing to well-known problems of comparability to other disease areas and 'double-counting' when estimating the ICER.[59,60]

To our knowledge, this is the first study reporting an economic evaluation of upright versus lying-down positions during the second stage of labour in nulliparous women with an epidural. The most comprehensive systematic review of economic evaluations of potential interventions during intrapartum care has been recently updated in a NICE clinical guideline.[31] The review aimed to identify all published cost-effectiveness evaluations in the areas within the remit of the guideline that included the second stage of labour, but no published economic evaluations were identified. Therefore, the results reported here should be considered the most up-to-date evidence about the cost-effectiveness of alternative position strategies during the second stage of labour in women with an epidural.

We were not able to collect HRQoL data at trial entry (or late pregnancy) or in the early postnatal period, precluding the estimation of QALYs. Therefore, one of the limitations of the current analysis is the limited comparability of our study with evaluations in other health areas using a cost-per-QALY approach, as recommended by NICE.[58] The use of QALYs has the potential to be a feasible and responsive outcome measure to evaluate the effectiveness of delivery position interventions during labour. A recent study has assessed the impact of mode of delivery on maternal HRQoL postnatally, suggesting that caesarean section is associated with larger quality-of-life decrements, followed by instrumental delivery and then SVB.[61]

Collecting quality-of-life information during late pregnancy and in the early postnatal period to use in cost-effectiveness analysis is controversial, because there is limited evidence about the validity of recommended instruments such as the EQ-5D-3L in this context.[62,63] However, it would be possible to estimate QALYs in the BUMPES study using a modelling exercise that synthesises available quality-of-life information during late pregnancy and in the early postpartum period from a literature review with the collected EQ-5D-3L data at 12-month follow-up. Such analysis is of interest to the research team and will be explored in future research. However, we feel that our cost–consequences analysis provides important evidence that can be considered by decision-makers in obstetrics when making recommendations about position during the late stages of labour in women with an epidural.

Chapter 7 Discussion and conclusion

BUMPES is the largest RCT yet undertaken of different positions in labour and their effects on the mode of birth. There is clear evidence of a benefit of adopting a lying-down position in the second stage of labour for nulliparous women with epidural analgesia, and there are no apparent disadvantages in relation to either short- or long-term outcomes for either mother or baby. Thus, a clinical improvement (increase in SVBs) could be achieved by encouraging nulliparous women with epidural analgesia to adopt a lying-down position during the second stage of labour. The intervention has no resource implications and has no additional risk to women or their babies, and thus could be implemented rapidly without additional cost.

Like all pragmatic trials, the study has limitations. The reporting of adherence is complex for this trial. Various options were considered for recording adherence, but, given the size of the trial, many of these, such as video recordings of the second stage of labour, were both impractical and intrusive. As midwives recorded observations of the women and the fetus in utero every 15 minutes during labour, it was felt that asking the midwife to record position of these epochs would facilitate good data collection. However, it was also recognised that there were a number of clinical reasons why position could not be maintained as allocated, for example to facilitate the taking of a fetal blood sample or because the fetal heart could not be easily monitored using an external monitor. Representing these as non-adherent in the analysis would have been unhelpful.

With an intervention such as this, masking is impossible, so the results may be influenced by the women's and the midwives' perceptions of the different positions in their ability to achieve a SVB. Given that existing NICE guidance suggests that women with an epidural should be encouraged to adopt whatever upright position they find comfortable, we might expect the trial results to suggest an improvement in SVB with an upright position if midwives' and women's behaviour was altered in these positions because of a firm belief that these were preferable. The finding that the lying-down position increases the chances of achieving a SVB suggests that this potential bias was either absent or minimal in its impact, or that the benefit of the lying-down position may be even greater in leading to a SVB.

The original commissioning brief for this trial asked for a measure of maternal satisfaction with the allocated position during labour. This proved particularly challenging, as there are no validated quantitative measures of maternal satisfaction specific to the labour and birth episode, and unpicking which aspects of care could improve an individual woman's satisfaction with her allocated position is difficult. The measure that was used was therefore created for this trial and so has limited external validity, even though it has internal validity.

The incidence of SVB in the trial overall was lower than anticipated when the study was being designed. The estimate of the risk of SVB was calculated using the COMET, which was published in 2001.[5] In the COMET, there were almost no caesarean sections undertaken during the second stage of labour, reflecting the change in clinical practice in obstetrics between the late 1990s and now.

We can only speculate about the mechanism by which a lying-down position increases the chance of a SVB. We have no direct measurements of the density of the epidural block in the two positions nor the level of the block. It is possible that women in the upright position acquired a more dense block around the birth canal because of the effect of gravity on the epidural drugs, which could have made expulsive efforts more difficult; however, the similarity of drug doses used in each group would suggest that this is unlikely. In women in the upright group, who may have been sitting, the pelvic outlet may have been restricted by the position on the coccyx or by lower genital tract oedema and venous obstruction causing swelling of the soft tissues obstructing the pelvic outlet. In addition, it is possible that lying down, by easing pressure of the fetal head on the pelvis, results in improved uterine blood flow and therefore improved uterine activity. This would suggest a difference in the risk of operative delivery associated with failure to progress; however, the distribution of indications for operative delivery appeared to be the same

in both groups. In addition, there was little difference in the use of oxytocin because of delay in labour progress after trial entry.

The mechanism by which the lying-down position improves the risk of SVB remains unknown; however, the results of this trial are clear. Among women with an epidural during their first birth, adopting a lying-down position in the second stage of labour increases the chance of achieving a SVB. The results cannot be directly extrapolated to multiparous women with an epidural, or to women who do not have an epidural, in whom the situation may be very different.

Longer-term outcomes

The response rate to the 1-year follow-up was 61%. Therefore, there is a possibility that the follow-up results are less than robust because of non-response bias. This poor response, despite many attempts to improve the rate (described in *Chapter 8*), is a phenomenon increasingly being seen with contemporary clinical trials in this area. We provided a variety of options for women to complete their questionnaire: on paper, via the internet or by telephone. The majority of women still prefer to use paper, but, despite these various offers, the response rate remained poor. Responders and non-responders exhibited clear differences in a variety of demographic and clinical factors that were anticipated. Women who responded were more likely to be older, more likely to be white, less likely to live in a deprived area and less likely to have achieved a SVB. There were, however, no apparent differences between the two randomised groups in their response rates or characteristics, suggesting that there were minimal biases in the comparison between the two groups.

The lack of an impact of the risk of SVB on longer-term outcomes, such as faecal incontinence, is of interest. The observation that IVD is associated with increased risks of faecal incontinence is robust; however, in the BUMPES trial the differences between the randomised groups of women in their risk of SVB and instrumental delivery were relatively small, so, although there are associations between different modes of birth and long-term outcomes, these are likely to be diluted in a trial in which these differences in actual mode of birth are relatively modest (only a 6% absolute difference in the risk of SVB). This is likely to explain the lack of an observed difference in long-term outcomes.

Adherence

Adherence is clearly important when considering an intervention of this nature. The observation that there was greater adherence in the upright group than in the lying-down group suggests that there may be even greater benefit from adopting a lying-down position if adherence could be improved. However, the ability to comply with the allocated intervention may be a function of the intervention itself. For example, women in the lying-down group may be more difficult to monitor when using an external cardiotocograph monitor because of the ability to position the monitor accurately to pick up the fetal heart rate. If this is the case, then non-adherence for clinical reasons is to be expected. It would therefore be difficult to improve adherence in these women if that meant that they could not be effectively and safely monitored. Further work needs to be undertaken on the association between adherence and various characteristics of the nature of the non-adherence, and the risk of the various outcomes, before much more can be said about whether or not improved adherence may improve the benefit of the lying-down position.

Challenges with equipoise

Although the trial was initially expected to recruit from five UK centres, the expansion to 41 centres suggests that the results have good generalisability, in that a large number of centres participated throughout the country. However, the reason for the expansion in the number of centres was because of

the concerns expressed by midwives in terms of recruiting to the trial. It was clear that many midwives did not have equipoise about position in the second stage of labour for women with an epidural, and in all of the participating centres it was a relatively small number of midwives who recruited the women in those centres. At no stage in the trial was there any suggestion that women were expressing a preference not to participate in the trial if they were approached. This effect of midwives having particular views about the benefits of position may limit the generalisability if midwives are not prepared to accept the evidence produced by the BUMPES trial. When there are strong views, for example that an upright position is preferable to a lying-down position, if the results of BUMPES fail to be implemented, then the population benefit of a lying-down position in these women will be relatively small. By producing results that contradict current NICE guidance and what is widely accepted, that is, that an upright position improves the chances of achieving a SVB, these results challenge an orthodoxy that may make their implementation more challenging. The results of the trial, however, are clear. If women giving birth to their first babies and their carers are keen to increase the chances of achieving a SVB, then adopting a lying-down position in the second stage of labour, for as much of that second stage of labour as can be achieved, results in a modest but real increase in their chances of doing so. There is no evidence to suggest that this improvement carries a risk either to the women themselves, in relation to perineal trauma, or to their babies, in relation to newborn compromise. Similarly, there is no evidence of any long-term risks to the health and well-being of the women or their babies. Given that there was no evidence of increasing resource consumption with the intervention, the authors believe that it could be straightforward to implement and therefore realise benefits for a substantial number of women having their first babies throughout the UK and other countries.

Monitoring adherence

Another observation from the conduct of this trial is whether or not a trial management group can and should monitor adherence. In general, adherence is often monitored by the DMC, which is the only group that sees any data by allocated intervention. For drug trials, in which monitoring of adherence may be relatively straightforward, this may not be a problem. But for interventions that are less well circumscribed, such as that in BUMPES, it is important that people with a good knowledge of the trial and its interventions are able to monitor adherence to ensure that there is reasonable separation between the arms of the trial. This can be achieved by the DMC; however, given the complexity of monitoring adherence to this intervention, particularly with respect to taking account of clinically acceptable reasons for periods of non-compliance, such as fetal blood sampling, the nature of DMCs (in that they tend to meet annually) means that the DMC is removed from the conduct of the trial, which may be a disadvantage. In a pragmatic trial, there is a clear reluctance to impose strict adherence rules, but it is helpful and useful to identify centres or particular individuals with very poor adherence so that behaviour can be modified. In BUMPES, with 41 centres, it was possible to monitor adherence by centre and identify at least one outlier centre that had particularly poor adherence to one of the allocated arms, which was at odds with all the other participating centres. This difference did not come to light until the trial investigators had received agreement from the DMC that the trial management group should be able to monitor adherence by allocated intervention on an ongoing basis. We believe that there is an important lesson to be learnt here about the nature of monitoring adherence, and agreements should be in place early in the trial on who should undertake this, what parameters should be monitored and how this should be overseen carefully to ensure that the degree of monitoring is reasonable, and that monitoring adherence cannot be used by the trial management group to make any inferences about outcomes.

Chapter 8 Nested study

This chapter describes a nested study within the BUMPES trial, which has been published.[64]

Rationale for nested study

The return rate of 1-year follow-up questionnaires for BUMPES was lower than expected and the use of incentives to evaluate the impact on questionnaire return rate was discussed by the TSC. It was noted by the TSC that there was a lack of evidence relating to the value of incentives to increase collection of follow-up data in trials. As the evidence base for incentives included a variety of populations, it could be that postnatal women respond differently. A proposal for a nested study within a trial (SWAT) was therefore developed.

Background

Maximising follow-up rates for postal questionnaires for RCTs is an important aspect of a well-designed and well-conducted study. Loss to follow-up can lead to bias and compromise the internal and external validity of the results.

Use of incentives to promote questionnaire return in clinical trials has been researched. Existing systematic reviews suggest that they are effective,[65,66] but not all studies have sufficient funds to use them. Promising an incentive once data are returned can reduce the cost burden of this approach. Brueton *et al.*[66] found that an offer of a monetary incentive was comparable with the addition of a monetary incentive with the questionnaire (pooled RR 1.04, 95% CI 0.91 to 1.19). However, it may be possible to provide further cost-savings if the offer was restricted to the reminder letters only.

We evaluated the effect of promising a monetary incentive at first mail-out versus a promise on reminder letters only, with the incentive being posted out on receipt of a completed follow-up questionnaire.

Objective

To assess the effectiveness on the return rate of the 1-year follow-up postal questionnaires for BUMPES of the promise of a monetary incentive made at the point of sending the questionnaire for the first time compared with a promise made on reminder letters only.

Trial design

Parallel-group RCT nested within BUMPES.

Study setting

All women randomised into the BUMPES study who consented to be contacted at 12 months and who had not yet been sent their 1-year follow-up questionnaire were included.

Participant eligibility

Inclusion criteria

- Recruited to BUMPES.
- Consented at recruitment to receive follow-up questionnaire.
- One-year questionnaire not sent.

Exclusion criteria

- Women who had a stillbirth.
- Women whose infant had died.
- Address details unknown.
- Woman and infant not living at the same address.

Interventions

Women were randomly allocated to the following two groups.

1. Incentive cover letter: this contained details of the promise of a monetary incentive when the questionnaire was first sent. A £10 gift voucher redeemable at high-street shops was sent to the woman on return of a completed questionnaire. The cover letter included a sentence explaining that the voucher was to thank participants for their time and effort. All reminder letters included a sentence about the incentive.
2. Incentive reminder letters: the standard cover letter did not mention any incentive. All subsequent reminder letters sent if the questionnaire was not returned detailed the promise of an incentive. A £10 gift voucher redeemable at high-street shops was sent to the woman on return of a completed questionnaire.

For both groups, women were contacted electronically and via text messaging if the contact details had been collected. The content of the e-mails and texts sent reflected the group to which the woman was randomised. All women were provided with an option of completing the questionnaire online.

Outcome measure

Primary outcome measure

The primary outcome measure was questionnaire return, defined as receipt of a completed or partially completed questionnaire at the BUMPES office.

Secondary outcome measures

The following secondary outcomes were analysed:

- the number of questionnaires returned without chasing by the study team
- the total cost of the vouchers sent out by nested study arm.

Data collection

Recording of questionnaire receipt, date received and voucher sent was made using internal trial administration systems. Postal versus online receipt was also recorded.

Sample size

The sample size was predetermined by the numbers of questionnaires remaining to be sent at the point of start of the nested study.

BUMPES started recruiting in October 2010 and finished in January 2014. A total of 3236 women were randomised. It was estimated that approximately 1150 women remained to be followed up at the start date of this study (beginning August 2014). Assuming that approximately 15% of these women would be excluded from receiving the questionnaire due to stillbirth, infant death, or address details unknown or different from the infant, 980 women would be eligible to be randomised in the nested study (approximately 490 per group).

In order to assess the detectable effect size possible with the given sample size, we estimated the control group risk based on current literature. Khadjesari *et al.*[67] investigated the use of an offer of an incentive [a £10 Amazon (Amazon.com, Inc., Bellevue, WA, USA) gift voucher] versus no offer of an incentive on follow-up rates in an online trial. They found an increase of 9% (95% CI 5% to 12%) when using the offer of an incentive. Kenyon *et al.*[68] investigated the use of a monetary incentive included in reminder letters versus no incentive and found an improvement in the response rate between the two groups of 11.7% (95% CI 4.7% to 18.6%).

The follow-up questionnaire return rate for BUMPES up to June 2014 was 59%. Assuming that this could increase by at least 5% with use of the offer of an incentive either with an incentive cover letter or with an incentive reminder letter only, a sample size of 980 would be sufficient to demonstrate an increase in questionnaire return rate of 8% from 64% in the incentive reminder letter group to 72% in the incentive cover letter group at a two-sided 5% significance level with 80% power. *Figure 13* illustrates the proportion detectable in the incentive cover letter group for control group risk varying between 60% and 70%. The detectable difference lies between 8% and 8.5% for varying control group estimates.

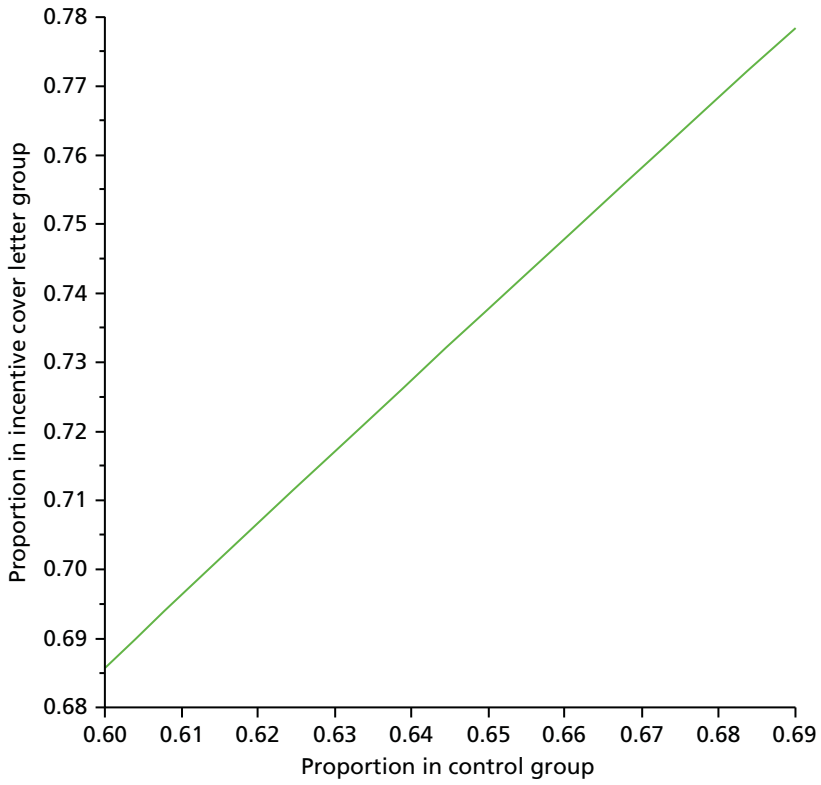

FIGURE 13 Proportion in incentive cover letter group by proportion in control group. Significance = 0.05; power = 0.80; sample size per group = 490.

Randomisation

Allocation was by computerised random number generation stratified by BUMPES allocation and by centre. Randomisation to incentive cover letter or incentive reminder letter occurred at each woman's next follow-up point during the conduct of the BUMPES study, with a block size of four. Each BUMPES participant was randomised to incentive cover letter or incentive reminder letter once only.

Blinding

Trial staff were aware of allocation as a result of the nature of the interventions and the practicalities involved in sending the letters and the vouchers.

Statistical analysis

For all analyses, participants were analysed in the groups into which they were randomly allocated, that is, comparing outcomes for women allocated to the incentive cover letter with outcomes for women allocated to the incentive reminder letter, regardless of allocation received.

All analyses were based on all women randomised for whom data were available.

The flow of participants through the trial was summarised using a CONSORT flow diagram (see *Figure 14*). Specifically, the number of women recruited to the BUMPES main trial and subsequently recruited to the BUMPES SWAT is reported along with reasons for not being included in the SWAT.

Participants in the two randomised groups are described separately with respect to baseline demographics and clinical characteristics, including the primary outcome for the main BUMPES study, and recorded on the BUMPES DCB.

Numbers (with percentages) for binary and categorical variables and means (and SDs) or medians (with lower and upper quartiles) for continuous variables are reported.

The return rate and chase rate before the introduction of the randomised interventions (i.e. before the SWAT started) and at the end of the study (with both SWAT trial arms combined) are presented using numbers and percentages.

The return rate and chase rate by method of completion (online vs. postal) are described by trial arm using numbers and percentages.

An adjusted analysis was performed on the two return rate outcomes adjusting for centre (the stratification factor at randomisation) as a random effect. The analysis was carried out using log-binomial regression models and results are presented as adjusted RRs with 95% CIs.

To examine whether or not the effect of when vouchers were sent was consistent across specific subgroups of women, a subgroup analysis by IMD quintile was prespecified. Results are presented as RR plus 95% CI for each subgroup, by intervention group, with the *p*-value for the statistical test of interaction.

Stata/SE for Windows (version 13.1) was used for all analyses.

Results

Randomisation to the incentive nested study started on 31 July 2014 and continued until all questionnaires and reminders had been sent (last letter sent 6 March 2015). The total number of women in the SWAT was 1026. Eight women were excluded from the analysis as it was discovered after they had been randomised to the SWAT that they had changed address (*Figure 14*).

Balance between the SWAT trial arms in baseline characteristics and centre of recruitment to BUMPES was good. There were only small imbalances in onset of labour (spontaneous or induced), diagnosis of pre-eclampsia and SVB (the BUMPES primary outcome) (*Table 29*).

The percentage of questionnaires returned before the SWAT started was considerably lower than the overall percentage returned from participants included in the SWAT (55.6% vs. 73.0%, respectively). This trend is also seen in the percentage returned without any reminder letters being sent [35.3% vs. 46.8%, respectively (*Table 30*)].

Return rates by postal and online completion between the two SWAT arms are presented in *Table 31*. A total of 152 questionnaires (20.5% of all questionnaires returned) were completed online, with slightly more being returned online in the reminder letter group than in the cover letter group (18.0% vs. 23.0%).

Figure 15 and *Table 32* present the percentages of questionnaires returned, according to how many times a reminder letter was sent, and broken down by postal versus online completion. A higher percentage of questionnaires were returned without chasing after receipt of a cover letter promising an incentive than in the group receiving a standard cover letter (51.5% vs. 42.1%, respectively). However, if a reminder was sent, fewer women returned the questionnaire in the group receiving the promise of an incentive in the

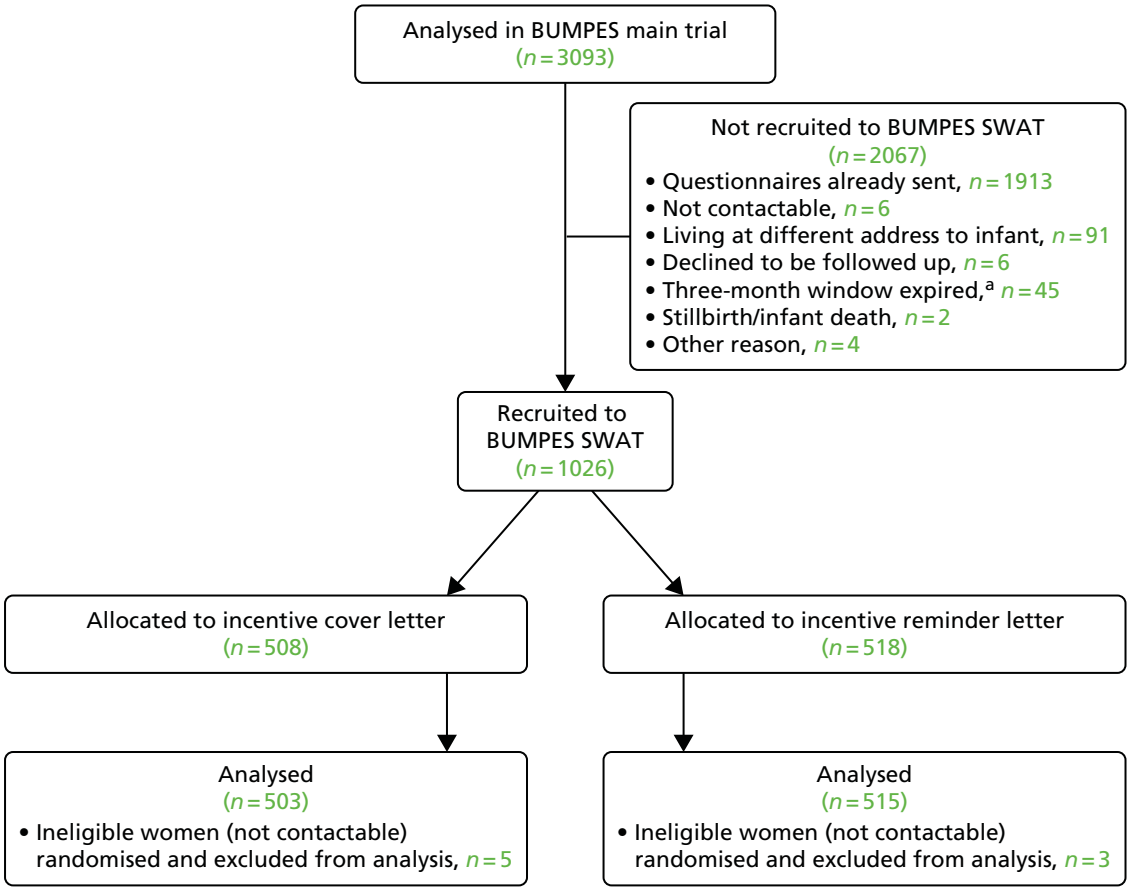

FIGURE 14 Nested study participant flow diagram. a, If not contactable after 15 months since randomisation, questionnaire was not sent.

TABLE 29 Characteristics prior to study entry

Characteristic	Letter	
	Cover (*N* = 503)	Reminder (*N* = 515)
Centre, *n* (%)		
Birmingham Women's Hospital	13 (2.6)	16 (3.1)
St Thomas' Hospital	61 (12.1)	60 (11.7)
Queen Alexandra Hospital, Portsmouth	9 (1.8)	8 (1.6)
University Hospital of Wales	36 (7.2)	36 (7.0)
Royal United Hospitals Bath	27 (5.4)	31 (6.0)
Bradford Royal Infirmary	10 (2.0)	12 (2.3)
Jessop Wing, Sheffield Teaching Hospital	20 (4.0)	20 (3.9)
Princess of Wales Hospital	3 (0.6)	2 (0.4)
Singleton Hospital, Swansea	3 (0.6)	1 (0.2)
Royal Gwent Hospital, Newport	17 (3.4)	14 (2.7)
Gloucestershire Royal Hospital	9 (1.8)	9 (1.8)
Nevill Hall Hospital	4 (0.8)	4 (0.8)
Frimley Park Hospital	25 (5.0)	25 (4.9)
Sunderland Royal Hospital	4 (0.8)	6 (1.2)
Pinderfields Hospital	15 (3.0)	14 (2.7)
Warrington Hospital	8 (1.6)	9 (1.8)
Tameside Hospital	4 (0.8)	5 (1.0)
Medway Maritime Hospital	2 (0.4)	1 (0.2)
South Tyneside District Hospital	1 (0.2)	4 (0.8)
Queen Mary's Hospital, London	13 (2.6)	13 (2.5)
Queen Charlotte's and Chelsea Hospital	3 (0.6)	4 (0.8)
Queen Elizabeth Hospital	6 (1.2)	7 (1.4)
Great Western Hospital	12 (2.4)	10 (1.9)
Royal Cornwall Hospital	12 (2.4)	12 (2.3)
Bedford Hospital	9 (1.8)	9 (1.8)
University College Hospital, London	12 (2.4)	12 (2.3)
Royal Sussex County Hospital	7 (1.4)	9 (1.8)
North Manchester General Hospital	14 (2.8)	16 (3.1)
New Cross Hospital, Wolverhampton	8 (1.6)	10 (1.9)
James Paget Hospital	11 (2.2)	10 (1.9)
St George's Hospital	24 (4.8)	23 (4.5)
Princess Royal University Hospital	2 (0.4)	1 (0.2)
King's College Hospital, London	36 (7.2)	37 (7.2)
St Mary's Hospital	1 (0.2)	2 (0.4)
Dorset County Hospital	8 (1.6)	8 (1.6)
Kingston Hospital	38 (7.6)	38 (7.4)
Hillingdon Hospital	6 (1.2)	6 (1.2)

TABLE 29 Characteristics prior to study entry (*continued*)

Characteristic	Letter	
	Cover ($N = 503$)	Reminder ($N = 515$)
Arrowe Park Hospital	6 (1.2)	6 (1.2)
Lewisham Hospital	1 (0.2)	2 (0.4)
Prince Charles Hospital	3 (0.6)	3 (0.6)
Maternal age (years)		
Mean (SD)	28.9 (5.6)	29.3 (5.5)
< 20, *n* (%)	24 (4.8)	24 (4.7)
20–24, *n* (%)	93 (18.5)	79 (15.3)
25–29, *n* (%)	133 (26.4)	148 (28.7)
30–34, *n* (%)	177 (35.2)	180 (35.0)
35–39, *n* (%)	66 (13.1)	71 (13.8)
≥ 40, *n* (%)	10 (2.0)	13 (2.5)
Missing	0	0
Gestational age at entry (weeks)		
Mean (SD)	40.4 (1.2)	40.3 (1.2)
37^{+0} to 39^{+6}, *n* (%)	150 (29.9)	167 (32.5)
40^{+0} to 41^{+6}, *n* (%)	320 (63.8)	315 (61.3)
≥ 42^{+0}, *n* (%)	32 (6.4)	32 (6.2)
Missing	1	1
IMD: quintile, *n* (%)		
First (least deprived)	64 (15.0)	72 (16.3)
Second	72 (16.9)	63 (14.2)
Third	83 (19.5)	91 (20.5)
Fourth	112 (26.3)	129 (29.1)
Fifth (most deprived)	95 (22.3)	88 (19.9)
Wales – not derived	66	59
Postcode missing	11	13
Ethnic group, *n* (%)		
White	415 (83.7)	434 (85.1)
Indian	20 (4.0)	14 (2.8)
Pakistani	9 (1.8)	7 (1.4)
Bangladeshi	2 (0.4)	1 (0.2)
Black African	14 (2.8)	10 (2.0)
Black Caribbean	7 (0.7)	2 (0.4)
Any other ethnic group	29 (5.9)	42 (8.2)
Not known/missing	7	5

continued

TABLE 29 Characteristics prior to study entry (*continued*)

Characteristic	Letter	
	Cover (*N* = 503)	Reminder (*N* = 515)
BMI at booking visit (kg/m^2)		
Mean (SD)	25.2 (5.2)	25.2 (5.3)
Height and/or weight not known	17	11
Woman undergone FGM, *n* (%)	2 (0.4)	0 (0.0)
Missing	1	1
Onset of labour, *n* (%)		
Spontaneous	309 (61.6)	293 (56.9)
Induced	193 (38.5)	222 (43.1)
Missing	1	0
Duration of first stage (minutes)		
Median (IQR)	490 (345–675)	505 (360–720)
Geometric mean	473.8	492.2
Missing	4	6
Diagnosis of pre-eclampsia, *n* (%)	12 (2.4)	22 (4.3)
Missing	2	1
Continuous electronic fetal monitoring, *n* (%)	484 (96.4)	492 (95.7)
Missing	1	1
Diagnosis of delay requiring intervention, *n* (%)	266 (53.1)	272 (52.8)
Missing	2	0
Systemic opioids given prior to epidural, *n* (%)	142 (28.3)	137 (26.6)
Pethidine	103 (72.5)	97 (70.8)
Diamorphine	38 (26.8)	38 (27.7)
Remifentanil	0 (0.0)	1 (0.7)
Morphine	0 (0.0)	0 (0.0)
Meptid	3 (2.1)	3 (2.2)
Missing	1	0
Epidural technique, *n* (%)		
Epidural	485 (96.6)	496 (96.5)
Combined spinal epidural	17 (3.4)	18 (3.5)
Missing	1	1
Epidural maintained with PCEA/infusion, *n* (%)	359 (73.1)	369 (73.1)
Missing	12	10
Woman's pain score for last contraction		
Median (IQR)	10 (0–32)	10 (0–30)
Missing	59	55
Able to perform straight leg raise, *n* (%)	381 (80.4)	408 (82.8)
Missing	29	22

TABLE 29 Characteristics prior to study entry (*continued*)

Characteristic	Letter	
	Cover (*N* = 503)	Reminder (*N* = 515)
Time from VE diagnosing second stage to study entry (minutes)		
Median (IQR)	13 (7–26)	15 (8–26)
Apparently randomised before diagnosis of second stage[a]	33	19
Time apparently > 180 minutes[b]	4	2
Missing	1	1
Time from study entry to start of recording positions (minutes)		
Median (IQR)	0 (–4 to 5)	1 (–3 to 5)
Time from study entry to recording position of > 15 minutes,[a] *n* (%)	38 (7.7)	44 (8.7)
Time apparently > 15 minutes before study entry[b]	79	68
Missing	9	7
SVB, *n* (%)	197 (39.2)	181 (35.2)
Missing	0	0

FGM, female genital mutilation; IQR, interquartile range; VE, vaginal examination.
a Values included.
b Values set to missing.

TABLE 30 Return rates by pre and post SWAT

Return rate, *n* (%)	SWAT	
	Pre (*N* = 2067)	Post (*N* = 1018)
Questionnaire returned	1149 (55.6)	743 (73.0)
Missing	0	0
Questionnaire returned without chasing by study team	729 (35.3)	476 (46.8)
Missing	0	0

TABLE 31 Return rates: mode of completion, by incentive

Return rate, *n* (%)	Letter	
	Cover (*N* = 503)	Reminder (*N* = 515)
Questionnaire returned	373 (74.2)	370 (71.8)
Postal	306 (82.0)	285 (77.0)
Online	67 (18.0)	85 (23.0)
Questionnaire returned without chasing by study team	259 (51.5)	217 (42.1)
Postal	207 (79.9)	161 (72.2)
Online	52 (20.1)	56 (25.8)

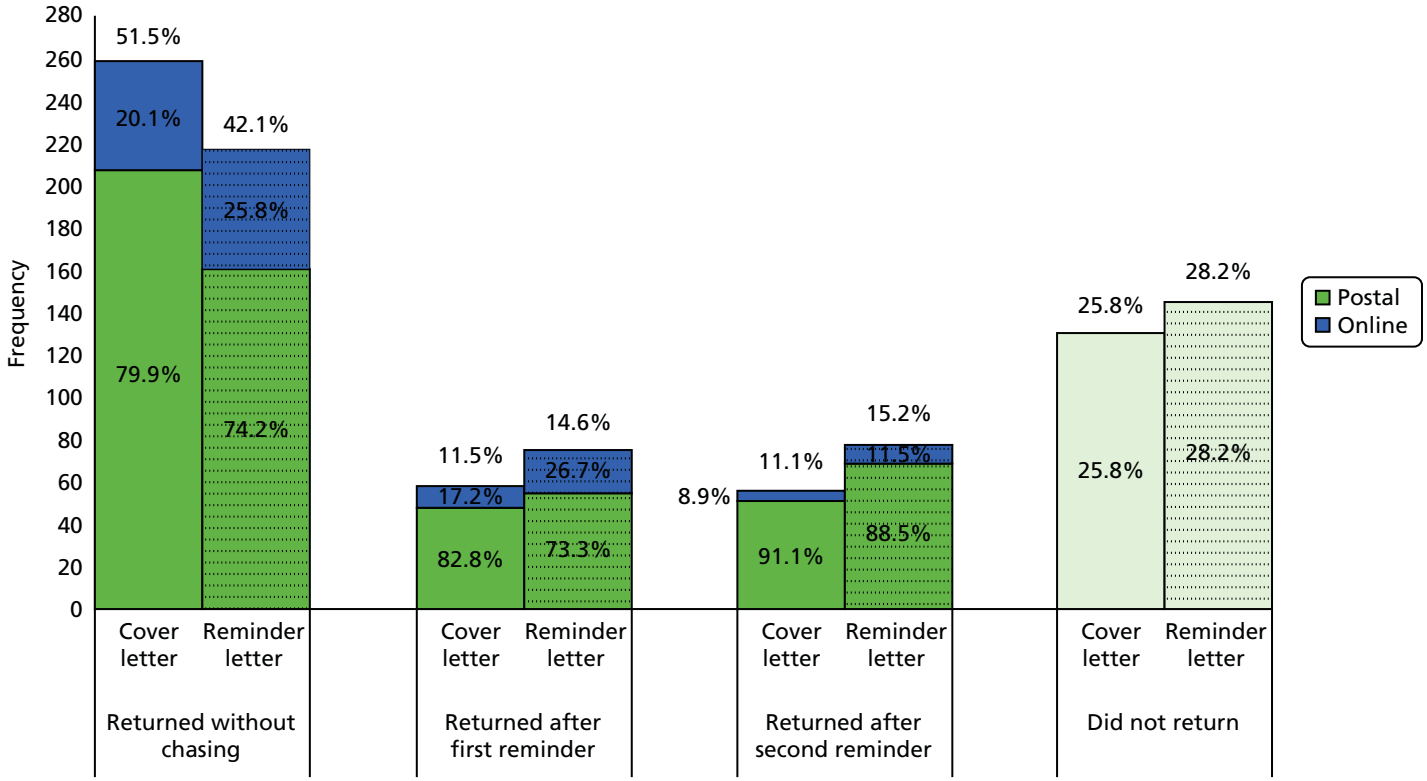

FIGURE 15 Percentages of questionnaires returned according to how many times a reminder letter was sent, broken down by postal vs. online completion.

TABLE 32 Return rates by letter and method of completion

Rate, *n* (%)	Letter	
	Cover (*N* = 503)	Reminder (*N* = 515)
Questionnaire returned without chasing by study team	259 (51.5)	217 (42.1)
Postal	207 (79.9)	161 (74.2)
Online	52 (20.1)	56 (25.8)
Questionnaire returned after first reminder	58 (11.5)	75 (14.6)
Postal	48 (82.8)	55 (73.3)
Online	10 (17.2)	20 (26.7)
Questionnaire returned after second reminder	56 (11.1)	78 (15.2)
Postal	51 (91.1)	69 (88.5)
Online	5 (8.9)	9 (11.5)
Did not return questionnaire	130 (25.8)	145 (28.2)

cover letter than those receiving a promise in the reminder letter (11.5% vs. 14.6%, respectively, for the first reminder, and 8.9% vs. 11.5%, respectively, for the second reminder).

For the primary outcome, the percentage of questionnaires returned overall for those receiving the incentive cover letter was slightly higher than those receiving the incentive reminder letter (74.2% vs. 71.8%, respectively), but this was not statistically significant at the 5% level (adjusted RR 1.03, 95% CI 0.96 to 1.11) suggesting no evidence of an effect resulting from when the incentive is offered (*Table 33*). However, women who received a cover letter promising an incentive were more likely to return their questionnaire without a reminder letter being required than those who received a standard cover letter (adjusted RR 1.22, 95% CI 1.07 to 1.39). The mean difference in the total cost of the vouchers was £4.56 (95% CI £4.02 to £5.11), with the cost being higher in the group receiving the standard cover letter.

The pre-specified subgroup analysis is presented as a forest plot in *Figure 16*. There is no evidence of heterogeneity for IMD subgroups for the primary outcome of overall response rate ($p = 0.43$).

TABLE 33 Outcomes

Outcome	Letter		Adjusted effect measure (95% CI)
	Cover (*N* = 503)	Reminder (*N* = 515)	
Primary outcome			
Questionnaire returned, *n* (%)	373 (74.2)	370 (71.8)	RR[a] 1.03 (0.96 to 1.11)
Missing	0	0	
Secondary outcomes			
Questionnaire returned without chasing by study team, *n* (%)	259 (51.5)	217 (42.1)	RR[a] 1.22 (1.07 to 1.39)
Missing	0	0	
Total cost of vouchers (£)	3790	1530	
Cost of vouchers,[b] mean (SD)	7.5 (0.2)	3.0 (0.2)	MD 4.56 (4.02 to 5.11)
Missing	0	0	

MD, mean difference.
a Adjusted for centre.
b Per participant.

	Cover letter *Number of events/total number (%)*	Reminder letter *Number of events/total number (%)*	Adjusted[a] RR (95% CI)	Interaction *p*-value
IMD: quintile				
First (least deprived)	52/64 (81.3)	55/72 (76.4)	1.08 (0.91 to 1.28)	0.43
Second	63/72 (87.5)	49/63 (77.8)	1.12 (0.96 to 1.31)	
Third	61/83 (73.5)	72/91 (79.1)	0.91 (0.77 to 1.08)	
Fourth	85/112 (75.9)	89/129 (69.0)	1.11 (0.95 to 1.29)	
Fifth (most deprived)	62/95 (65.3)	54/88 (61.4)	1.06 (0.85 to 1.32)	

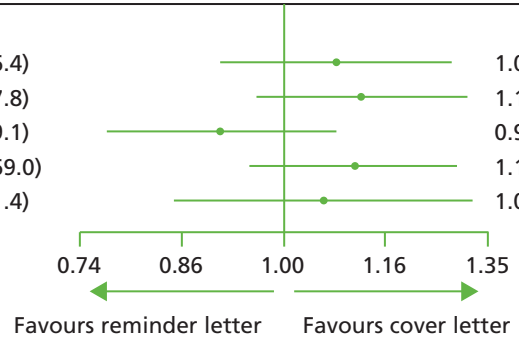

FIGURE 16 Subgroup analysis for questionnaires returned.

Discussion

In this SWAT, there is no evidence to suggest that the offer of a monetary incentive at first mail-out, compared with only when a reminder letter is sent, makes a substantial difference to the overall return rate of a 1-year follow-up postal questionnaire. Although slightly more questionnaires were returned in the group receiving the offer at first mail-out (an absolute difference of 3.4%), the corresponding RR of 1.03 (95% CI 0.96 to 1.11) was not statistically significant at the 5% level.

The return rate for women included in the SWAT compared with that before the SWAT was introduced showed a marked improvement (absolute difference 17%). Although this is not a randomised comparison, it is consistent with that found by Kenyon *et al.*[68] in a randomised study investigating the inclusion of a high-street voucher versus no voucher sent with a reminder letter to parents of 7-year-old children, which showed an increase in the return rate of 11.7% (95% CI 4.7% to 18.6%). This study is included in a systematic review that showed that the addition of monetary incentives was more effective than no incentive at increasing response rates to postal questionnaires (RR 1.18, 95% CI 1.09 to 1.28).[66]

This SWAT used a £10 high-street gift voucher as a monetary incentive. The mean cost of vouchers per participant was greater in the group receiving the offer at first mail-out (£7.50 vs. £3.00). Coupled with the lack of evidence of a difference in the overall return rate, this would indicate that sending the offer of an incentive with a reminder letter only is a cost-effective approach to improving return rates. However, there is evidence to suggest that the return rate without requiring reminders is higher in the group for whom the incentive is offered in the first mail-out (absolute difference 9.4%). The cost of administering the additional reminder letters was not calculated, but is a serious consideration that would need to be offset against the expected cost of the vouchers and could depend on the resources available as well as the sample size of the study.

There are ethical issues to consider with the approach of only sending an offer of an incentive to those participants who do not return their questionnaire promptly. Consideration should be given to the chance that participants in a study may communicate with each other, and share their experiences regarding whether or not they received an incentive.

This is the first known SWAT to investigate the use of incentives for improving questionnaire return rates in a population of first-time mothers with infants around 1 year old. This study suggests that offering incentives when a reminder is required could be cost-effective depending on the sample size of the study and hence the resources required to administer the reminder letters.

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Data sharing statement

Data can be obtained from the corresponding author.

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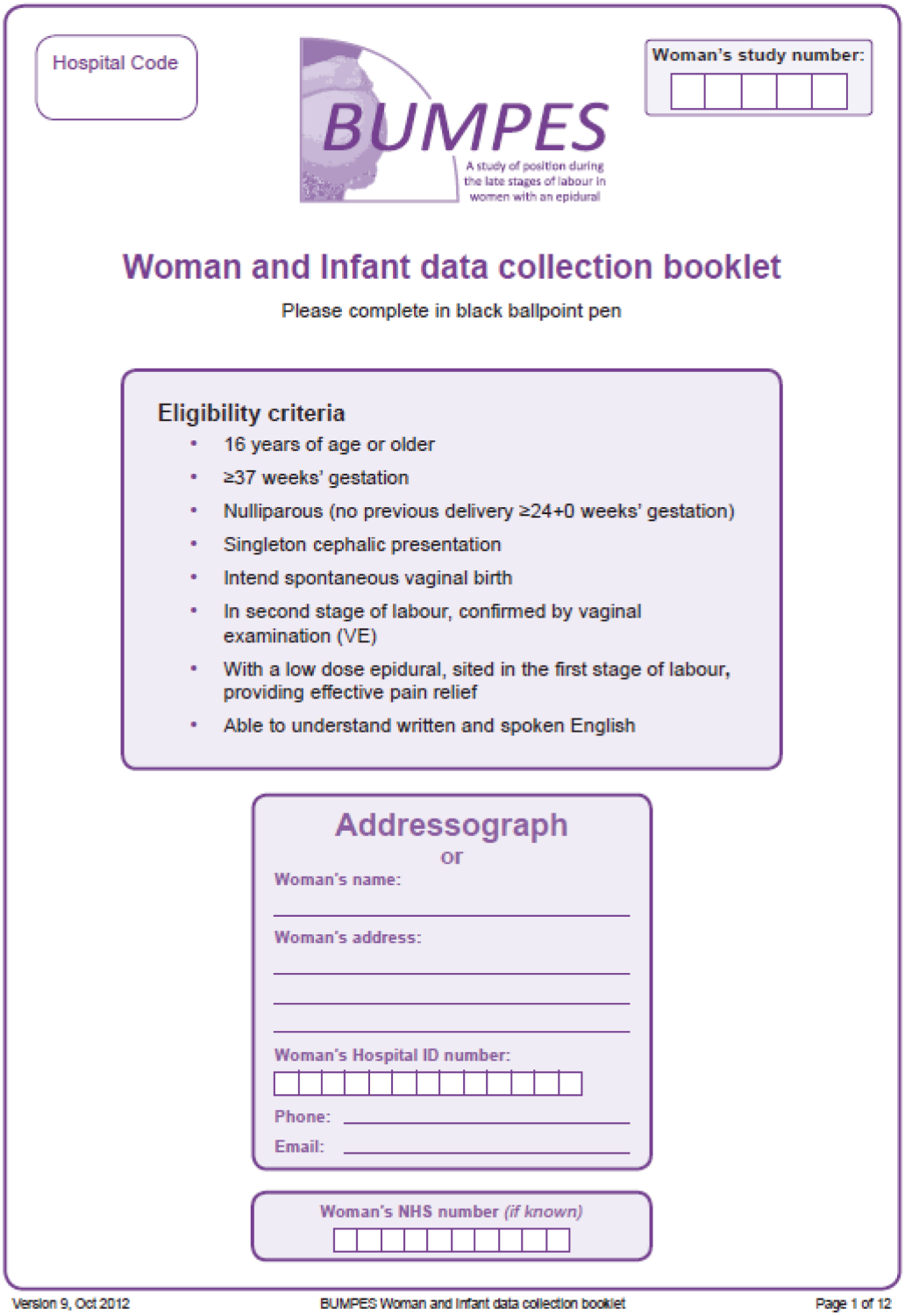
Appendix 1 BUMPES: woman and infant data collection booklet (version 9.0)



Hospital Code

BUMPES

A study of position during the late stages of labour in women with an epidural

Woman's study number:

Woman and Infant data collection booklet

Please complete in black ballpoint pen

Eligibility criteria

- 16 years of age or older
- ≥37 weeks' gestation
- Nulliparous (no previous delivery ≥24+0 weeks' gestation)
- Singleton cephalic presentation
- Intend spontaneous vaginal birth
- In second stage of labour, confirmed by vaginal examination (VE)
- With a low dose epidural, sited in the first stage of labour, providing effective pain relief
- Able to understand written and spoken English

Addressograph

or

Woman's name:

Woman's address:

Woman's Hospital ID number:

Phone:

Email:

Woman's NHS number *(if known)*

Version 9, Oct 2012 BUMPES Woman and Infant data collection booklet Page 1 of 12

Part 1

Data to be collected at time of occurrence.

Section 1: Eligibility checklist

Please complete this section before logging on to the BUMPES website to obtain the study number.

1.1 **What is the woman's date of birth?** D D / M M / Y Y

1.2 **What is the expected date of delivery (EDD)?** D D / M M / Y Y

1.3 **Hospital number:**

1.4 **Is the woman nulliparous (no previous delivery greater than or equal to 24+0 weeks' gestation)?** Yes ☐ No ☐

1.5 **Is this a singleton cephalic presentation?** Yes ☐ No ☐

1.6 **Is spontaneous vaginal birth intended?** Yes ☐ No ☐

1.7 **Is the woman in the second stage of labour, confirmed by VE?** Yes ☐ No ☐

1.8 **Is a low dose epidural, sited in the first stage of labour, providing effective pain relief?** Yes ☐ No ☐

1.9 **Is the woman able to understand written and spoken English?** Yes ☐ No ☐

If all the criteria are fulfilled, the woman in your care is eligible to participate in the BUMPES study.

Please ensure that the consent form for participation in the study has been signed prior to randomisation. The original consent form should be sent back to the coordinating centre. A copy of the consent form should be given to the woman, a copy should be filed in the study site file and a copy should be filed in the woman's notes.

1.10 **Has the woman given written consent for participation in BUMPES?** Yes ☐ No ☐

Name of person completing this section of the form:

Name: *(Print)* _____ **Signature:** _____

Section 2: Randomisation

After completion of section 1, log on to the BUMPES randomisation website via the internet: https://rct.npeu.ox.ac.uk/bumpes and follow the instructions on the screen.

The randomisation system will provide you with a unique study number and group allocation for the woman in your care. Please enter these below.

2.1 **Study number:** ☐☐☐☐☐

2.2 **Group allocation:** *(Please tick only one)* Upright ☐ OR Lying down ☐

2.3 **Date and time of randomisation:** D D / M M / Y Y h h : m m

Please go to section 4.1 and record the woman's position prior to study entry.

Then support and encourage the woman to assume the allocated position. Once the woman's position is established, record the start time in the row marked '0'.

Section 3: Pain and Pain Relief at Study Entry

3.1 **How painful was the woman's last contraction at its peak?**

Using the "Visual Analogue Scale" slide rule in your recruitment pack, ask the woman in your care to rate how painful her last contraction was at its peak. Explain to her that "0" represents "No pain at all" and "100" represents "The worst pain imaginable".

VAS recording: (0-100) ☐☐☐

3.2 **Can the woman perform a "Straight leg raise" with one leg?** Yes ☐ No ☐

3.3 **Was the epidural pain relief maintained with PCEA/infusion up until study entry?** Yes ☐ No ☐

If Yes, please record the pump reading at study entry: ☐☐☐ ml

Please note: you will need to make a note of the pump reading post birth (in section 5) prior to turning the pump off or disposing of the infusion bag.

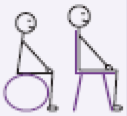
Section 4: Maternal position recordings after study entry

This section records the actual position that a woman adopts after study entry. It provides the study with information which cannot be retrieved at a later time. Therefore, it is important that it is filled in as accurately as possible during labour.

4.1 Please record maternal position every quarter of an hour after entry to the study.

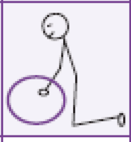
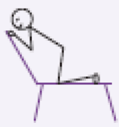
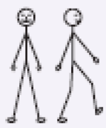
At the end of each time interval, please note down the position that the woman in your care has adopted for the majority of the previous 15 minutes, by ticking the relevant box in the position chart. The images above the matrix act as a guide to chart completion.

Group allocation *(as recorded on page 3)*: Upright ☐ OR Lying down ☐

		Predominant maternal position in last 15 minutes						
		Lying (elevation of head of bed up to a maximum of 30°)				Sitting		
				Tilted with a wedge				
Study time (min)	Actual time (24h)	Left lateral	Right lateral	Wedge on left side	Wedge on right side	Out of bed	In bed	
								
Position prior to study entry		☐	☐	☐	☐	☐	☐	
0	:							
15	:	☐	☐	☐	☐	☐	☐	
30	:	☐	☐	☐	☐	☐	☐	
45	:	☐	☐	☐	☐	☐	☐	
60	:	☐	☐	☐	☐	☐	☐	
75	:	☐	☐	☐	☐	☐	☐	
90	:	☐	☐	☐	☐	☐	☐	
105	:	☐	☐	☐	☐	☐	☐	
120	:	☐	☐	☐	☐	☐	☐	
135	:	☐	☐	☐	☐	☐	☐	
150	:	☐	☐	☐	☐	☐	☐	
165	:	☐	☐	☐	☐	☐	☐	
180	:	☐	☐	☐	☐	☐	☐	
195	:	☐	☐	☐	☐	☐	☐	
210	:	☐	☐	☐	☐	☐	☐	
225	:	☐	☐	☐	☐	☐	☐	
240	:	☐	☐	☐	☐	☐	☐	
255	:	☐	☐	☐	☐	☐	☐	
270	:	☐	☐	☐	☐	☐	☐	
285	:	☐	☐	☐	☐	☐	☐	
300	:	☐	☐	☐	☐	☐	☐	

4.1 Maternal position at time of birth Upright ☐ Lying down ☐ Lithotomy ☐ Other ☐

If Other, please describe _____

	Predominant maternal position in last 15 minutes				If the woman changes from her allocated position to a non-allocated position, please record the reason
	Supported kneeling		Standing/ walking	Other including lithotomy	
	Out of bed	In bed		*Please briefly describe*	
					
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Version 9, Oct 2012 BUMPES Woman and Infant data collection booklet Page 5 of 12

Section 5: Pain and Pain Relief after Study Entry

5.1 **Was PCEA/infusion used after study entry?** Yes ☐ No ☐

If Yes, please record the concentration of the epidural solution given and record the PCEA pump reading at time of delivery:

Bupivacaine 0.☐☐☐ %

Fentanyl ☐☐ µg/ml

Pump reading ☐☐☐ ml

5.2 **How painful was the birth of the woman's baby?**

Using the "Visual Analogue Scale" slide rule in your BUMPES recruitment pack, ask the woman in your care to rate how painful the birth of her baby was. Explain to her that "0" represents "No pain at all" and "100" represents "The worst pain imaginable".

VAS recording: (0-100) ☐☐☐

Section 6: Maternal labour and birth questionnaire

Please ask the woman to complete the questionnaire entitled 'Your labour and birth experience' as soon as practicable while she is in the delivery suite.

Please confirm that the questionnaire was given to the woman by ticking this box: ☐

Name and signature of person who completed Part 1:

Name: *(Print)* _____ **Signature:** _____

What to do now:-

Please either complete Part 2 of this form or put it in the midwives recruitment envelope and place in the designated area for the research midwife to complete.

Part 2

Section 1: Information about the woman at study entry

Maternal characteristics

1.1 **Maternal ethnic group:**

White – British/Irish	☐	Asian – Indian	☐
White – Other	☐	Asian – Pakistani	☐
Mixed – White and Black Caribbean	☐	Asian – Bangladeshi	☐
Mixed – White and Black African	☐	Asian – Other	☐
Mixed – White and Asian	☐	Black – Caribbean	☐
Mixed – Other	☐	Black – African	☐
Chinese	☐	Black – Other	☐
Any other ethnic category	☐	Not known	☐

1.2 **Booking weight:** ☐☐☐.☐ kg OR ☐☐ stones ☐☐ lbs OR tick if not known ☐

1.3 **Height:** ☐☐☐ cm OR ☐ feet ☐☐ inches OR tick if not known ☐

1.4 **Has the woman undergone FGM?** Yes ☐ No ☐

Information on this pregnancy and labour

1.5 **Was the onset of labour:** Spontaneous ☐ OR Induced ☐

1.6 **What was the duration of first stage?** ☐☐ hours ☐☐ mins

1.7 **What was the date and time of VE diagnosing second stage?** *(Full cervical dilatation = 10cm)* D D / M M / Y Y h h : m m (24hr)

1.8 **Was there any maternal diagnosis of pre-eclampsia?** Yes ☐ No ☐

1.9 **Was continuous electronic fetal monitoring used prior to study entry?** Yes ☐ No ☐

1.10 **Was there a diagnosis of delay made prior to study entry?** Yes ☐ No ☐

If Yes, which of the following interventions were used?

None ☐

ARM ☐

Syntocinon ☐

Pain relief up until study entry

1.11 **Were any systemic opioids given in labour prior to epidural pain relief?** Yes ☐ No ☐

If Yes, which drug was given? *(Please tick all that apply)*: Pethidine ☐

Diamorphine ☐ Remifentanil ☐

Morphine ☐ Other ☐

If Other, please specify _____

1.12 **What epidural technique was used?** *(Please tick only one)*

Epidural ☐ OR Combined Spinal Epidural ☐

1.13 **Date and time first dose epidural/spinal pain relief given:** D D / M M / Y Y h h : m m (24hr)

Section 2: Events after study entry

Please refer to time of randomisation to ensure that events recorded in this section did occur after study entry.

2.1 **Were any epidural drugs administered by "top-up" after study entry?** Yes ☐ No ☐

Please do not include top-ups given for instrumental delivery or caesarean section.

If yes, please provide details below:

Time	Local Anaesthetic		Opioid		Volume (ml)
	Drug	% Conc.	Drug	µg/ml	
:					
:					
:					
:					
:					

2.2 **Was augmentation (syntocinon) commenced after study entry?** Yes ☐ No ☐

2.3 **Was fetal blood sampling performed after study entry?** Yes ☐ No ☐

2.4 **Was a fetal scalp clip applied for the first time after study entry?** Yes ☐ No ☐

2.5 **Did the woman complain of dizziness after study entry?** Yes ☐ No ☐

2.6 **Did maternal hypotension occur after study entry?**
Systolic blood pressure <100 mm Hg at any time Yes ☐ No ☐

2.7 **Were any drugs to increase the woman's blood pressure given after study entry?** Yes ☐ No ☐

These are known as vasopressors and include ephedrine, phenylephrine and metaraminol (aramine). They are usually only administered by anaesthetists for severe maternal hypotension.

Section 3: Birth details

3.1 **Date and time pushing commenced:** D D / M M / Y Y h h : m m (24hr)

3.2 **Date and time of birth:** D D / M M / Y Y h h : m m (24hr)

3.3 **Mode of birth:** *(Please tick only one)*

- Spontaneous vaginal birth ☐
- Instrumental vaginal birth
  - Forceps ☐
  - Ventouse ☐
  - If instrumental birth, was this in theatre? Yes ☐ No ☐
- Caesarean section ☐
  - If caesarean section, give category *(as per RCOG guidelines, see back page of booklet)* 1 ☐ 2 ☐ 3 ☐

3.4 ***Primary* indication for assisted (non-spontaneous) birth:** *(Please tick only one)*

- Fetal distress ☐
- Failure to progress ☐
- Breech presentation ☐
- Other ☐
  - If Other, please specify _____

3.5 **Was anaesthesia required for instrumental birth or caesarean section?**
This refers to anaesthesia additional to the routine epidural pain relief given in labour Yes ☐ No ☐

If Yes, please record the additional anaesthetic technique used: *(Please tick all that apply)*

- Local infiltration ☐
- Pudendal (cervical) block ☐
- High dose epidural top-up ☐
- Spinal anaesthesia ☐
- General anaesthesia ☐

3.6 **Was active management of third stage required?** Yes ☐ No ☐

3.7 **Was an episiotomy performed?** Yes ☐ No ☐

3.8 **Was any perineal tear evident after birth, including perineal tear with episiotomy?** Yes ☐ No ☐

If Yes, please record using standard classification system recommended by the 2007 NICE Intrapartum guidelines, see back page of booklet.

Severity: Degree: 1 ☐ 2 ☐ 3a ☐ 3b ☐ 3c ☐ 4 ☐

3.9 **Was the perineum sutured?** Yes ☐ No ☐

3.10 **Was any anterior tear evident after birth?** Yes ☐ No ☐

If Yes, was any anterior tear sutured? Yes ☐ No ☐

3.11 **Was manual removal of the placenta performed?** Yes ☐ No ☐

3.12 **Was there a post-partum haemorrhage requiring blood transfusion?**
(Whole blood or packed cells) Yes ☐ No ☐

If Yes, how many units were transfused? ☐☐

3.13 **Date and time of maternal discharge from delivery/birth centre care:** D D / M M / Y Y h h : m m (24hr)

3.14 **Maternal destination after leaving delivery/birth centre:**

- Home (early discharge) ☐
- Ward ☐
- High Dependency Unit (HDU) ☐
- Intensive Care Unit (ICU) ☐
- Other ☐

If Other, please specify _____

Infant outcomes

3.15 **Infant's hospital ID number:** ☐☐☐☐☐☐☐☐☐☐☐☐

3.16 **Infant's NHS number:** *(if known)* ☐☐☐☐☐☐☐☐☐☐

3.17 **Apgar score at 5 minutes:** ☐☐

3.18 **Birth weight:** ☐☐☐☐ g

3.19 **Umbilical cord pH and base deficit at birth:** *(if done)*
If paired samples taken record arterial sample.

pH ☐.☐☐ base deficit ☐☐.☐ mmol/l OR tick if not done ☐

3.20 **Was meconium stained liquor noted at birth?** Yes ☐ No ☐

3.21 **Was neonatal resuscitation required at birth?** Yes ☐ No ☐

If Yes, please tick all that apply:

- Facial oxygen ☐
- Suction ☐
- Bag and mask ventilation ☐
- Intubation ☐
- Complex resuscitation ☐

3.22 **Was skin-to-skin contact achieved in the first hour?** Yes ☐ No ☐

3.23 **Did the woman initiate breastfeeding within the first hour of birth?** Yes ☐ No ☐

3.24 **Infant's destination *immediately* after leaving the delivery/birth centre:** *(Please tick only one)*

- Home (early discharge) ☐
- Ward ☐
- Transitional care ☐
- Neonatal unit ☐

Section 4: Maternal and Neonatal Discharge and Higher Level of Care Information

4.1 Date and time of maternal discharge from hospital: D D / M M / Y Y h h : m m (24hr)

4.2 Date and time of infant discharge from hospital: D D / M M / Y Y h h : m m (24hr)

4.3 Was the woman admitted to a higher level of care (high dependency / intensive care) during her hospital stay? Yes ☐ No ☐

4.4 Was the infant admitted to a higher level of care (transitional care / neonatal unit) during their hospital stay? Yes ☐ No ☐

Name and signature of person who completed Part 2:

Name: *(Print)* _____ **Signature:** _____

What to do now:-

Please put the completed booklet into the midwives recruitment envelope and place in the designated area.

Thank you for completing this form

[redacted]

Definitions

EDD: Use the best estimate (dates or ultrasound) based on a 40 week gestation

RCOG Caesarean section classifications

1. Immediate threat to the life of the woman or fetus
2. Maternal or fetal compromise which was not immediately life-threatening
3. No maternal or fetal compromise but needs early delivery
4. Delivery timed to suit woman or staff *(not applicable for BUMPES)*

2007 NICE Intrapartum guidelines on perineal trauma

1. First degree – injury to skin only
2. Second degree – injury to the perineal muscles but not the anal sphincter
3. Third degree – injury to the perineum involving the anal sphincter complex:
    a. Less than 50% of external anal sphincter thickness torn
    b. More than 50% of external anal sphincter thickness torn
    c. Internal anal sphincter torn
4. Fourth degree – injury to the perineum involving the anal sphincter complex (external and internal anal sphincter) and anal epithelium

Appendix 2 BUMPES: higher level of care data collection form – woman (version 2.0)

Woman's date of birth: D D / M M / Y Y

Woman's study number:

BUMPES

A study of position during the late stages of labour in women with an epidural

Higher Level of Care data collection form WOMAN post study entry

Please complete this form for a woman who received a higher level of care and/or who had surgery following her delivery.

Please liaise with your local Principal Investigator (PI) to complete this form.

Please complete in black ballpoint pen.

[redacted]

Version 2, Feb 2012 Woman Higher Level of Care data collection form Page 1 of 4

ICNARC HDU Definitions of Care

Level 0: patients whose needs can be met through general ward care

Level 1: patients who are at risk of their condition deteriorating, or those who have recently been relocated from higher levels of care whose needs can be met on the general ward with additional advice and support from the critical care team.

Level 2: patients requiring more detailed monitoring and support, including support for a single failing organ system, or postoperative care and those stepping down from higher levels of care.

Level 3: patients needing monitoring and support for two or more organs systems, one of which may be basic or advanced respiratory support.

Section 1: Level of care details

1.1 **Please give details of this woman's higher level of care:**

	Level of care required *(please tick as appropriate - n.b. full day = 24 hrs)*							
	Level 0		Level 1		Level 2		Level 3	
Day 1	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐
Day 2	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐
Day 3	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐
Day 4	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐
Day 5	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐
Day 6	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐
Day 7	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐
Day 8	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐	Full day ☐	Partial day ☐

1.2 **Please state the primary reason for admission into higher care:**

_____

_____

_____

Section 2: Surgery

2.1 **Did the woman undergo any additional surgery at the time of, or following delivery (excluding initial perineum or anterior suturing) prior to her discharge or transfer from this hospital?** Yes ☐ No ☐

If Yes, please give details below:

Surgery 1: Date of surgery: ..... D D / M M / Y Y

Type of surgery: _____

Surgery 2: Date of surgery: ..... D D / M M / Y Y

Type of surgery: _____

Surgery 3: Date of surgery: ..... D D / M M / Y Y

Type of surgery: _____

Surgery 4: Date of surgery: ..... D D / M M / Y Y

Type of surgery: _____

Please use an additional form if necessary.

Section 3: Investigations

3.1 **Did the woman have any X-rays, CT scans or MRI scans following delivery and prior to her discharge or transfer from this hospital?** Yes ☐ No ☐

If Yes, please indicate which investigations were performed:

X-rays ☐ If ticked, how many? ☐☐

CT-scans ☐ If ticked, how many? ☐☐

MRI ☐ If ticked, how many? ☐☐

Section 4: Outcome *(Please complete only one of the outcome sections below)*

4.1 Discharge home

Was the woman discharged home from this hospital? Yes ☐

If Yes, please give date of discharge home: D D / M M / Y Y

4.2 Transfer to another hospital

Was the woman transferred to another hospital? Yes ☐

If Yes, name of the transfer hospital: _____

Please specify how the woman was transferred:

Ambulance ☐ Helicopter ☐ Own transport ☐ Other ☐

If Other, please specify: _____

Date of transfer: D D / M M / Y Y

4.3 Death

Did the woman die during her stay in this hospital? Yes ☐

If Yes, has the cause of death been identified? Yes ☐ No ☐

Principal cause of death:

_____

Date of death: D D / M M / Y Y

Form completed by: *(Please print)* _____ **Date completed:** D D / M M / Y Y

Name of hospital: _____

Principal Investigator's signature: _____

Please agree the content of this form with your local Principal Investigator (PI) then return this completed form to the BUMPES Co-ordinating Centre using the FREEPOST envelope.

Thank you for completing this form

Appendix 3 BUMPES: higher level of care data collection form – infant (version 2.0)

Woman's date of birth: D D / M M / Y Y

Woman's study number:

BUMPES

A study of position during the late stages of labour in women with an epidural

Higher Level of Care data collection form INFANT

Please complete this form if an infant delivered to a woman randomised in the BUMPES study was admitted to a higher level of care.

Please liaise with the local Principal Investigator and neonatal staff to complete this form.

Please complete in black ballpoint pen.

[redacted]

Version 2, Feb 2012 Infant Higher Level of Care data collection form Page 1 of 4

Section 1: Higher level of care details

1.1 Please give details of the infant's higher level of care (not including transitional care): *(please see definitions)*

Level of care required *(Please tick all that apply)*	Time in each setting	
	Number of Hours *(if <24 hrs)*	Number of Days *(1 day = 24 hrs)*
Special Care ☐	☐☐	☐☐☐
High Dependency Intensive Care ☐	☐☐	☐☐☐
Intensive Care ☐	☐☐	☐☐☐

1.2 Please state the primary reason for admission into higher care:

_____

_____

_____

_____

_____

_____

_____

Section 2: Surgery

2.1 Did the infant undergo any surgery after birth and prior to discharge or transfer from this hospital? Yes ☐ No ☐

If Yes, please give details below:

Surgery 1: Date of surgery: ..... D D / M M / Y Y

Type of surgery: _____

Surgery 2: Date of surgery: ..... D D / M M / Y Y

Type of surgery: _____

Surgery 3: Date of surgery: ..... D D / M M / Y Y

Type of surgery: _____

Surgery 4: Date of surgery: ..... D D / M M / Y Y

Type of surgery: _____

Section 3: Investigations

3.1 **Did the infant have any X-rays, CT scans or MRI scans after birth and prior to discharge or transfer from this hospital?** Yes ☐ No ☐

If Yes, please indicate which investigations were performed:

X-rays ☐ If ticked, how many? ☐☐

CT-scans ☐ If ticked, how many? ☐☐

MRI ☐ If ticked, how many? ☐☐

Section 4: Outcome *(Please complete only one of the outcome sections below)*

4.1 **Discharge home**

Was the infant discharged home from this hospital? Yes ☐ No ☐

If Yes, please give date of discharge home: D D / M M / Y Y

4.2 **Transfer to another hospital**

Was the infant discharged to another hospital? Yes ☐ No ☐

If Yes, name of the transfer hospital: _____

Please specify how the infant was transferred:

Ambulance ☐ Helicopter ☐ Other ☐

If Other, please specify: _____

Date of transfer: D D / M M / Y Y

4.3 **Death**

Did the infant die during their stay in this hospital? Yes ☐ No ☐

If Yes, has the cause of death been identified? Yes ☐ No ☐

Please provide brief details of what was written on the death certificate:

_____

Date of death: D D / M M / Y Y

Form completed by: *(Please print)* _____ **Date completed:** D D / M M / Y Y

Name of hospital: _____

Principal Investigator's signature: _____

British Association of Perinatal Medicine Definitions of Care

Special Care: A nurse should not be responsible for care of more than four babies receiving Special or Normal Care.

- special care is provided for all other babies who could not reasonably be expected to be looked after at home by their mother.

High Dependency Care: A nurse should not be responsible for the care of more than two babies in this category:

- receiving NCPAP for any part of the day and not fulfilling any of the criteria for intensive care
- below 1000g current weight and not fulfilling any of the criteria for intensive care
- receiving parenteral nutrition
- receiving oxygen therapy and below 1500g current weight
- requiring treatment for neonatal abstinence syndrome
- requiring specific procedures that do not fulfil any criteria for intensive care:
  - care of an intra-arterial catheter or chest drain
  - partial exchange transfusion
  - tracheostomy care until supervised by a parent
- requiring frequent stimulation for severe apnoea

Intensive Care: These babies have the most complex problems. They need 1:1 care by a nurse with a neonatal qualification. The possibility of acute deterioration is such that there should be the constant availably of a competent doctor:

- receiving any respiratory support via a tracheal tube and in the first 24 hours after its withdrawal
- receiving NCPAP for any part of the day and less than five days old
- below 1000g current weight and receiving NCPAP for any part of the day and for 24 hours after withdrawal
- less than 29 weeks gestational age and less than 48 hours old
- requiring major emergency surgery, for the pre-operative period and post-operatively for 24 hours
- requiring complex clinical procedures:
  - full exchange transfusion
  - peritoneal dialysis
  - infusion of an inotrope, pulmonary vasodilator or prostaglandin and for 24 hours afterwards
- any other very unstable baby considered by the nurse-in-charge to need 1:1 nursing: for audit, a register should be kept of the clinical details of babies recorded in this category
- a baby on the day of death

Please agree the content of this form with your local Principal Investigator (PI) then return this completed form to the BUMPES Co-ordinating Centre using the FREEPOST envelope.

Thank you for completing this form

Appendix 4 BUMPES: 'your labour and birth experience' form (version 6.0)

Hospital code:

BUMPES
A study of position during the late stages of labour in women with an epidural

Study number:
to be completed by the midwife

Your labour and birth experience

Many congratulations on the birth of your baby! We would be very grateful if you could spend a couple of minutes completing this short questionnaire to tell us what you thought about your labour and birth.

All of the questions can be answered with a 'tick (☑)'. The information we collect is confidential and no names will ever be used. Only the research team will have access to this information.

1. **After your cervix was fully dilated and before you started pushing, in which position did you spend the majority of the time?** *(Please tick only one box below, see reverse for diagrams of positions)*

   Upright ☐ Lying down ☐ Other ☐ please state: _____ Can't remember ☐

2. **Once you were pushing and before your baby was born, in which position did you spend the majority of the time?** *(Please tick only one box below, see reverse for diagrams of positions)*

   Upright ☐ Lying down ☐ Other ☐ please state: _____ Can't remember ☐

3. **Birth Experience** *(Please tick only one box per line)*

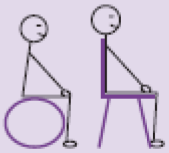
	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
I was satisfied with my overall childbirth experience	☐	☐	☐	☐	☐
I was treated with respect by all of the staff	☐	☐	☐	☐	☐
I was involved in making decisions as much as I wanted to be	☐	☐	☐	☐	☐
My expectations for labour and birth were met	☐	☐	☐	☐	☐
I felt safe at all times	☐	☐	☐	☐	☐
Good communication from the staff kept me well informed	☐	☐	☐	☐	☐
I felt in control	☐	☐	☐	☐	☐
I was able to move as much as I wanted after my cervix was fully dilated	☐	☐	☐	☐	☐
I was satisfied with my position before I started pushing	☐	☐	☐	☐	☐
I was satisfied with my position while pushing to give birth	☐	☐	☐	☐	☐
I was satisfied with my labour pain relief	☐	☐	☐	☐	☐

Thank you very much for completing the questionnaire.

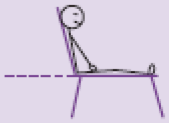
Please place it in the self addressed **FREEPOST** envelope provided and hand it back to your midwife.

ISRCTN35706297 REC Ref: 09/H0605/114 Maternal Satisfaction Form Version 6, Aug 2013

Upright

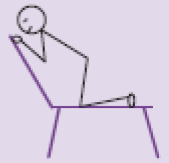


Sitting - Out of bed

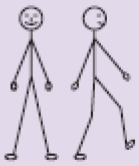


Sitting - In bed

Supported kneeling - Out of bed

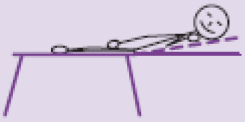


Supported kneeling - In bed

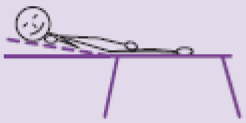


Standing/walking

Lying Down



Left side



Right side

Wedge on left side

Wedge on right side

Appendix 5 BUMPES: 1-year follow-up (version 3.0)

Pages of the 1-year follow-up questionnaire that contained copyrighted material have been removed.

Section 5: Hospital visits for you

The following section asks about your use of hospital services **following discharge home from hospital after the birth of your first child.** *Please answer all questions as fully as possible.*

5.1 **Have you been admitted to hospital in the past year?** Yes ☐ No ☐

If Yes, please provide details for each individual admission.

Hospital admission 1

a) Reason: ____

b) Did you stay overnight in hospital? Yes ☐ No ☐

If Yes, please give number of days you stayed in hospital: ____ days

c) Did you have an operation? Yes ☐ No ☐

If Yes, please tell us what operation you had:

____

Hospital admission 2

a) Reason: ____

b) Did you stay overnight in hospital? Yes ☐ No ☐

If Yes, please give number of days you stayed in hospital: ____ days

c) Did you have an operation? Yes ☐ No ☐

If Yes, please tell us what operation you had:

____

If you have had more than 2 admissions, please enter them on the back page.

5.2 **Have you attended an outpatient clinic in a hospital for your health since the birth of your first child?** Yes ☐ No ☐

If Yes, please provide details for each individual visit. *Please do not include visits to antenatal clinics.*

Outpatient Clinic attendance

Type of clinic	Attended *(please tick)*	Number of times	Reason
Perineal care clinic	Yes ☐		
Gynaecological	Yes ☐		
Surgical	Yes ☐		
Other *(please specify)* ____	Yes ☐		
Other *(please specify)* ____	Yes ☐		
Other *(please specify)* ____	Yes ☐		

If you have had more than 3 "Other" clinic visits, please enter them on the back page.

Section 6: Your first child's health

The following question asks about your first child's use of hospital services **following discharge home from hospital after birth.** *Please answer all questions as fully as possible.*

6.1 **Has your first child been admitted to hospital in the past year?** Yes ☐ No ☐

If Yes, please provide details for each individual admission.
(If more than 4 visits use the back page)

Hospital admission 1

a) Reason:

b) Did your child stay overnight in hospital? Yes ☐ No ☐
If Yes, please give number of days your child stayed in hospital: ☐☐ days

c) Did your child have an operation? Yes ☐ No ☐
If Yes, please tell us what operation your child had:

Hospital admission 2

a) Reason:

b) Did your child stay overnight in hospital? Yes ☐ No ☐
If Yes, please give number of days your child stayed in hospital: ☐☐ days

c) Did your child have an operation? Yes ☐ No ☐
If Yes, please tell us what operation your child had:

Hospital admission 3

a) Reason:

b) Did your child stay overnight in hospital? Yes ☐ No ☐
If Yes, please give number of days your child stayed in hospital: ☐☐ days

c) Did your child have an operation? Yes ☐ No ☐
If Yes, please tell us what operation your child had:

If your child had more than 3 admissions, please enter them on the back page.

6.2 **Has your first child attended an outpatient clinic in the last year?** Yes ☐ No ☐

If Yes, please provide details for each individual visit.

Outpatient Clinic attendance

Type of clinic	Attended *(please tick)*	Number of times	Reason
Orthopaedic	Yes ☐		
Paediatric	Yes ☐		
Hearing	Yes ☐		
Eye	Yes ☐		
Dermatology	Yes ☐		
Other *(please specify)*	Yes ☐		
Other *(please specify)*	Yes ☐		

If your child had more than 2 "Other" outpatient visits, please enter them on the back page.

Section 7:

The following questions ask about your child's development. You might find it helpful to refer to the red book (Child Health Record) and comments made by your health visitor and doctor.

7.1 **Has your first child been diagnosed with cerebral palsy?** Yes ☐ No ☐

7.2 **Has your first child been diagnosed with any other major health problem?** Yes ☐ No ☐

If Yes, **please specify:**

8.1 **What date did you finish completing this questionnaire?** D D / M M / Y Y

8.2 **What is your date of birth:** D D / M M / Y Y

Thank you for completing this questionnaire

Please return it to us in the FREEPOST envelope provided.
No stamp is required.

Please only use this page to provide *additional* information to questions 5.1, 5.2, 6.1 and 6.2 *if necessary*.

Additional hospital admissions (5.1 or 6.1 continued)

Additional hospital admission

Additional hospital admission for: You ☐ Your child ☐

a) Reason: _____

b) Did you/your child stay overnight in hospital? Yes ☐ No ☐

If Yes, please give number of days you/your stayed in hospital: ____ days

c) Did you/your child have an operation? Yes ☐ No ☐

If Yes, please tell us what operation you/your had:

_____

Additional hospital admission

Additional hospital admission for: You ☐ Your child ☐

a) Reason: _____

b) Did you/your child stay overnight in hospital? Yes ☐ No ☐

If Yes, please give number of days you/your stayed in hospital: ____ days

c) Did you/your child have an operation? Yes ☐ No ☐

If Yes, please tell us what operation you/your had:

_____

Additional outpatient clinic attendance (5.2 or 6.2 continued)

Additional attendance

Additional outpatient clinic addition for: You ☐ Your child ☐

Type of clinic	Attended *(please tick)*	Number of times	Reason
Please specify _____	Yes ☐	____	_____

Additional attendance

Additional outpatient clinic addition for: You ☐ Your child ☐

Type of clinic	Attended *(please tick)*	Number of times	Reason
Please specify _____	Yes ☐	____	_____

[redacted]

Appendix 6 Membership of the Trial Steering Committee, Data Monitoring Committee and Clinical Investigator Group

Clinical Investigator Group

- Professor Debra Bick, Professor of Evidence Based Midwifery Practice, King's College London.
- Dr Annette Briley, Consultant Midwife, Guy's and St Thomas' NHS Foundation Trust (replaced Geraldine O'Sullivan in 2012).
- Professor Peter Brocklehurst, Professor of Women's Health at UCL.
- Oya Eddama, Health Economist, National Perinatal Epidemiology Unit, University of Oxford.
- Professor Janesh Gupta, Professor/Honorary Consultant in Obstetrics and Gynaecology, Birmingham University/Birmingham Women's Foundation NHS Trust.
- Pollyanna Hardy, Senior Trials Statistician, National Perinatal Epidemiology Unit, University of Oxford.
- Professor Edmund Juszczak, Associate Professor–Director, National Perinatal Epidemiology Unit, University of Oxford.
- Lynn Lynch, Senior Research Midwife, Cardiff University.
- Professor Christine MacArthur, Professor of Maternal and Child Epidemiology, University of Birmingham.
- Professor Rona McCandlish, Epidemiologist: Maternal Health, National Perinatal Epidemiology Unit, University of Oxford (until 2012).
- Dr Phillip Moore, Consultant Anaesthetist, University Hospital Birmingham NHS Trust.
- Professor Mary Nolan, Professor of Perinatal Education, University of Worcester.
- Dr Felicity Plaat, Lead Clinician and Consultant Anaesthetist, Queen Charlotte's and the Hammersmith Hospital/Senior Lecturer, Imperial College London.
- Dr Dean Regier, Senior Health Economist, National Perinatal Epidemiology Unit, University of Oxford (until 2012).
- Dr Julia Sanders, Consultant Midwife/Reader in Midwifery, Cardiff University.
- Professor Andrew Shennan, Professor of Obstetrics, King's College London.
- Dr Geraldine O'Sullivan, Lead Clinician in Obstetric Anaesthesia, Guy's and St Thomas' NHS Foundation Trust (deceased 2012).
- Dr Matt Wilson, Consultant in Obstetric Anaesthesia/Senior Lecturer in Anaesthesia, Sheffield Teaching Hospital/University of Sheffield.

Trial Steering Committee

Independent members:

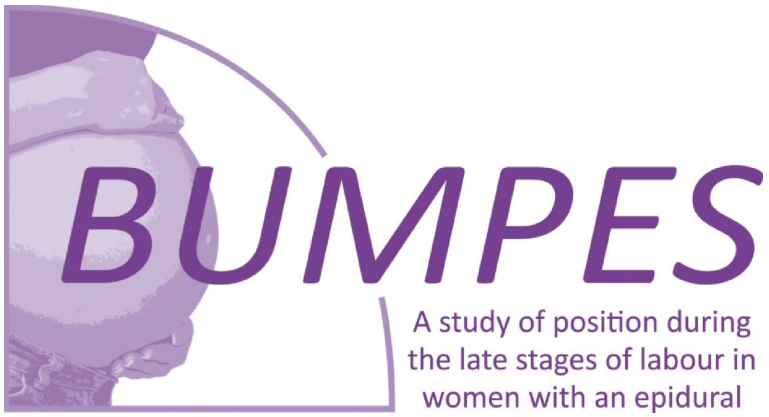
- Dr Paul Howell, Consultant Anaesthetist, St Bartholomew's Hospital
- Professor Dame Tina Lavender, Professor in Midwifery, University of Manchester
- Professor Alan Montgomery (Vice-Chairperson), Professor of Medical Statistics and Clinical Trials, Nottingham Clinical Trials Unit
- Professor Stephen Palmer, Professor of Health Economics, University of York
- Ms Justine Pepperell (Consumer Representative)
- Professor Steve Robson (Chairperson), Professor of Fetal Medicine, Medical School, University of Newcastle.

Data Monitoring Committee

Independent members:

- Professor Christine Kettle, Professor of Women's Health, Academic Unit of Obstetrics and Gynaecology, University Hospital of North Staffordshire and Staffordshire University
- Mr Stephen Walkinshaw (Vice-Chairperson), Consultant in Maternal and Fetal Medicine, Liverpool Women's NHS Foundation Trust
- Dr Steve Yentis (Chairperson), Consultant Anaesthetist, Chelsea and Westminster Hospital
- Dr Pat Yudkin, Emeritus Reader in Medical Statistics, University of Oxford.

Appendix 7 BUMPES: statistical analysis plan



The BUMPES study

HTA project number: 08/22/02

MREC number: 09/H0605/114

ISRCTN35706297

Statistical Analysis Plan

Version 1, May 2015

Contributors:

Pollyanna Hardy, National Perinatal Epidemiology Unit Clinical Trials Unit, University of Oxford

Peter Brocklehurst, Institute for Women's Health, University College London

Background: As the most effective form of pain relief in labour, epidural analgesia is chosen by up to 30% of women. Previous randomised controlled trials have shown that epidural analgesia is associated with an increased risk of instrumental delivery (IVD), prolonged labour and oxytocic augmentation. These effects have been attributed to dense epidural motor block. "Low dose epidurals" which use low-dose local anaesthetic in combination with opioids (fentanyl) are now routine practice and have been shown to result in a lower risk of IVD. However, the risk of IVD is still higher compared with women with no epidural. Although low dose epidurals preserve motor function, allowing greater mobility throughout labour and can enable women to adopt upright positions, there is controversy about whether an upright posture in second stage increases the spontaneous vaginal delivery (SVD) rate. This pragmatic randomised controlled trial will test the hypothesis that amongst women in first time labour with a low-dose epidural who enter second stage, a policy of enabling upright position increases the incidence of SVD compared to a policy of lying down.

INTRODUCTION

This document details the proposed presentation and analysis for the main paper(s) reporting results from the NIHR HTA-funded multicentre randomised controlled trial investigating position during late stages of labour in women with an epidural (BUMPES).

The results reported in these papers will follow the strategy set out here. Subsequent analyses of a more exploratory nature will not be bound by this strategy, though they are expected to follow the broad principles laid down here. The principles are not intended to curtail exploratory analysis (for example, to decide cut-points for categorisation of continuous variables), nor to prohibit accepted practices (for example, data transformation prior to analysis), but they are intended to establish the rules that will be followed, as closely as possible, when analysing and reporting the trial.

The analysis plan will be available on request when the principal papers are submitted for publication in a journal. Suggestions for subsequent analyses by journal editors or referees, will be considered carefully, and carried out as far as possible in line with the principles of this analysis plan; if reported, the source of the suggestion will be acknowledged.

Any deviations from the statistical analysis plan will be described and justified in the final report of the trial. The analysis should be carried out by an identified, appropriately qualified and experienced statistician/analyst, who should ensure the integrity of the data during their processing. Examples of such procedures include quality control and evaluation procedures. This document and the interim and final analyses have been and will be produced in line with NPEU Standard Operating Procedures ST 105 Statistical Analysis Plan; ST 104 Interim Statistical Analysis; and ST 106 Final Statistical Analysis and Reporting.

BACKGROUND INFORMATION

Objectives of the Trial

The primary objective

The main objective of the trial is to evaluate whether, in nulliparous women who choose low dose epidural analgesia, a policy of adopting an "upright position" throughout the second stage of labour is associated with an increase in the incidence of spontaneous vaginal delivery compared with a policy of adopting a "lying down" position.

Secondary objectives

Secondary objectives are:

- to evaluate whether there are differences between the two policies in important clinical outcomes for women and babies around the time of birth and 12 months postpartum;
- to evaluate cost-effectiveness of the two policies for position during second stage from an NHS perspective;
- to measure women's satisfaction with and experience of labour and delivery.

Trial Design

The BUMPES study is a pragmatic, multicentre, individually randomised controlled trial that had a target recruitment of 3,000 nulliparous women who had a low dose epidural in situ. It is a two-arm parallel group trial with one arm allocated to adopting an "upright" position during the second stage of labour and one arm allocated to adopting a "lying down" position during the second stage of labour.

Date of start of recruitment:	October 2010
End date of recruitment:	January 2014
Target number of participants:	3,000 (1,500 per arm)
Target number of centres:	30
Follow up:	12 months

Eligibility

Women who were admitted to a participating labour ward who fulfilled all of the following criteria were eligible to be randomised in the trial:

- 16 years of age or older
- ≥37 weeks' gestation
- nulliparous (no previous delivery greater than or equal to 24 + 0 weeks' gestation)
- singleton cephalic presentation
- intended spontaneous vaginal birth
- in second stage of labour
- with a low dose epidural in situ during the first stage of labour, providing effective pain relief
- able to understand printed documentation produced in English
- able to give written answers in English

Planned Interventions

Intervention group

Women were allocated to a policy of **upright maternal position which would maintain the pelvis in as vertical a plane as possible** during second stage of labour with the intention of continuing this until the birth. Women allocated to the "upright" group were encouraged by their midwife to adopt positions which were as upright a posture as possible (this would include walking, standing, sitting out of bed, supported kneeling or bolt upright in an obstetric bed) for as much of the second stage as possible.

Control group

Women were allocated to a policy of **lying down maternal position which would maintain the pelvis in as horizontal a plane as possible** during second stage of labour with the intention of continuing this until the birth. Women allocated to the "lying down" group were encouraged to adopt a lying down position which would mean lateral positions or lying down in bed for as much of second stage as possible. The bed could be tilted at up to a maximum of 30 degrees from the horizontal.

Note: a truly supine position (i.e. flat on the back) should not be used during labour because of aorto-caval compression from the gravid uterus.

Principal Comparisons of Interest

The objective of the trial is to determine whether there are any differences in mode of delivery, post study entry interventions during second stage of labour, duration of labour, genital tract trauma, infant clinical outcomes, women's satisfaction of their birth experience, cost effectiveness, and longer term woman and infant outcomes between the group allocated to "upright" position and the group allocated to "lying down" position.

Definition of Primary and Secondary Outcomes

Primary outcome

Incidence of spontaneous vaginal delivery (SVD).

Secondary outcomes

Mode of delivery

Instrumental delivery (forceps and ventouse)
- and primary indication

Caesarean section
- and primary indication

Outcomes from randomisation until delivery

Augmentation
Major interventions to maintain blood pressure (eg Vasopressors)
Hypotension (systolic BP < 100 mmHg prior to delivery)
Application of fetal scalp clip
Fetal blood sampling
Total doses of epidural local anaesthetic and opioids administered after randomisation
Duration of active second stage
Duration of second stage of labour
Additional anaesthesia used for operative delivery

Immediate post delivery outcomes

Active management of the third stage
Episiotomy
Pain during delivery
Genital tract trauma (location and severity)
Manual removal of the placenta
Primary PPH requiring blood transfusion

Postnatal period – Woman

Duration of in-patient stay after delivery
Satisfaction with experience of birth

Postnatal period - Infant

Cord-artery pH <7.05 in second stage (this is 2 standard deviations below the mean) with base deficit ≥ 12 mmol/l (this is a threshold above which the risks of neurological damage increase)
Presence of meconium stained liquor
Apgar score <4 at 5 minutes
Resuscitation at birth
Skin to skin contact within the first hour of birth
Initiation of breastfeeding within the first hour of birth
Duration of in-patient stay
Admission to neonatal unit and duration of stay

1 year after birth - Woman

Urinary incontinence
Faecal incontinence
Other bowel 'problems'
Dyspareunia
General physical and psychological health

1 year after birth - Infant

Major morbidity e.g. gross neurodevelopmental delay including cerebral palsy (if a diagnosis has been made)

Hospital admissions

Cost effectiveness – see separate document

Data Collection Schedule

Woman and Infant Data Collection Booklet (DCB) – completed by the attending midwife during labour and immediately after delivery.
For all participating women and infants

Higher Level of Care Form: Woman – completed by the attending midwife during the woman's admission and/or immediately after discharge from hospital; checked by the local Principal Investigator.
For women receiving a higher level of care following delivery

Higher Level of Care Form: Infant – completed by the attending midwife during the infant's admission and/or immediately after discharge from hospital; checked by the local Principal Investigator.
For infants receiving a higher level of care following birth

Maternal Satisfaction Form – completed by the woman as soon as possible after delivery.
For all participating women

One Year Form – postal questionnaire completed by the woman.
For all women for whom their babies are alive and both are resident at the same address

Withdrawal Form - completed by the attending midwife at the time of withdrawal from the study.
For women who decide to withdraw from BUMPES after study entry

Sample Size and Power

The proposed sample size was a total of 3,000 women.

At the time of writing the funding application an assumed rate for the primary outcome spontaneous vaginal delivery (SVD) was made as 55% in the control group derived from data published on the COMET trial. [5] A total sample size of 3,000 women (1,500 in each arm) would have 90% power to detect a clinically significant (absolute) difference of 6% in the SVD rate between the two policies (with 95% confidence). The cost of implementing this technology is low, therefore even modest differences in outcome are likely to be cost-effective. Detecting the smallest and clinically relevant effect size possible is therefore desirable. A 6% absolute risk difference, which equates to a 10% relative risk reduction (approximately) is well within the uncertainty of the existing evidence (despite the existing trials' heterogeneity) and is considered sufficient to change clinical practice.

The proportion in the 'upright' group achieving a spontaneous vaginal delivery (SVD) was anticipated to be 0.61 (61%) under the null hypothesis and the proportion in the 'control' group was 0.55 (55%). The test statistic used is the two-sided Z test with pooled variance. The significance level of the 2-sided test was targeted at 5%. A trial of this size will also give more than 80% power to detect important differences in secondary outcomes, such as faecal incontinence at 1 year after birth which affects around 6% of women.

On collation of the pilot data for an interim analysis presented to the Data Monitoring Committee in 2011, it was recognised that the combined primary outcome event rate was lower than anticipated. As at 6th December 2011 the overall SVD rate for BUMPES (combining upright and lying down groups) was 33.8%; 95% CI 26.1% to 42.1% (based on 49/145 events). With a reduction in the control group event rate (from an anticipated 55% to between 30% and 40%), keeping the sample size fixed at 3000 would mean that a relative risk of between 1.13 and 1.19 would be detectable, equivalent to an absolute risk reduction of 5-6%. Although there is not sufficient power to detect a relative risk as small as the planned 1.11, the absolute risk detectable is similar and the Trial Steering Committee (TSC) agreed that changes to the target sample size were unnecessary.

Intervention Allocation

When a woman in a participating centre had an effective epidural established during the first stage of labour written informed consent was obtained by a health professional. The woman had to meet most of the eligibility requirements at this stage, though did not have to be in second stage to give consent.

When a woman with an effective low dose epidural was diagnosed as being in the second stage of labour and she fulfilled all of the eligibility criteria outlined above, and she gave consent, she was randomised.

Randomisation to the allocated intervention (allocation ratio 1:1) used a web-based central service. To confirm eligibility investigators needed to confirm the woman's gestation, age, that this was the woman's first birth and that the fetus was a singleton with cephalic presentation, and that an effective epidural was *in situ*, as well as signed consent.

The randomisation software used random permuted blocks of variable sizes to ensure that the staff recruiting women to the trial could not reliably predict the next allocation. Because of the large numbers of women recruited in each centre, no stratification by clinical characteristics was planned although there was stratification by centre. The procedures for randomisation were fully documented and tested prior to the start of the trial and monitored by the co-ordinating centre during the trial.

Interim analyses: The Independent Data Monitoring Committee

An independent Data Monitoring Committee (DMC) was established for the trial and met as and when the DMC requested. The terms of reference for the DMC were agreed at their first meeting. A DMC charter was completed following the recommendations of the DAMOCLES Study. [32]

During the period of recruitment to the trial, interim analyses were supplied, in strict confidence, to the DMC, together with any other analyses the DMC may request. The data were supplied to the Chair of the DMC as frequently as they requested. Meetings of the committee were arranged periodically, as considered appropriate by the Chair. In the light of interim data, and other evidence from relevant studies (including updated overviews of the relevant randomised controlled trials), the DMC would inform the TSC, if in their view there was proof beyond reasonable doubt that the data indicated that any part of the protocol under investigation was either clearly indicated or contra-indicated, either for all women or for a particular subgroup of trial participants. A decision to inform the TSC would be based on statistical, clinical and ethical considerations.

Appropriate criteria for proof beyond reasonable doubt cannot be specified precisely. A difference of at least 3 standard errors in the interim analysis of a major endpoint may be needed to justify halting, or modifying, such a study prematurely. If this criterion were to be adopted by the DMC, it would have the practical advantage that the exact number of interim analyses would be of little importance, and so no fixed schedule was proposed. Unless modification or cessation of the protocol was recommended by the DMC, the TSC, collaborators and administrative staff (except those who supply the confidential information) remained blind to the results of the interim analysis. Collaborators and all others associated with the study could write through the trial office to the DMC, to draw attention to any concern they may have had about the possibility of harm arising from the treatment under study, or any other matters that may have been relevant.

Independent Data Monitoring Committee Membership

Dr Steve Yentis (chair) - Consultant Anaesthetist, Chelsea & Westminster Hospital

Mr Stephen Walkinshaw - Consultant in Maternal and Fetal Medicine, Liverpool Women's NHS Foundation Trust

Dr Pat Yudkin - Emeritus Reader in Medical Statistics, University of Oxford

Professor Christine Kettle - Professor of Women's Health, University Hospital of North Centre

Trial reporting

The trial will be reported according to the principles of the CONSORT statement. [63]

DATA MANAGEMENT

Data Collection

Information at trial entry, including eligibility and maternal characteristics, were collected from hospital notes onto the Data Collection Booklet (DCB). The position to which the woman was allocated was recorded on the DCB in two places – once in the eligibility section and again on the worksheet used to record the woman's actual positions. As soon as possible after the woman was randomised, the attending midwife encouraged her into the allocated position and started recording in the DCB what position the woman was in "for the majority of the time in the last 15 minutes" and if this position had changed from the allocated position and the reasons for this. Information on drugs taken after study entry and during labour were also recorded, as well as other clinical information about the labour. The DCB also collected clinical outcome information on the delivery as well as neonatal outcomes and hospital stay.

If either the woman or infant received a higher level of care, the relevant Higher Level of Care form was completed by the attending midwife.

As soon as possible after delivery, the woman was asked to complete a one page questionnaire asking about her satisfaction with her birth experience, as well as asking her to provide an overview of what position she was in most of the time after study entry.

Women with surviving infants are followed up at one year with a self-administered postal questionnaire asking about their general health and wellbeing, with specific questions relating to any urinary and bowel problems. This questionnaire also requests information on the use of health services for themselves or their child. Prior to contact, mortality status and place of residence of both mother and infant is checked using NHS Summary Care Records. Only women whose infants reside at the same address are contacted.

Data Entry, Cleaning and Validation

Data will be double entered at UCL CTU using MACRO, by independent data clerks. Validation routines will check for missing data and inconsistencies on an ongoing basis. This will include screening for out-of-range data, with cross-checks for conflicting data within and between data collection forms using computerised logic checking screens. Any validation errors on the DCB and Higher Level of Care Forms will be queried and documented. Queries will be communicated as soon as possible to the appropriate centres by the Trial Co-ordinator. Errors on the Maternal Satisfaction Questionnaire and the One-Year Follow-up form are not queried with the woman.

Derivation of Variables

See Table 2.

Process outcomes

As described in 3.1 above, every 15 minutes a record was made of what position the woman was in "for the majority of the time since the last assessment" and if this position had changed from the previous assessment with the reasons for this. These data will be used to assess to what extent the women were able to adhere to the allocated intervention during (i) the passive second stage (i.e. before pushing commenced); (ii) the active second stage (i.e. pushing) and (iii) the whole of the second stage. These data will be summarised to indicate what proportion of time of each of these three stages women adhered to the intervention. Reasons for a change from a woman's allocated position are recorded as text which will be coded into categories.

Positions recorded on DCB V9 Part 1 Question 4.1 are categorised according to whether they are 'lying down', 'upright' or 'other' positions for each 15 minute interval. For each interval the categorised position is compared to the position allocated for the woman, and where the allocated position is the same as the categorised position, this is coded as 'adherent' for that 15 minute interval. All other positions are coded as 'non-adherent'. Some manual coding will be required for positions recorded as text. Positions recorded as lithotomy will be categorised as 'lying down' since the pelvis is in a horizontal position.

See section 8.5 for details on the analysis of the process outcomes.

Reliability

All outcome data, except for Maternal Satisfaction Questionnaire data and 1 Year Form data, are recorded in women's hospital notes. Site monitoring visits verified a random sample of data collected on the DCBs and Higher Level of Care Forms, by making comparisons with information recorded in hospital notes. Self-administered forms were not verified.

Data relating to the calculation of the process outcomes (i.e. maternal position at 15 minute intervals since study entry) was recorded by the midwife on the DCB only and is itself the source documentation and can therefore not be verified directly with any other source. The Maternal

Satisfaction Questionnaire aims to confirm these data with a question asking the woman to record what position they were in for the majority of the time during the passive and active stages of labour.

The coding of position data and reasons for a change from allocated position recorded as text will be validated by an independent clinician.

SERIOUS ADVERSE EVENT REPORTING

Serious Adverse Events (SAE) should be reported to the UCL BUMPES Trial Office within 48 hours. The BUMPES Trial Office would then notify the Chair of the DMC and the Research Ethics Committee. All SAEs occurring during the trial observed by the investigator or reported by the participant, whether or not attributed to the trial, would be reported on the data collection form. SAEs considered to be related to the trial by the investigator would be followed up until resolution or the event is considered stable. The investigator could have been asked to provide follow-up information. All related SAEs that could have resulted in a participant's withdrawal from the trial or are present at the end of the trial, should be followed up until a satisfactory resolution occurs.

The Chief Investigator shall submit, once a year throughout the clinical trial, or on request, a safety report to the Research Ethics Committee that includes all SAEs.

Although no serious adverse events were anticipated, it was possible that these could have occurred, for example, in the upright group, if ambulation was allowed and encouraged in the participating centre, it is possible that women could fall. This would be considered a serious adverse event.

PROTOCOL VIOLATIONS AND DEVIATIONS

Protocol Violation

A protocol violation is the failure to comply fully with the final study protocol as approved by the Research Ethics Committee and Research Department, for example, a serious non-compliance with the protocol resulting from error, fraud or misconduct and results in the exclusion of a patient from the analysis for the study. Any violations would be reported to the Sponsor and Research Ethics Committee as soon as possible.

Protocol Deviation

A protocol deviation is an allowable departure from the final study protocol as approved by the Research Ethics Committee, with minor consequences on the integrity of the data. Protocol deviations would be reported in the final publication but not excluded from the analysis.

UNBLINDING OF RANDOMISED INTERVENTIONS

Due to the nature of the intervention all recruiting and attending midwives and clinicians as well as the trial participant and staff at the UCL trial co-ordinating centre are aware of the allocation of each woman. All persons involved in the trial (except for the Trial Statistician and Trial Programmer), including the UCL trial co-ordinating centre, do not have access to the aggregate list of

randomisation codes. The data entry and storage system (OpenClinica and Macro) does not allow data to be aggregated, and all forms are filed according to study number.

PATIENT GROUPS FOR ANALYSIS

Post-randomisation Exclusions

Losses to the trial post randomisation are defined as any of the following:-

- Women for whom a valid consent was not received;
- Women for whom consent to use their data was withdrawn;
- Women not in second stage of labour when randomised and didn't reach second stage before delivery
- Women not in labour or without an epidural in place at the time of randomisation

The numbers (with percentages of the randomised population) of post-randomisation exclusions will be reported by randomised treatment group, and reasons summarised.

Women can specify whether data collected up to the point of withdrawal can be used. If the response is 'No', then they will be considered post-randomisation exclusions. If the response is 'Yes', then they will be reported as 'missing' for any data not collected after withdrawal.

Primary Analysis Strategy

For the primary analysis, participants will be analysed in the groups into which they were randomly allocated, i.e. comparing the outcomes of all women and infants for women allocated to a policy of enabling upright position with a policy of lying down, regardless of position recorded at any time during the second stage of labour (see section 10.3 for a description of sensitivity analyses according to adherence to position). Post-randomisation exclusions, as set out in section 7.1, will be excluded from all analyses.

The unit of analysis is the woman for all maternal outcomes and the infant for all infant outcomes. Women with multiple births are not eligible for the trial and hence non-independence of observations is not a cause of concern.

Descriptive analysis population

Baseline demographic and clinical characteristics will be reported for all women randomised for whom we have data available excluding post-randomisation exclusions (see section 7.1).

Comparative analysis population

- Maternal outcomes
  All women randomised for whom we have data available, excluding post-randomisation exclusions (see section 7.1).

- Short term neonatal outcomes
  All infants born to women randomised for whom we have data available, excluding post-randomisation exclusions (see section 7.1).

- 1 year maternal health outcomes
  All women randomised for whom we have data available, excluding post-randomisation exclusions (see section 7.1).

- 1 year infant health and development outcomes
  All infants born to women randomised for whom we have data available, excluding post-randomisation exclusions (see section 7.1).

Interim analysis population

Different denominators will be used for each of the interim analyses, based on the number of women randomised and data available:

- The total number of trial participants randomised at the time of data freeze, excluding post-randomisation exclusions (see section 7.1).
- The number of women and infants with 1 year follow up data available, excluding post-randomisation exclusions (see section 7.1).

Safety reporting analysis population

All women randomised, excluding women for whom a valid consent was not received and women who withdrew and did not consent to use of their data.

DESCRIPTIVE ANALYSES

Representativeness of Trial Population and Participant Throughput

The flow of participants through each stage of the trial will be summarised using a CONSORT diagram.[68] Specifically, for each intervention group we will report the numbers of women randomly assigned and women for whom the incorrect allocation was recorded in the eligibility section of the DCB (Part 1, section 2 of the DCB). The number of ineligible women randomised, if any, will be reported, with reasons for ineligibility. The number of post-randomisation exclusions and women analysed for the primary outcome will also be reported. We will also report numbers for the 1 year follow-up, women lost to follow up, women who withdrew before 1 yr, or withdrew after 1 year and did not consent to use of their data.

The total number of eligible women was not collected during the conduct of this study as it was considered heavy on resources and would not be sufficiently reliable.

Baseline Comparability of Randomised Groups

Participants in the two randomised groups will be described separately with respect to baseline demographics and clinical characteristics recorded on the Woman and Infant Data Collection Booklet. Data summarised will include:

- Centre
- Maternal age
- Gestational age at trial entry
- Index of Multiple Deprivation
- Ethnic group
- BMI at booking visit (if recorded)
- If woman had undergone Female Genital Mutilation
- Labour induction
- Diagnosis of pre-eclampsia
- First stage of labour history (duration of first stage, Electronic Fetal Monitoring, diagnosis of delay, opioids given)
- Epidural information (technique, PCEA, pain score, straight leg raise)

- Position prior to study entry
- study durations (from diagnosing second stage to randomisation, from randomisation to start of recording position).

Numbers (with percentages) for binary and categorical variables and means (and standard deviations), or medians (with lower and upper quartiles), or geometric means for continuous variables will be presented; there will be no tests of statistical significance performed nor confidence intervals calculated for differences between randomised groups on any baseline variable.

Losses to Follow-up

The number (with percentages) of losses to follow up among women selected for the 1 year assessment will be reported in the CONSORT flow chart (see section 8.1) by trial arm, and the reasons will be reported. Any deaths (and their causes) will also be reported in the CONSORT flow chart. Selected demographic and clinical characteristics, the primary outcome and selected short-term outcomes of women and their infants with 1 year data available will be compared with those for whom no follow-up data were received, using tests of statistical significance.

Description of Available Data

Missing data for primary and secondary outcomes, from baseline to the end of follow-up, will be summarised for the two trial arms.

Not all data may be routinely collected by all hospitals, e.g. BMI, cord artery pH and base deficit. The DCB allows midwives to tick “Data not recorded”. These data will be summarised by trial arm and reported separately to data missing or unknown.

Description of Adherence to Allocation

A summary of adherence to allocated position will be reported by trial arm for (i) the passive second stage (i.e. before pushing commenced); (ii) the active second stage (i.e. pushing) and (iii) the whole of the second stage. Summaries of adherence data will be presented calculated as the proportion of 15 minute intervals a woman spends in the position to which she was allocated out of the total number of 15 minute intervals recorded in the passive, active or whole of the second stage of labour. Medians and inter-quartile ranges will be presented due to the skewed distribution of the data. Data will be presented by randomised group and differences in medians will be calculated with corresponding 95% confidence intervals.

There are a variety of reasons why women change from their allocated position. Changing position to perform fetal blood sampling or to enable fetal heart rate monitoring is considered unavoidable. All reasons for change will be reviewed and classified as avoidable or unavoidable according to these criteria. The analysis will be performed for adherence treating periods where changes to a non-allocated position are considered necessary for unavoidable reasons as adherent.

Reasons for change from allocated position are recorded as free text on the DCB. These will be coded by the trial statistician and an independent assessor and presented by trial arm using counts and percentages.

The self-complete Maternal Satisfaction Questionnaire includes a question asking the woman to record what position they were in for the majority of the time during the passive and active stages of labour (see section 3.4) with responses “lying down”,“upright”, “other” and “can’t remember”.

These data will be summarised by trial arm using counts and percentages along with 95% confidence intervals for differences in percentages. A qualitative comparison will be made between these results and the results from the DCB data provided by the midwife, to ascertain the extent to which reporting bias may have occurred, if at all.

PRIMARY EFFECTIVENESS ANALYSES

Statistical Methods Used for Primary Analysis

Outcomes will be summarised by trial arm using counts and percentages for categorical variables, means and standard deviations for normally distributed continuous variables, or medians and interquartile ranges for other continuous variables. In addition geometric means will be presented for durations of stages of labour, as these are inherently highly skewed data.

An adjusted analysis will be performed on all comparative analyses adjusting for centre (the stratification factor at randomisation) as a random effect. [69] Binary outcomes will be analysed using log binomial regression models and results will be presented as adjusted risk ratios with corresponding confidence intervals (CI). If the model does not converge then log Poisson regression models with robust variance estimation will be used. [33] If the model is still unstable then centre will be removed and unadjusted risk ratios will be presented. Continuous outcomes will be analysed using linear regression models and results will be presented as adjusted differences in means with associated confidence intervals. Transformations will be applied for non-normal data if possible. Otherwise unadjusted median differences (plus CIs) for skewed continuous variable will be presented. In addition geometric mean ratios will be presented for durations of stages of labour.

Comparisons between randomised groups of all primary and secondary outcomes will be reported in full for completeness and transparency i.e. there will be no selective reporting of outcomes.

Adjustment for Multiplicity

In order to take account of the number of comparisons, 95% confidence intervals will be presented for the primary outcome and 99% confidence intervals for all other outcomes.

Missing Data

Missing data for the primary outcome are likely to be negligible. If any data items are missing on the data collection forms every effort will be made to extract these data from the hospital involved.

Statistical Software Employed

The most recent version of Stata/SE for Windows (version 13.1 at the time of writing this document) will be used for all analyses.

ADDITIONAL EFFECTIVENESS ANALYSES

Adjusted Analyses

The primary analysis will be adjusted further for the primary outcome to investigate the impact of the following known prognostic factors (in addition to centre) : age as a continuous variable, ethnicity, diagnosis of delay, onset of labour – induced vs. spontaneous.

Pre-specified Subgroup Analysis

To examine whether the effect of policy of position during the second stage of labour is consistent across specific subgroups of women, the following subgroup analyses will be undertaken:

- Gestational age (37+0 to 38+6; 39+0 to 40+6; and 41+0 or more)
- Maternal age (Up to 24, 25-29, 30-34, 35 and over)
- Augmentation with syntocinon in the first stage of labour (Yes/No)
- Index of Multiple Deprivation (population based quintiles 1 to 5)
  (derived using the postcode of the woman's last known address based on Office of National Statistic Indices of Multiple Deprivation 2010 and Ordnance Survey Code-Point Open Feb 2013).

For the trial primary outcome, results will be presented on forest plots showing the risk ratio plus 95% CI for each subgroup , [37] by intervention group, with the p value for the statistical test of interaction or test for trend where appropriate. [38]

Centre was included as a stratifying factor in the original protocol as we were expecting to recruit to target using 5 centres only. Recruitment rates were poor and we expanded the number of recruiting centres to 40. A subgroup analysis on 40 centres is therefore not considered relevant.

Pre-specified Sensitivity Analysis

A sensitivity analysis on the one year maternal outcomes will be carried out on a restricted dataset that excludes all women who are pregnant or have had another child at the time of completing the 1 year follow-up questionnaire.

In some cases women gave more than one response to a single question on the Maternal Satisfaction Questionnaire (MSQ). For the primary analysis, responses to these questions will be treated as missing. A sensitivity analysis will be undertaken if this occurs for more than 5% of the returned questionnaires for each individual question (i.e. if 2000 MSQs are received and for one question there are more than 100 responses treated as missing, then a sensitivity analysis will be performed on that question). This analysis will impute data according to the recorded worst and best case scenario.

Resource Use and Cost Data

See BUMPES Economic Evaluation Analysis Plan.

ADDITIONAL EXPLORATORY ANALYSES

The following further exploratory analyses will be performed to provide context to the results or to generate hypotheses for future testing:

To explore the relationship between adherence and outcome, an analysis will be undertaken to investigate whether there appears to be a threshold of duration of adherence (absolute or relative) which is associated with achieving a SVD. This will be performed for the passive stage only as this is the focus of the intervention. Receiver Operating Characteristic (ROC) curve analysis will be employed to determine a cut-off value of adherence using time as an absolute measurement, and proportion of time as a relative measurement. [70, 71, 72]The ROC curve will be used to provide a visual presentation of sensitivity versus specificity and a cut-off value of duration of adherence that maximises these will be examined. The accuracy of the measurement of duration of adherence as a predictor of SVD will be summarised using the area under the ROC curve. This analysis will be undertaken controlling for trial arm. Adherence will be defined according to the definition detailed in section 8.5.

Further exploratory analyses will also be undertaken after the main trial report is complete. These will include an exploration of whether there are other prognostic factors for the primary outcome (e.g. duration of passive second stage, time from first dose of epidural to randomisation). These analyses will be hypothesis-generating and pre-specified in a separate document, and the findings will be interpreted cautiously.

SAFETY DATA ANALYSIS

Serious Adverse Events

Any serious adverse event occurring whilst a woman is in the study (until discharge), will be recorded and tabulated in full.

DEVIATION FROM ANALYSIS DESCRIBED IN PROTOCOL

Centre was included as a stratifying factor in the list of subgroup analyses in the original protocol as we were expecting to recruit to target using 5 centres only. Recruitment rates were poor and we expanded the number of recruiting centres to 40. A subgroup analysis on 40 centres is therefore not considered relevant.

Table 1 Document History

Date	Version	Name	Details
27 May 2012	i	Pollyanna Hardy	First draft
29 July 2014	ii	Pollyanna Hardy	Reviewed and updated by PH and sent to PB for review.
13 August 2014	iii	Pollyanna Hardy	Incorporating PB's edits and comments for review by the CiG.
10 November 2014	iv	Pollyanna Hardy	Incorporating discussion from CiG held on 8th Sept 2014 – not finished
11 November 2014	v	Pollyanna Hardy	Incorporating Beth Howden's changes and finishing edits from CiG
14th May 2015	vi	Pollyanna Hardy	Accepting changes, incorporating PB's edits and amending methods for dose-response analysis
18th May 2015	vii	Pollyanna Hardy	After discussion with PB on 18th May 2015, changes accepted and minor amendments made. CACE analysis considered and not thought relevant for this study.
26th May 2015	viii	Pollyanna Hardy	Edited analysis of Maternal Satisfaction Questionnaire based on advice from Debbie Bick and PB.
27th May 2015	1	Pollyanna Hardy	Version 1 saved for sign off

TABLE 2: DERIVATION OF VARIABLES

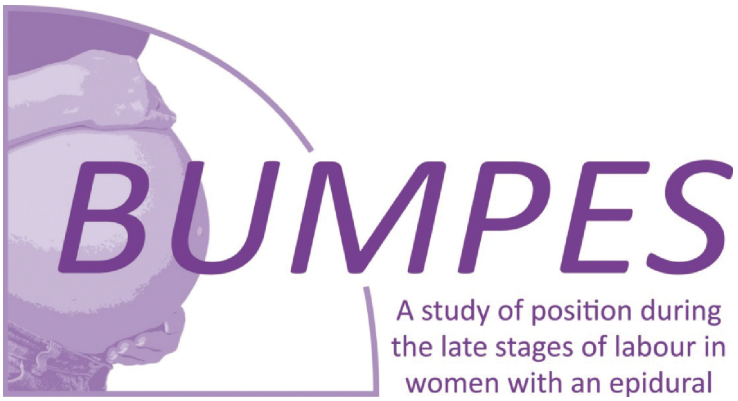
According to version 9 of the Data Collection Booklet (DCB)
Version 5 of the Maternal Satisfaction Questionnaire (MSQ)
Version 2 of the Higher Level of Care Forms (Infant and Mother)
Version 3 of the One Year Follow-up forms

Outcome	Part no./Question reference	Comments
Primary outcome		
Incidence of spontaneous vaginal delivery (SVD)	DCB P2 Q 3.3, 'Spontaneous vaginal birth'	Exclude if 'Breech presentation' ticked for P2 Q 3.4
Secondary outcomes		
Mode of delivery		
Instrumental delivery (forceps and ventouse)	DCB P2 Q 3.3, 'Forceps' or 'Ventouse'	
and primary indication	DCB P2 Q 3.4	
Caesarean section	DCB P2 Q 3.3, 'Caesarean section'	
and primary indication	DCB P2 Q 3.4	
Outcomes from randomisation until delivery		
Augmentation with syntocinin	DCB P2 Q 2.2, 'Yes'	
Major interventions to maintain blood pressure (eg Vasopressors)	DCB P2 Q 2.7, 'Yes'	
Hypotension (systolic BP < 100 mmHg prior to delivery)	DCB P2 Q 2.6, 'Yes'	
Application of fetal scalp clip	DCB P2 Q 2.4, 'Yes'	
Fetal blood sampling	DCB P2 Q 2.3, 'Yes'	
Total doses of epidural local anaesthetic and opioids administered after randomisation	DCB P1 3.3, pump reading DCB P1 5.1, pump reading DCB P2 Q 2.1	Separate outcomes for each type of anaesthetic using the general formula: Dose in milligrams = Local anaesthetic concentration in percent x volume in millilitres x 10 (e.g. 10 mls of 1% lignocaine, dose = 1 x 10 x 10 = 100mg of lignocaine). The opioid amount is calculated separately by multiplying the concentration by the volume.
Duration of active second stage *Time from when pushing commenced to when baby was born*	DCB P2 Q 3.2 – DCB P2 Q 3.1	Presented as minutes
Duration of second stage of labour	DCB P2 Q 3.2 – Date and time taken from randomisation	Presented as minutes

Time from entry into the study to when baby was born	data	
Additional anaesthesia used for operative delivery	DCB P2 Q 3.5, 'Yes'	
Immediate post delivery outcomes		
Active management of the third stage	DCB P2 Q 3.6, 'Yes'	
Episiotomy	DCB P2 Q 3.7, 'Yes'	
Pain during delivery	DCB P1 Q 5.2, Score from 0 to 100	
Genital tract trauma (location and severity)	Perineal tear: DCB P2 Q 3.8, 'Yes'(Perineal tear evident) Severity - degree 1, 2, 3a, 3b, 3c, 4 Sutured - DCB P2 Q 3.9 'Yes'(Perineum sutured) Anterior tear: DCB P2 Q 3.10, 'Yes'(Anterior tear evident) Sutured - sutured ticked 'Yes'	
Manual removal of the placenta	DCB P2 Q 3.11, 'Yes'	
Primary PPH requiring blood transfusion	DCB P2 Q 3.12, 'Yes' AND Units transf>0	
Postnatal period – Woman		
Duration of in-patient stay after delivery	DCB P2 Q 4.1 - DCB P2 Q 3.2	Days from date of delivery to date of maternal discharge from hospital
Satisfaction with experience of birth	The individual items from the MSQ Q 3.	Multiple responses to one question to be treated as missing for the primary analysis.
Postnatal period – Infant		
Cord-artery pH <7.05 in second stage with base deficit ≥ 12 mmol/l	DCB P2 Q 3.19, pH<7.05 AND (base deficit ≥ 12 OR base deficit ≤ -12)	A pH <7.4 will always produce a base deficit (rather than a base excess)
Presence of meconium stained liquor	DCB P2 Q 3.20, 'Yes'	
Apgar score <4 at 5 minutes	DCB P2 Q 3.17, Apgar<4	
Resuscitation at birth	DCB P2 Q 3.21, 'Yes'	
Skin to skin contact within the first hour of birth	DCB P2 Q 3.22, 'Yes'	
Initiation of breastfeeding within the first hour of birth	DCB P2 Q 3.23, 'Yes'	
Duration of in-patient stay	DCB P2 Q 4.2 - DCB P2 Q 3.2	Days from date of delivery to date of infant discharge from hospital
Admission to neonatal unit and duration of stay	DCB P2 Q 3.24, 'Neonatal Unit' Higher Level of Care Form – Infant, Q 1.1, Total number	

	of days in 'Special Care', 'High Dependency Intensive Care' and 'Intensive Care'	
1 year after birth – Woman		
Urinary incontinence	1 Yr Form Qs 4.1 to 4.5. (ref 11) Leaking in first 3 months - Q 4.1 Overall ICIQ-UI score is sum of Qs 4.2, 4.3 x 2 and 4.4 When does Urine leak - Q 4.5	
Faecal incontinence	Individual items from 1 Yr Form Q 4.6	
Other bowel 'problems'	1 Yr Form Q 4.7 (constipation), nvr/frst 3 mnths/lst 4 wks/other time 1 Yr Form Q 4.8 (haemorrhoids), nvr/frst 3 mnths/lst 4 wks/other time	
Dyspareunia	1 Yr Form Q 4.9 (pain on intercourse), nvr/frst 3 mnths/lst 4 wks/other time/no intercourse	
General physical and psychological health	1 Yr Form Qs 2.1 to 2.6 (EQ-5D) (ref 12) – Overall score and overall health state 1 Yr Form Qs 3.1 to 3.7 (SF-12 V2) (ref 13)	See Health Economics Analysis Plan for details on scoring.
1 year after birth – Infant		
Major morbidity e.g. gross neurodevelopmental delay including cerebral palsy (if a diagnosis has been made)	1 Yr Form Q 7.1 (CP) AND/OR Question 7.2 (Other major health problem)	
Hospital admissions	1 Yr Form Q 6.1, 'Yes' and no. of admissions	

Appendix 8 BUMPES: health economics analysis plan



The BUMPES study

HTA project number: 08/22/02

MREC number: 09/H0605/114

ISRCTN35706297

Health Economics Analysis Plan

Version 5, May 2015

(Amendments made after receiving comments from Trial Steering Committee in November 2014)

Contributors: **Oya Eddama, NPEU, University of Oxford**
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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.

Appendix 9 List of hospitals contributing to the BUMPES study

Centre number	Centre name
384	Arrowe Park Hospital
373	Bedford Hospital
203	Birmingham Women's Hospital
152	Bradford Royal Infirmary
379	Dorset County Hospital Dorchester
356	Frimley Park Hospital
353	Gloucestershire Royal Hospital
365	Great Western Hospital
381	Hillingdon Hospital
369	James Paget University Hospital
112	Jessop Wing, Sheffield
380	King's College London
382	Kingston Hospital
377	Lewisham Hospital
363	Medway Maritime Hospital
358	Neville Hall Hospital
368	New Cross Hospital
370	North Manchester General Hospital
354	Pinderfields Hospital
378	Prince Charles Hospital
351	Princess of Wales Hospital
367	Princess Royal Hospital
279	Queen Alexandra Hospital, Portsmouth
140	Queen Charlotte's and Chelsea Hospital
364	Queen Elizabeth Hospital
361	Queen Mary's Hospital
374	Royal Cornwall Hospital
383	Royal Glamorgan Hospital
352	Royal Gwent Hospital, Newport
366	Royal Sussex County Hospital
350	Royal United Hospital, Bath
362	Singleton Hospital, Swansea
360	South Tyneside District Hospital
376	St George's Hospital
375	St Mary's Hospital

Centre number	Centre name
261	St Thomas' Hospital
227	Sunderland Royal Hospital
359	Tameside Hospital
355	University College Hospital, London
173	University Hospital of Wales
357	Warrington Hospital

Appendix 10 BUMPES: serious adverse event form (version 2.0)

BUMPES

A study of position during the late stages of labour in women with an epidural

Serious Adverse Event (SAE) Form

Please complete pages 1 - 3 and one form for each Serious Adverse Event

Please fax immediately to the BUMPES Co-ordinating office on [redacted]

Reporting information:

Date form completed: D D / M M / Y Y

Type of report: Initial ☐ Follow-up ☐

Name of hospital: _____

Name of person completing the form: _____

Clinical status: Doctor ☐ Midwife ☐ Other ☐

If Other, please specify: _____

Woman's Identification Details:

BUMPES study number: *(found in section 2 of the data collection form)* ☐☐☐☐☐

Woman's initials: ☐☐☐ **Date of birth:** D D / M M / Y Y

Treatment allocation: *(Please tick only one)* Upright ☐ OR Lying down ☐

Participant affected: *(Please tick only one)* Woman ☐ OR Infant ☐

Seriousness: *(Please tick only one)*

Results in death ☐

Life threatening ☐

Inpatient hospitalisation or prolongation of hospitalisation ☐

Persistent or significant disability/incapacity ☐

Medically significant or requires intervention to prevent one of the above outcomes ☐

Event description:

Please describe the event as fully as possible:

Event details:

Date and time event started: D D / M M / Y Y h h : m m (24hr)

Date and time event resolved: *(If applicable)* D D / M M / Y Y h h : m m (24hr)

Indicate the severity of the event: Mild ☐ Moderate ☐ Severe ☐

Event causality:

Indicate whether the event is considered related to participation in the study:

Unrelated ☐ Possibly related ☐ Probably related ☐ Definitely related ☐

Version 2, Mar 2012 Serious Adverse Event (SAE) form Page 1 of 2

Event outcome:

Recovered ☐ Recovering ☐ Continuing ☐ Patient died ☐ Unknown ☐

Are there any clinical sequelae? Yes ☐ No ☐

If Yes, please describe:

Treatment required:

Did the event require treatment with medication? Yes ☐ No ☐

If Yes, please list any medication administered in the table on the next page;

Medication name (generic)	Dose	Route of administration	Date and time started	Date and time stopped	Ongoing?
			D D / M M / Y Y h h : m m 24hr	D D / M M / Y Y h h : m m 24hr	☐
			D D / M M / Y Y h h : m m 24hr	D D / M M / Y Y h h : m m 24hr	☐
			D D / M M / Y Y h h : m m 24hr	D D / M M / Y Y h h : m m 24hr	☐
			D D / M M / Y Y h h : m m 24hr	D D / M M / Y Y h h : m m 24hr	☐
			D D / M M / Y Y h h : m m 24hr	D D / M M / Y Y h h : m m 24hr	☐

Did event require treatment with a procedure? Yes ☐ No ☐

If Yes, please list any procedures required in the box below:

Is there any other relevant information? Yes ☐ No ☐

If Yes, please detail in the box below:

Investigator's Review:

Investigator's name: _____

Investigator's signature: _____ **Date:** D D / M M / Y Y

Appendix 11 BUMPES: incentive trial protocol (version 1.0, 8 July 2009)

Ancillary study to BUMPES: Protocol for the evaluation of the effects of an offer of an incentive on the rate of questionnaire return

Version 1.0, 8th July 2014

Authors: Pollyanna Hardy, Beth Howden, Peter Brocklehurst

Chief Investigator(s):	Peter Brocklehurst
Centre:	[redacted]
Sponsoring Institution:	University College London
Funder:	NIHR Health Technology Assessment programme NIHR Evaluation, Trials and Studies Coordinating Centre University of Southampton Alpha House Enterprise Road Southampton SO16 7NS
HTA project number:	08/22/02
MREC number:	09/H0605/114
ISRCTN:	ISRCTN35706297
Approved	Substantial amendment 11 30th July 2014

1. Background

Maximising follow-up rates for postal questionnaires for randomised controlled trials is an important aspect of a well designed and well conducted study. Loss to follow-up can lead to bias and compromise the internal and external validity of the results.

Use of incentives to promote questionnaire return in clinical trials has been researched. Existing systematic reviews suggest they are effective,[65, 66] but not all studies have sufficient funds to use them. Promising an incentive once data are returned can reduce the cost burden of this approach. Brueton *et al.*[66] showed evidence that an offer of a monetary incentive was comparable to the addition of a monetary incentive with the questionnaire (pooled risk ratio 1.04, 95% confidence interval 0.91 to 1.19). However, it may be possible to provide further cost-savings if the offer was restricted to the reminder letters only.

We propose to evaluate the effect of promising a monetary incentive at first mail out versus a promise on reminder letters only, with the incentive being posted out on receipt of a completed follow-up questionnaire. This randomised controlled trial (RCT) will be nested within the BUMPES RCT (a study of position during the late stages of labour in women with an epidural) and will be carried out on a population of women in the UK one year after the birth of their first child.

2. Objective

To assess the effectiveness on the return rate of the 1 year follow-up postal questionnaires for BUMPES of a promise of a monetary incentive made at the point of sending the questionnaire for the first time compared to a promise made on reminder letters only.

3. Trial Design

Parallel group, randomised controlled trial nested within BUMPES.

4. Study setting

All women randomised into the BUMPES study, who consented to be contacted at 12 months and who have not yet been sent their 1 year follow-up questionnaire, will be included. The BUMPES study is a multicentre randomised controlled trial in women who are admitted to a participating labour ward ≥37 weeks' gestation with no previous pregnancy and with a low dose epidural in situ. A follow-up questionnaire is sent to the woman asking for information on their health and wellbeing, as well as health service use 1 year following the birth of their baby.

5. Eligibility criteria:

Inclusion criteria

- Recruited to BUMPES
- Consented at recruitment to receive follow up questionnaire
- 1 year questionnaire not sent

Exclusion criteria:

- Women who had stillbirths
- Women whose infants have died
- Address details unknown
- Woman and infant not living at same address

6. Interventions

Women will be randomly allocated to the following two groups:

1. Incentive cover letter. This will contain details of a promise of a monetary incentive when the questionnaire is first sent. A £10 gift voucher redeemable at high street shops will be sent to the woman on return of a completed questionnaire. The covering letter will include a sentence explaining that the voucher is to thank participants for their time and effort. All reminder letters will include a sentence about the incentive.
2. Incentive reminder letters. The standard cover letter (as currently used) will not mention any incentive. All subsequent reminder letters sent if the questionnaire is not returned, will detail the promise of an incentive. A £10 gift voucher redeemable at high street shops will be sent to the woman on return of a completed questionnaire.

For both groups women will also be contacted electronically or via text messaging if the contact details have been collected. The content of the emails and texts sent will reflect the group to which the woman was randomised. All women will also be provided with an option of completing the questionnaire online.

7. Outcomes

The primary outcome will be questionnaire return, defined as receipt of a completed or partially completed questionnaire at the BUMPES office. As a secondary outcome we will analyse the number of questionnaires returned without chasing by the study team. There is a standard procedure for chasing missing questionnaires; if the incentive increases the proportion returned without chasing this will save time for the study team. We will also report the total cost of the vouchers sent out by nested study arm.

8. Sample size and feasibility

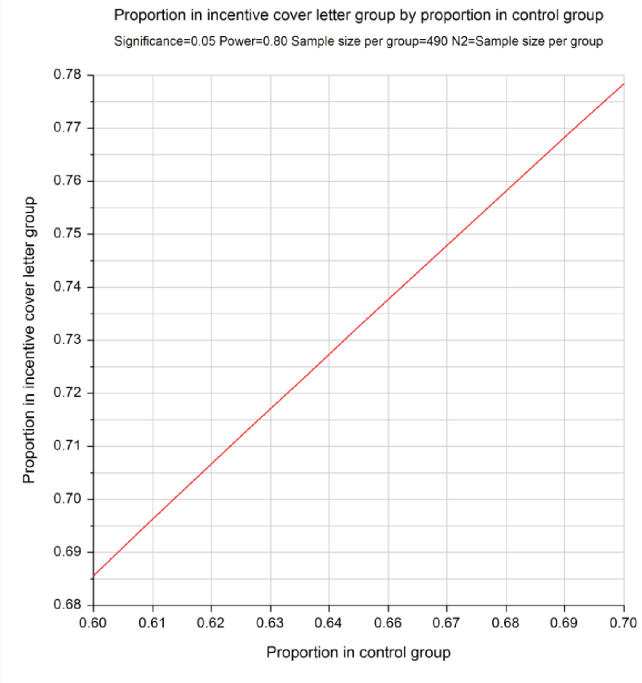
The sample size will be predetermined by the numbers of questionnaires remaining to be sent at the point of start of the nested study.

BUMPES started recruiting in October 2010 and finished in January 2014. A total of 3236 women were randomised. It is estimated that approximately 1,150 women will remain to be followed up at the start date of this study (currently estimated to be beginning August 2014). Assuming that approximately 15% of these women will be excluded from receiving the questionnaire due to stillbirth, infant death, address details unknown or different to the infant, 980 women will be eligible to be randomised in the nested study (approximately 490 per group).

In order to assess the detectable effect size possible with the given sample size, we need to estimate a control group risk based on current literature. Khadjesari *et al*[67] investigated the use of an offer of an incentive (a £10 Amazon gift voucher) versus no offer of an incentive on follow-up rates in an online trial. They found an increase of 9% (95% CI 5% to 12%) when using the offer of an incentive. Kenyon *et al*[68] investigated the use of a monetary incentive included in reminder letters versus no incentive and found an improvement in the response rate between the two groups of 11.7% (95% confidence interval 4.7% to 18.6%).

The follow-up questionnaire return rate for BUMPES up to June 2014 was 59%. Assuming that this could increase by at least 5% with the use of an offer of an incentive either with an incentive cover letter or an incentive reminder letter only, a sample size of 980 is sufficient to demonstrate an increase in questionnaire return of 8% from 64% in the incentive reminder letter group to 72% in the incentive cover letter group at a 2-sided 5% significance level with 80% power. Figure 1 illustrates the proportion detectable in the incentive cover letter group for control group risk varying between 60% and 70%. The detectable difference lies between 8% and 8.5% for varying control group estimates.

Figure 1: Proportion in incentive cover letter group by proportion in control group



Randomisation to the incentive nested study will start as soon as practical, and continue until all questionnaires and reminders have been sent.

9. Randomisation

Allocation will be by computer random number generation stratified by BUMPES allocation and by centre.

Randomisation to incentive cover letter or incentive reminder letter will occur at each woman's next follow-up point during the conduct of the BUMPES study. Each BUMPES participant will be randomised to incentive cover letter or incentive reminder letter once only.

10. Blinding

Trial staff will be aware of allocation due to the nature of the interventions, and the practicalities involved in sending the letters and the vouchers.

11. Data collection

Recording of questionnaire receipt, date received and voucher sent will be made using the current trial administration systems. Postal versus online receipt will also be recorded.

12. Statistical analysis

Baseline demographic information will be summarised by randomised group using frequency counts and percentages for categorical data and means and standard deviations, or medians with interquartile ranges for continuous data.
Differences in risk and risk ratios along with their 95% confidence intervals to compare the proportions of questionnaires returned between randomised group will be presented.

13. Consent

No consent from participants will be sought for this trial.

14. Dissemination

The results of this study will be submitted for publication in a peer reviewed journal, and disseminated to the relevant Cochrane review group. The Medical Research Council Methodology Hubs will also be notified as they are collecting information on such studies for a database of RCT methodological work.

15. Funding

No additional funding will be required to carry out this study. All costs will be covered by the BUMPES study Health Technology Assessment award.

Appendix 12 BUMPES: data collection worksheet (version 5.0)

BUMPES

A study of position during the late stages of labour in women with an epidural

Data Collection Worksheet

Please complete in black ballpoint pen

Hospital Code

Woman's study number:

Addressograph

or

Woman's name:

Woman's address:

Woman's telephone number(s):

Woman's email address:

Woman's Hospital ID number:

Woman's NHS number *(if known)*

1. **Does the woman meet the BUMPES eligibility criteria?**
   For full list of eligibility criteria please refer to the study protocol. ☐ Yes ☐ No

At Study Entry (Full dilatation confirmed by VE, randomisation completed)

2. **How painful was the woman's last contraction at its peak (using "Visual Analogue Scale")?** VAS recording: (0-100) ☐☐☐
3. **Can the woman perform a "straight-leg raise" with one leg?** ☐ Yes ☐ No
4. **Was the epidural pain relief maintained with PCEA/infusion up until study entry?** ☐ Yes ☐ No
   If Yes, please record pump reading at study entry: ☐☐☐ ml

After Study Entry (After birth has occurred, while still on delivery suite)

5. **Was the epidural pain relief maintained with PCEA/infusion after study entry?** ☐ Yes ☐ No
   If Yes, please record pump at time of delivery: ☐☐☐ ml
6. **How painful was the birth of the woman's baby (using "Visual Analogue Scale")?** VAS recording: (0-100) ☐☐☐
7. **Was the maternal satisfaction questionnaire given?** ☐ Yes ☐ No
8. **Date and time of discharge from delivery suite care:** D D / M M / Y Y h h : m m (24hr)

Name of person completing this section of the form:

Name: *(Print)* _____ **Signature:** _____

UCL Clinical Trials Unit

Version 5 Nov 2013

[redacted]

BUMPES Data collection worksheet

UCL

Page 1 of 2

Group allocation: Upright ☐ **OR** Lying down ☐

		Predominant maternal position in last 15 minutes										
		Lying (elevation of head of bed up to a maximum of 30°)				Sitting		Supported kneeling		Standing/ walking	Other including lithotomy	If the woman changes from her allocated position to a non-allocated position, please record the reason
		Left lateral	Right lateral	Tilted with a wedge		Out of bed	In bed	Out of bed	In bed		Please briefly describe	
				Wedge on left side	Wedge on right side							
Study time (min)	Actual time (24 h)											
Position prior to study entry		☐	☐	☐	☐	☐	☐	☐	☐	☐		
0	:											
15	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
30	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
45	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
60	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
75	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
90	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
105	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
120	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
135	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
150	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
165	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
180	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
195	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
210	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
225	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
240	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
255	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
270	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
285	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		
300	:	☐	☐	☐	☐	☐	☐	☐	☐	☐		

Maternal position at time of birth Upright ☐ Lying down ☐ Lithotomy ☐ Other ☐

If Other, please describe _____

Appendix 13 BUMPES: withdrawal form (version 4.0)

BUMPES
A study of position during the late stages of labour in women with an epidural

Withdrawal from BUMPES

Please complete using a black ballpoint pen
Please complete if a women decides to withdraw from BUMPES after study entry.

General information

Name of hospital: _____

Date and time of withdrawal: D D / M M / Y Y h h : m m (24hr)

Woman's identification

BUMPES study number: _____

Date of birth: D D / M M / Y Y

Withdrawal

Reason for withdrawal:

At the woman's request ☐ — *Reason if known:*

Other ☐ — *Please describe:*

May we use the woman's data up to point of withdrawal Yes ☐ No ☐

May we obtain outcome information from hospital records Yes ☐ No ☐

May we contact the woman at one year Yes ☐ No ☐

Health Professional's name in block capital letters: _____

Health Professional's position: _____

Signature: _____ **Date:** D D / M M / Y Y

Please fax this form to the BUMPES Co-ordinating Centre:

[redacted]

UCL Clinical Trials Unit

ISRCTN35706297 [redacted] REC Ref: 09/H0605/114 Withdrawal Form UCL Version 4, Mar 2012

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HTA
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PHR

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