Centre for Trials Research
Canolfan Ymchwil Treialon

UKCRC Registered Clinical Trials Units

NIHR | National Institute for Health Research

Statistical Analysis Plan

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1.0			

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Chief Investigator Date and Signature

Contents

List of abbreviations

AMU	Alongside Midwifery Unit
APH	Antepartum haemorrhage
BBA	Born Before Arrival
BMI	Body Mass Index
CI	Confidence interval
CTR	Centre for Trials Research
DAG	Directed acyclic graph
FMU	Freestanding Midwifery Unit
HR	Heart rate
ICH	International Council for Harmonisation
IRR	Incidence rate ratio
IV	Instrumental variables
NBM	Negative Binomial model
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NN	Nearest neighbour
NNRD	National Neonatal Research Database
NNU	Neonatal unit
OASI	Obstetric Anal Sphincter Injury
OBS	Obstetric Unit
OR	Odds ratio
OSF	Open science framework
PPH	postpartum haemorrhage
RECORD	Reporting of studies Conducted using Observational Routinely-collected Data
SAP	Statistical analysis plan
SMG	Study Management Group
SSC	Study Steering Committee
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
UKNC	United Kingdom Neonatal Collaborative
VBAC	Vaginal Birth after Caesarean

1. Purpose and scope of the plan

This statistical analysis plan (SAP) details the proposed presentation and analyses for the main paper reporting results from the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme (Project number 16/149/01) funded multi-centre cohort study to establish the safety of waterbirth for mothers and babies among women who are classified appropriate for midwifery-led intrapartum care (The POOL Study)[1].

It describes the analysis principles, definitions of outcomes, methods for primary analysis, pre-specified subgroup analysis, and secondary analysis. This SAP conforms to the published guidelines on the content for SAP in clinical trials and was finalised prior to completion of data collection from sites[2]. Any deviations from this plan will be described and justified in the final report of the trial.

Subsequent analysis 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 analyses (for e.g. to decide cut points for categorisation of continuous variables), nor to prohibit accepted practices (e.g. 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 study.

The analysis strategy will be available on request when the principal papers are submitted for publication in a journal but will also be made publicly available on the POOL Open Science Framework (OSF) website: https://osf.io/kwj53 and will be published. Suggestions for subsequent analyses by journal editors or referees, will be considered carefully, and conducted as far as possible in line with the principles of this analysis strategy; if reported, the source of the suggestion will be acknowledged.

The analysis should be conducted by an identified, appropriately qualified and experienced statistician, who should ensure the integrity of the data during their processing. Examples of such procedures include quality control and evaluation procedures.

2. Statistical analysis plan authorship

Rebecca Cannings-John is the study statistician for POOL study and the author of this SAP. All statistical analyses will be carried out by Rebecca Cannings-John. This SAP will be finalised for presentation to the Study Management Group (SMG) and will be agreed by them and signed off by the author, a senior statistician and the Chief Investigator. A copy will then be sent to the Study Steering Committee (SSC). This statistical analysis plan has been developed in compliance with 'Statistical Principles for Clinical Trials' (ICH E9)[3], 'Guidance for Good Clinical Practice' (ICH E6)[4], 'Structure and Contents for Clinical Study Reporting' (ICH E3)[5]. It adheres to the Centre for

[1] Milton R, Sanders J, Barlow C, Brocklehurst P, Cannings-John R, Channon S, et al. Establishing the safety of waterbirth for mothers and babies: a cohort study with nested qualitative component: the protocol for the POOL study. BMJ Open. 2021 Jan;11(1):e040684.
[2] Gamble C, Krishan A, Stocken D, Lewis S, Juszczak E, Doré C, et al. Guidelines for the content of statistical analysis plans in clinical trials. JAMA. 2017;318(23):2337–43. https://doi.org/10.1001/jama.201 7.18556
[3] ICH E9: Statistical principle for clinical trials (Notes for Guidance on Statistical Principles for Clinical Trials) September 1998, CPMP/ICH/363/96.
[4] ICH E3: ICH Harmonised Tripartite Guideline: Structure and Content of Clinical Study Report E3.
[5] ICH E6 (R1): Guideline for Good Clinical Practice. European Medicine Agency; CPMP/ICH/135/95.

Trials Research (CTR) Standard Operating Procedure[6]. Any amendment to this plan after the commencement of the analysis should be documented in the log provided.

Note on terminology

We use the terms 'women' and 'mother' throughout the document, but this document will also apply to people who do not identify as women and who are pregnant or have given birth.

3. Study overview

3.1 Study aim

The primary study aim is to establish whether for low-risk women who use a pool during labour, waterbirth, compared to leaving a pool prior to birth, is as safe for mothers and infants.

3.2 Primary objectives

To establish whether for low-risk women who use a pool during labour, waterbirth, compared to leaving a pool prior to birth, is as safe for mothers and infants.

3.3 Secondary objectives

The secondary study objectives will set pool use and waterbirth in the context of NHS care. The study will establish:

1. The overall proportion and characteristics of women who use a pool for labour or birth, compared to those who do not use a pool.
2. The characteristics of, and outcomes for, women with identified risk factors at labour onset, who use a pool during labour.
3. The characteristics of and outcomes for, women who develop labour complications who use a pool during labour.
4. Factors associated with rates of pool use in individual maternity units.

3.4 Study participants

All women who meet NICE criteria for being at low-risk of complications who use water immersion during labour. Descriptive data will be reported on all women at study sites.

4. Study design

A natural experiment using a cohort design will answer study objectives using a combination of retrospective and prospective data in electronic NHS maternity and neonatal information systems.

4.1 Sample size justification

The non-inferiority of birth in water compared to birth on land on rates of Obstetric Anal Sphincter Injury (OASI) will be examined by parity. The Birthplace in England study found that overall 4.6% and 1.6% of 'low-risk' nulliparous and parous women respectively, sustained OASI[7]. A sample size of 15,000 nulliparous and 15,000 parous low-risk women (7,500 each water and land) is required to obtain 90% power, and a 95% one-sided confidence interval around a treatment difference of zero. A non-inferiority margin of 1% or less, and 0.6% or less will be taken as

[6] Standard Operating Procedures for Statistical Analysis Plan SOP/008/2, Version 2.0, 14/02/2022

[7] Birthplace in England collaborative Group, Brocklehurst P, Hardy P, et al. perinatal and maternal outcomes by planned place of birth for healthy women with low-risk pregnancies: the birthplace in England national prospective cohort study. BMJ 2011;343:d7400

clinically non-significant amongst nulliparous and parous low-risk women respectively. Since nulliparous women birthing in water are regarded as the least prevalent of the four groups, a data collection period providing data on 7,500 would ensure adequate numbers in the other three, more prevalent groups. These data will be combined to assess the effects averaged across both strata at an increased power, with a combined required sample size of 30,000 low-risk women. We have assumed that 25% of the 6,600 waterbirths recorded in E3 in 2015 were nulliparous women (1650/annum). Allowing for staggered site set-up, six years of combined retrospective and prospective data collection would be required (January 2015 – June 2022). The exact ratio of nulliparous and parous women who give birth in water will be determined once the retrospective data are examined, but with increasing numbers of waterbirths, with 18 of the 35 E3 using sites, collectively undertaking 6,037 waterbirths in 2016, we are confident the study will have sufficient power to answer this important clinical question.

For the infant primary outcome, an estimate of 5% is used for the proportion of infants born to low-risk mothers experiencing 'adverse infant outcome or treatment'. A non-inferiority margin of 1.0% or less will be taken as clinically non-significant. A sample size of 16,200 infants (8,100 per group water / land) are required to have 90% power, and a 95% one-sided confidence interval (CI) around a treatment difference of zero.

5. Study outcomes

5.1 Primary outcome measure

The study has two primary outcomes:

The maternal primary outcome will be OASI. Such trauma is important to women and the NHS as it requires more complex repair and follow-up, and is associated with short term morbidity (pain, infection, incontinence) as well as longer term morbidity; (dyspareunia, urinary and faecal incontinence, future caesarean section).

The infant primary outcome will be composite of 'adverse infant outcomes or treatment' to include:

(a) Any neonatal unit (NNU) admission requiring respiratory support;
(b) Intravenous antibiotic administration within 48 hours of birth (with or without culture proven infection); and
(c) Intrapartum stillbirth or all deaths prior to NNU/postnatal ward discharge.

Such outcomes are important as they cause distress to parents, are associated with potential long-term damage to infants and with cost to the NHS. Composite infant outcomes combining mortality and morbidity are credible and provide more power to detect differences between groups, but the level of incidence of individual components will remain insufficient to detect differences in each outcome.

5.2 Secondary outcomes measure(s)

Secondary outcomes of parental, clinical and financial importance have been identified. Data relating to maternal or infant readmission to hospital within seven days of birth are already reported by community midwives and captured in Wellbeing Software's E3 systems at the point of discharge from midwifery care. Data relating to some primary and secondary outcomes are not currently captured in Wellbeing Software's E3 maternity information systems and at site opening the Wellbeing Software's E3 systems at sites will be amended to prospectively collect these data.

Maternal secondary outcomes:

Maternal Intrapartum:

- Shoulder dystocia and required management,
- Management of the third stage of labour (whether the placenta was intended to be, or delivered in or out of water),
- Obstetric involvement in care (including sepsis, treatment for haemorrhage),
- Incidence and management of perineal trauma,
- Maternal position at birth.

Maternal Postnatal:

- Duration of postnatal stay,
- Breastfeeding (initiation and continuation),
- Need for higher-level care,
- Maternal readmission to hospital within seven days of birth.

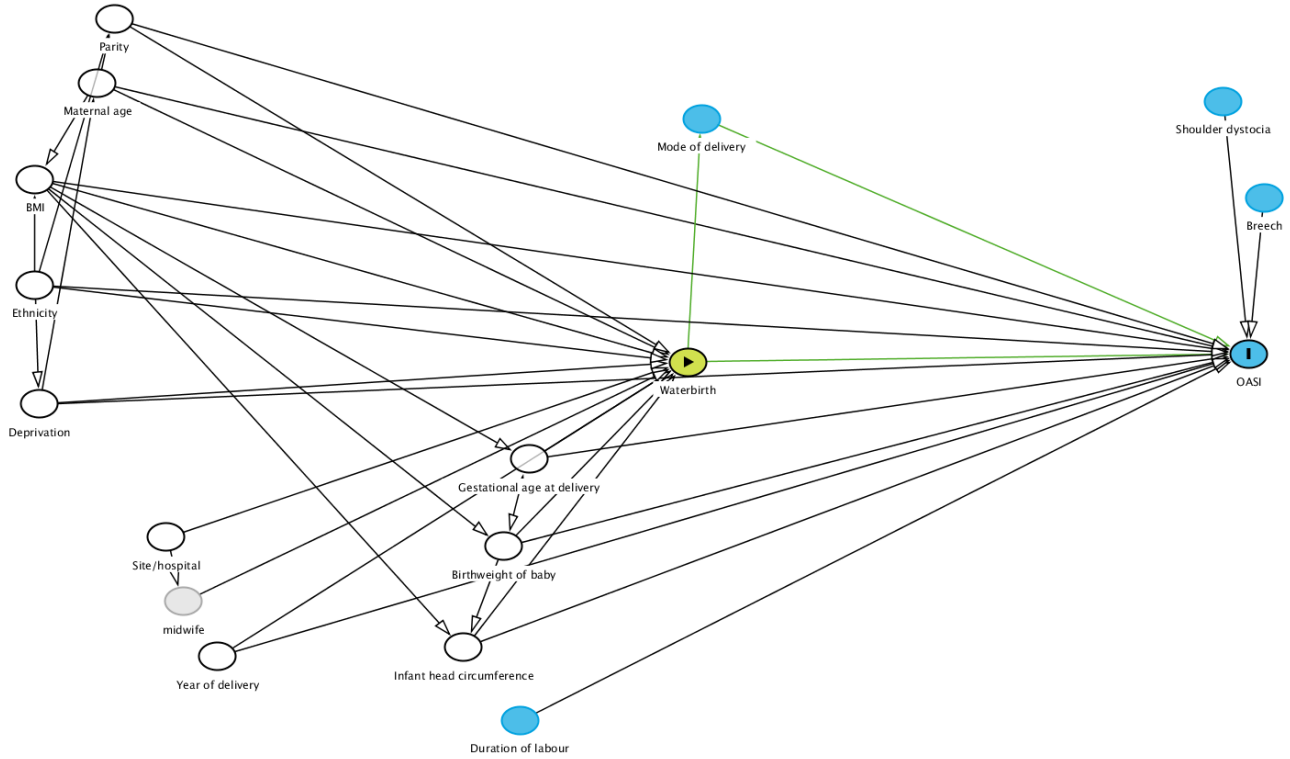
Infant secondary outcomes:

- Timing of cord clamping,
- Apgar scores (1, 5 and 10 minutes),
- Intrapartum stillbirth or neonatal death prior to NNU/postnatal ward discharge occurring within seven days of birth,
- Cause of intrapartum stillbirth or death prior to NNU/postnatal ward discharge,
- NNU admission requiring respiratory support,
- Antibiotic administration within 48 hours of birth (with/without culture proven infection),
- Neonatal resuscitation,
- Snapped umbilical cord prior to clamping,
- Skin-to-skin contact at birth,
- First breastfeed within first hour,
- Culture proven infection,
- Brachial plexus injury,
- Treatment for jaundice,
- Readmission to hospital within seven days of birth,
- Receipt of therapeutic hypothermia,
- Neonatal unit admissions,
- Respiratory support,
- Highest CRP results,
- Successful / attempted lumbar puncture,
- Blood culture positive with a recognised pathogen (excluding skin commensal organisms).

5.3 Confounders

A confounder is a variable that is associated with both exposure and outcome (a mutual cause), that occurs before the exposure (i.e., waterbirth). Conditioning for these measured confounders may then result in a more precise effect estimate. Visual representations of causal assumptions will be used to identify the potential confounders of confounders using directed acyclic graphs (DAGs). Figure 1 show the DAG for the maternal primary outcome of OASI.

Figure 1. Directed acyclic graphs for Obstetric Anal Sphincter Injury (OASI)



5.4 Datasets, linkage and handling

5.4.1 Datasets

To answer the research questions, it is planned to use two datasets, data extracted from Wellbeing Software's maternity information systems and data held by the National Neonatal Research Database (NNRD).

1. Wellbeing Software's Maternity Information System, "E3", forms a comprehensive clinical data set and is currently used by 35 maternity NHS Trusts and Health Boards in the UK.

2. All 200 neonatal units in England, Wales and Scotland form the United Kingdom Neonatal Collaborative (UKNC) and contribute electronic health record data to the NNRD from 2014 to present. The NNRD is a national resource formed of the Neonatal Data-Set (an NHS Information Standard), comprising 450 clearly defined variables extracted at patient level from the commercial Electronic Health Record used by all UK neonatal units.

5.4.2 Time-period

To provide necessary denominator data, and to be able to compare characteristics of pool and non-pool users, a minimal data set will be extracted relating to women who did not use a pool in labour, whilst a more extensive dataset will be extracted for women who did use a pool in labour. An important clinical question is whether there is a differential effect of waterbirth on severe perineal trauma (OASI) amongst nulliparous and parous women. To undertake this subgroup analysis will require a necessarily large sample (N=30,000). As data relating to perineal trauma

and waterbirth are already captured, and to avoid unnecessarily prolongation of the study, this analysis will use a combination of retrospective and prospectively collected data, including births from January 2015 to June 2022.

The sample required for the infant primary outcome is smaller (N=16,200) and, as all essential data are not currently collected for one component of this composite outcome (antibiotic administration within 48 hours of birth on postnatal wards) additional data fields will to be added to maternity systems at participating NHS sites. Therefore, we will collect these data on births prospectively during the period from site opening (around June 2018) to June 2022. Some infant outcomes of interest, including hypoxia, respiratory support or mortality, are already held by study sites or by the NNRD. Where available and where the risk status, and pool usage of mothers can be determined, retrospective data will be used to increase the power of the analysis around secondary infant outcomes.

5.4.3 Linkage and handling

To obtain detailed treatment and outcome information on any infant who required admission to a neonatal unit, following their mother's pool use in labour, the identifiers (NHS number) of all infants born to women who used a pool during the period of prospective data collection will be extracted and matched to any records held by the NNRD. Data will be received from Wellbeing Software and the NNRD at regular intervals and processed by the data manager. Cardiff University will receive only pseudonymised data.

5.5 Study population

5.5.1 Inclusion criteria

All women, at low-risk of complications who use water immersion during labour as recorded from NHS maternity services using Wellbeing Software's E3 Maternity Information System between January 2015 and June 2022 are eligible (Figure 2).

5.5.2 Exclusion criteria

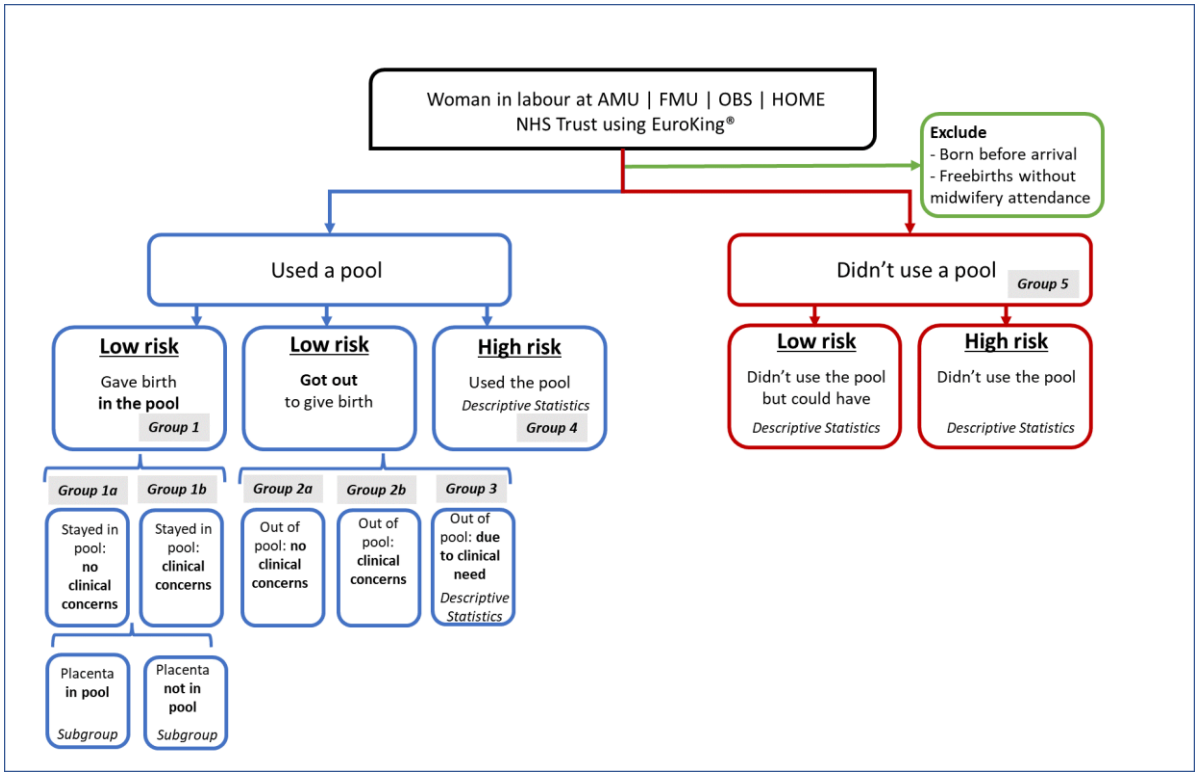
- Data from women who opt out from the study will not be received;
- Women and infants recorded in E3 as being 'Born Before Arrival' (BBA) or recorded as freebirths.

Women who do not use a pool (Group 5) are also excluded but will be described, as will women who used a pool but are not at low-risk of complications (Group 4).

5.5.3 Use of water

To capture data relating to women who use any form of water immersion during labour 'use of a pool' during labour, will pragmatically be any women for whom water immersion analgesia is recorded in Wellbeing Software's E3 system.

Figure 2. Study population groups: overview of the five groups of women within the POOL study population



AMU=Alongside Midwifery Unit; FMU=Freestanding Midwifery Unit; OBS=Obstetric Unit.

5.5.4 Defining women at 'low-risk' of complications at the commencement of labour and use a pool during labour

The criteria of 'low-risk' is one of exclusion of known risk factors; the NICE Intrapartum Care Guidelines[8] will be used to identify these conditions. The intrapartum guidelines provide information on conditions that, if present, should be regarded as an indication to either advise birth in an obstetric unit, or that suggest individual assessment should be undertaken prior to making a recommendation on the planned place of birth. The guidelines do not specifically relate to use of a pool for labour or birth.

Appendix 1, tables 1 and 2 lists medical conditions or situations in which additional observation or care would be recommended in an obstetric unit for the woman or baby during or shortly after labour, to reduce associated risks. The factors listed in tables 3 and 4 are not reasons in themselves for advising birth within an obstetric unit, but indicate that further consideration of birth setting may be required.

Existing historic E3 fields (data between study start and end (2015 to June 2022)) completed during the pregnancy, mapped to the NICE guidelines, and fields completed by the midwife following birth, but relating to the point of pool entry (from site opening in ~2019) will both be

[8] Intrapartum care for healthy women and babies. Clinical guideline [CG190]Published: 03 December 2014 Last updated: 21 February 2017. https://www.nice.org.uk/guidance/cg190/chapter/recommendations

used to identify women with an identified risk factor. Women with identified risk factors will form Group 4, irrespective of whether they gave birth in water or not (Figure 1). Those with no risk factor identified in the antenatal records/or by the midwives at the time of pool entry will form Groups 1, 2 and 3.

Classification of risk may differ between these two sources:

- risk classification categorisation based on the existing E3 antenatal fields is likely to provide a lower threshold for risk, potentially identifying women who experienced a complication in the past or during pregnancy, but for whom this was no longer present at pool entry, e.g. a woman with an episode of hypertension during pregnancy, but who is later normotensive.
- risk classification categorisation used by the midwife at pool entry is likely to provide a more pragmatic definition and reflects the opinion of the midwife providing intrapartum care.

For all outcomes, risk will be defined using a combination of the existing historic E3 fields/ completed by the midwife following birth to ensure a consistent definition of risk in study populations across all outcomes. However, consideration of the potential differences in risk classification will be reflected by running sensitivity analyses based on the midwives' assessment at pool entry alone (see section 6.4.1).

For women who gave birth prior to site opening, for whom the risk classification question relating to the time of pool entry is not available, if there is any record of risk factor in the antenatal notes, the woman will be classified as 'high-risk' (Group 4).

For women who gave birth after site opening, if risk factors that cannot change over time are recorded in the antenatal notes, the woman will be classified as 'high-risk' regardless of whether this was also identified by the midwife providing intrapartum care, e.g. a previous caesarean section.

For women who gave birth after site opening, if risk factors that can change over time are recorded in the antenatal notes, but not identified by the midwife providing intrapartum care, the woman will be classified as 'low-risk' e.g. hypertension, suspected macosomia.

5.5.5 Defining women who leave, or do not return to the pool due to a clinical need (a complication developed during labour with interventions that could not have been provided in the pool) – Group 3

Women leaving the pool due a clinical need i.e., develop a complication during labour, or by their own choice but subsequently developed a complication, will move to Group 3. These include women who received interventions including:

- caeserean section or instrumental birth,
- syntocinon augmentation of labour,
- pain relief incompatable with use in water (e.g,, epidural, remifentanil, pudendal block).

5.5.6 Defining women giving birth in water (Intervention - Group 1) or Women leaving the pool to give birth (Comparator – Group 2).

Intervention - Group 1
The primary study aim is to establish whether for low-risk women who use a pool during labour, waterbirth, compared to leaving a pool to give birth (Group 1 vs Group 2 respectively), is as safe for mothers and infants. We will identify Group 1 - women who give birth in water, by using the Waterbirth field in E3. To capture births commenced in, but completed, out of water, such as in the event of shoulder dystocia or previously unrecognised breech presentation, 'waterbirth' will be defined in the study as 'A birth in which the fetus is partially or totally expelled under water' (POOLWaterbirth). This information will only be available from records after site-opening. For the period of data collection where this additional data is not available, we will take any recording of waterbirth as such. We will examine rates of waterbirth using both definitions and be satisfied that there are no substantial differences.

Within this group will be mothers for whom staff recorded no clinical concerns prior to birth (Group 1a) but will also include women for whom staff recorded some clincial concern prior to birth (e.g.fetal heart rate concerns) but still gave birth to their baby in the pool (Group 1b). To identify women in Group 1b we will use a combination of existing fields (e.g. Maternal/Fetal intrapartum problems "Were there any maternal/fetal problems during labour?") and new E3 fields (POOLLabourComplications).

Comparator group
Women who leave the pool prior to birth, will be categorised as having left either:

a) due to their own choice and did not subsequently develop a complication (Group 2)

or

b) due to their own choice but who subsequently developed a complication prior to birth.

Women leaving the pool due to their own choice who do not subsequently develop a complication prior to birth will be allocated to Group 2 using a combination of new E3 fields (POOLLeftPoolNoReturn= Left pool for vaginal examination/use bathroom and did not return, Maternal decision to leave pool and did not return, Left pool for further analgesia and did not return, Planned to labour but not give birth in water) and an absence of information in the existing E3 fields: Maternal/Fetal intrapartum problems.

Within this group will be mothers for whom staff recorded no clinical concerns prior to birth (Group 2a) but will also include women for whom staff recorded some clincial concern prior to birth (e.g.fetal heart rate concerns) (Group 2b).

To identify women in Group 2b we will use a combination of existing fields (e.g. Maternal/Fetal intrapartum problems "Were there any maternal/fetal problems during labour?") and new E3 fields (POOLLabourComplications/ POOLLeftPoolNoReturn - Clinical reason for leaving pool or not getting back in" (Table 1).

Table 1: Clinical reason for leaving pool or not getting back in

Delay in 1st stage	Maternal tachycardia
Delay in 2nd stage	Maternal hypertension
Abnormalities in fetal heart rate	Breech presentation
Meconium stained liquor	Antepartum haemorrhage (APH)
Maternal pyrexia	

Women who leave the pool due to their own choice but who subsequently developed a complication prior to birth (making a pool birth contraindiated) can either remain in Group 2b (got out - some clincial concerns prior to birth) or move to Group 3 (got out due to clinical need). All women receiving obstetric interventions prior to birth will move to Group 3.

These two study populations will be used to address these different clinical questions:

	Pros	Cons
Primary Analysis: Groups 1b and 2b* will remain in primary analysis	This study population reflects real life with some clinical concerns resulting in the woman leaving the pool but without time or subsequent indication for transfer for obstetric intervention. This answers the question, "what are the outcomes for babies born in /out of water whose mother used water immersion analgesia during labour?"	Potential bias in favour of waterbirth group
Sensitivity Analysis: Groups 1b and 2b excluded from primary analysis	This study population excludes cases where outcomes are likley to be poorer but answers the question: "Does birth in water (in itself, and in the absence of any clincial concerns) influence maternal and neonatal outcomes?".	Potential to underestimate adverse neonatal events across whole primary analysis

** providing they did not undergo interventions incompatable with waterbirth (apart from episiotomy)*

The study will report outcomes for both of these study populations as it is important to reflect the intervention effect in both a pure risk and real life risk scenario.

Primary analysis: (Group 1a+1b versus Group 2a +2b as the 'reflects real life' practice

Sensitivity analysis: Group 1a (birth in pool+no clinical concerns) versus Group 2a (birth in /out of pool+no clinical concerns) as the 'pure' low-risk

5.6 Missing data

We will distinguish empty cells by:

(a) sites not collecting certain fields (partial or full study period) or entirely halting data collection (e.g. ceasing to use the E3 maternity information system);
(b) cells that are expected but are empty (and coded as NULL).

For (b) we will distinguish between fields that are:

1. expected to be well completed (e.g., mode of birth, birthweight, breastfeeding). Empty cells will be defined as true missing and imputation will be considered (See section 6.5).
2. likely to only be completed when an event has occurred (e.g., hypertension). Empty cells will be defined as absence of event.
3. only expected when relevant pre-screening questions are used (e.g., duration of antibiotics only applicable for those that receive antibiotics). Empty cells will be defined as 'not applicable', unless the screening question is positive in which case an empty field would be defined as missing.

5.7 Pooling of investigational sites

Records from all sites will be pooled for the analysis. Sites will be identified by their Site ID number (and not named) and will be included in the regression models as a random factor.

5.8 Withdrawals

- All mothers giving birth after site opening could opt out of the study. We will not receive these records from Wellbeing Software. We will however receive and report aggregate data on the number of opt outs per site over the period.
- Sites ceasing to use Wellbeing Software (e.g. crossing over to a new system). Data relating to births recorded in the new maternity information system will not be extracted.

5.9 Outliers

Any outliers in the data will be discussed as part of the project team and, if necessary, the Study Management Team. In such scenarios, outliers will either be retained or deleted from the study database (and documented using syntax); there will be no opportunity to go back to sites to verify the data item.

5.10 Analysis Time Frame

Analysis will be performed when all data has been received and cleaned. No emerging results will be presented as the study proceeds. Maternal and infant outcomes will be reported concurrently.

6. Statistical analyses

6.1 Descriptive analysis

We will describe the numbers of records received from Wellbeing Software across all sites and depict in a flow chart the total number of women and babies for Groups 1 to 5.

We will describe the following by each NHS site:

- number and rate of opt-outs;
- number and rate of women not using a pool (Group 5);
- number and rate of women using a pool (Groups 1-4);
    - by risk status (low-risk (Groups 1-3)/ underlying condition (Group 4));
        - rate of waterbirth.

Maternal and infant characteristics such as age, parity and ethnicity of all women giving birth in the study sites during data collection will be obtained and the characteristics of women who do and who not use a pool during labour, will be compared and described (see Table 2 for list of characteristics).

Table 2. Maternal and infant characteristics

	Group				
	5	4	3	2	1
Maternal characteristics					
Age at birth (years)*	✓	✓	✓	✓	✓
Maternal ethnicity	✓	✓	✓	✓	✓
Lead professional at labour onset	✓	✓	✓	✓	✓
Smoker at time of booking	✓	✓	✓	✓	✓
Issues with language/literacy	✓	✓	✓	✓	✓
Deprivation score quintile (Townsend)	✓	✓	✓	✓	✓
Risk factor	✓	✓	✓	✓	✓
Type of condition:					
Vaginal Birth after Caesarean (VBAC)	✓	✓	✓	✓	✓
Induction	✓	✓	✓	✓	✓
Previous OASI	✓	✓	✓	✓	✓
Gestational diabetes	✓	✓	✓	✓	✓
Para 4+	✓	✓	✓	✓	✓
Multiple pregnancy	✓	✓	✓	✓	✓
Thyroid disease**	✓	✓	✓	✓	✓
Other	✓	✓	✓	✓	✓
Complications per woman (none, 1, 2, 3,4+)	✓	✓	✓	✓	✓
Parity (primiparous / multiparous)*	✓	✓	✓	✓	✓
Body Mass Index (BMI) (Height/weight)*	✓	✓	✓	✓	✓
Gestational age at birth (weeks)*	-	✓	✓	✓	✓
Duration of labour*	-	✓	✓	✓	✓
Complications of labour	-	-	✓	✓	✓
Manual removal of placenta	-	✓	✓	✓	✓
Mode of birth	-	✓	✓	✓	✓
Meconium stained liquor at birth **	-	✓	✓	✓	✓
How was fetal heart rate (HR) monitoring performed?	-	✓	✓	✓	✓
CTG and syntocinon use in pool	-	✓	✓	✓	✓
Birth position	-	✓	✓	✓	✓
Reason for leaving pool prior to birth (maternal/infant intrapartum problems)	-	✓	✓	✓	✓
Perinatal deaths	-	✓	✓	✓	✓
Maternal and infant outcomes (for women with risk factors who use a pool)	-	✓	-	-	-
Infant					
Birthweight (g)*	-	✓	✓	✓	✓
Small for gestational age (<10th centile)**	-	✓	✓	✓	✓
Infant head circumference (cms)*	-	✓	✓	✓	✓
Sex of baby**	-	✓	✓	✓	✓
Duration ruptured membranes to birth**	-	✓	✓	✓	✓
Intrapartum fever**	-	✓	✓	✓	✓
Fetal heart rate concerns in labour	-	✓	✓	✓	✓

**potential confounders for maternal primary outcome; ** potential confounders for infant primary outcome*

6.2 Main comparative analysis: Group 1a+1b versus Group 2a +2b – 'low-risk' mothers by birth in water or not, in whom there was no clinical concerns prior to birth.

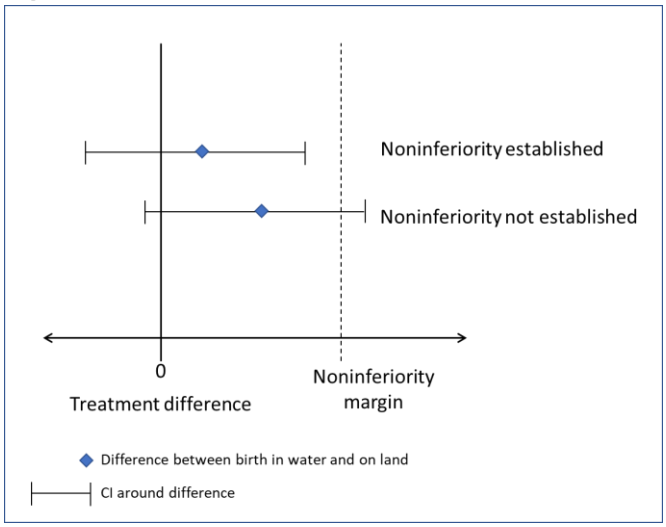
6.2.1 Primary outcomes

The primary analyses are based on a non-inferiority test of births occurring in water versus births occurring out of water comparing:

1. the proportion of mothers that have OASI (based on retrospective and prospective Wellbeing Software data), and
2. the proportion of infants with a composite outcome of 'adverse infant outcome or treatment' (based on prospective Wellbeing Software and National Neonatal Research Database (NNRD) data).

A non-inferiority trial aims to demonstrate that birth in water is not worse than birth out of water by more than the non-inferiority margin and is established at the 5% (one-sided) if the upper limit of the CI for the difference between groups is below the margin (Figure 3).

Figure 3. One-sided test procedure and the noninferiority margin in noninferiority testing.



Maternal outcome: Non-inferiority will be concluded if the upper limit of the 95% CI for the difference in the proportion of OASI between the groups is less than 1.0% (Odds ratio (OR) <1.23) in nulliparous low-risk women and less than 0.6% (OR<1.38) in parous women. The data will then be combined to assess the effects averaged across both strata.

Infant outcome: Non-inferiority will be concluded if the upper limit of the 95% CI for the difference in infant outcome between the groups is less than 1.0% (OR<1.21).

To test the primary hypothesis of non-inferiority between babies born in water versus leaving the pool before birth, both the maternal and infant primary outcomes will be evaluated for non-inferiority using logistic regression models. Three sets of ORs will be presented alongside a one-sided 95% CI: unadjusted odds ratio, adjusted OR for selected confounders (no imputation), adjusted OR for selected confounders (with imputation).

For maternal outcomes, women will be the unit of analysis (denominator) and those leaving the pool to give birth will be used as the reference group for all comparative analyses. For infant

outcomes, babies will be the unit of analysis (denominator) and those with mothers leaving the pool to birth will be used as the reference group for all comparative analyses. All analyses will use a mixed-effects two-level regression model to allow for clustering of outcomes by site. As we anticipated a small number of twins, we will not be accounting for the clustering of infants within mothers within site.

6.2.1.1 Secondary analyses

If non-inferiority is shown, then a superiority analysis will be conducted as a secondary analysis of the primary outcomes using logistic regression and will again be presented as an (unadjusted and adjusted) OR, alongside a 95% CI.

An important secondary analysis of the infant primary composite outcome using both retrospective and prospective data Wellbeing Software and NNRD data will be examined, thus increasing the sample size and the power of this analysis. NNU admissions requiring respiratory support and intrapartum stillbirth, or early neonatal death are captured over both periods of data collection in both sources. However, this outcome will not include administration of intravenous antibiotic within 48 hours of birth among babies not admitted to an NNU.

6.2.1.2 Delivery of placenta in water

An important subgroup is that of women who birthed in water, by whether the placenta was delivered in water, or the woman left the pool during the third stage. We will examine the primary maternal and infant outcomes and postpartum haemorrhage of >1000ml between these two groups.

6.2.2 Secondary outcomes

Secondary outcomes will have non-inferiority testing as detailed above. All outcomes listed in table 3 alongside the study population used, sensitivity analyses and analysis model. In addition, for mothers who give birth in water, we will examine the rates and management of postpartum haemorrhage (PPH) of >1,000 ml. We will also describe the rates and treatment of haemorrhage for the subgroup of 'low-risk' women who, following birth in water (Group 1a + 1b), deliver the placenta underwater and for those that leave the water prior to delivery of the placenta.

The method of analysis is dependent on the outcome type e.g., binary (yes/no, presence or absence of events), continuous, and count data. Binary outcomes will be modelled using logistic regression models and effect estimates presented as ORs comparing the odds of an event in waterbirth compared to land. For continuous outcomes, a multilevel linear model will be fitted, and results presented as difference in means (waterbirth minus birth on land). Count data will be analysed using a Poisson multilevel model. If the distribution of events displayed signs of over dispersion (greater variance than might be expected in a Poisson distribution), then a Negative Binomial model (NBM) will be used. Estimates will be presented as the incidence rate ratio (IRR) in waterbirth compared to on land. All parameter estimates will be accompanied by a 1-sided 95% confidence interval and p-value.

Table 3: All POOL outcomes, study populations used, sensitivity analyses and analysis model

Outcomes	Study population: Whole data (W) / from site open (P)	Outcome definition	Analysis
Maternal outcomes			
Primary			
Obstetric Anal Sphincter Injury	W	Presence/ absence	LO
Secondary			
Intrapartum			
Shoulder dystocia	W	Presence/ absence	LO
Required management of shoulder dystocia	W	See categories in Appendix 2	ORD
Planned and actual Management of the third stage of labour	P	Placenta delivered into water; Placenta delivered out of water	LO
Need for obstetric involvement in woman's care including sepsis	W	Yes, need for obstetric involvement. No need.	LO
Reason for obstetric involvement in woman's care	W	Categorical to include Sepsis; caesarean section	ORD
Incidence of perineal and other genital trauma	W	Presence/absence	LO
Management of perineal and other genital trauma	W	See categories in Appendix 2	ORD
Maternal position at birth	W	See categories in Appendix 2	ORD
Haemorrhage (PPH defined as blood loss>500ml)	W	Yes /no	LO
Treatment for haemorrhage	W	3rd stage drugs/3rd stage fluids	ORD
Maternal postnatal			
Duration of postnatal stay	W	Count of days	PO/NBM
Breast feeding initiation	W	Yes – Breast (expressed/maternal milk) No – artificial/breast (donor), No feed given	ORD
Breast feeding continuation (at community discharge of care)	W	Yes – Exclusively Breast (EBM) No – artificial milk feeding/combined	ORD
Need for higher-level care	W	Yes /no	LO
Maternal readmission to hospital (within seven days of birth)	W	Yes /no	LO
Infant outcomes			
Primary			
Adverse infant outcomes or treatment	P	Presence/absence	LO
Secondary			
Timing of cord clamping	W	Delayed cord clamping >60 seconds after birth or not	LO
Apgar scores @ 1, 5 and 10 min	W	Low score = <7 Healthy score = 7+	LO
Neonatal unit admission requiring respiratory support	W	Yes/No	LO

Outcomes	Study population: Whole data (W) / from site open (P)	Outcome definition	Analysis
Neonatal unit admission length of stay	W	Count of days	PO/NBM
Antibiotic administration commenced within 48 hours of birth (with/without culture proven infection)	W (among babies admitted to an NNU) P	Yes/No/Attempted but unsuccessful	ORD
For babies receiving IV antibiotics above, duration of antibiotics	W (among babies admitted to an NNU) P	<48 hours, 5 days, 6-7 days, >7 days, Other	ORD
Intrapartum stillbirth or neonatal death prior to NNU/postnatal ward discharge occurring within 7days of birth	W	Neonatal death/ Stillbirth (Antepartum/Intrapartum resuscitation attempted /not attempted)	ORD
Neonatal resuscitation	W	Yes/No	LO
Snapped umbilical cord prior to clamping	P	Yes/No	LO
Skin-to-skin contact at birth	W	Yes/No	LO
First breastfeed within first hour	W	Yes/No	LO
Culture proven infection	W (among babies admitted to an NNU) P	Yes/No	LO
Brachial plexus injury	W	Yes/No	LO
Treatment for jaundice	W	Yes/No	LO
Readmission to hospital within 7 days of birth	W	Yes/No	LO
Receipt of therapeutic hypothermia	W (NNRD only)	Yes/No	LO
NNU admissions	W (NNRD only)	Count of admissions	PO/NBM
Respiratory support	W (NNRD only)	Yes/No	LO
Highest C reactive protein (CRP) results	P	Continuous CRP result	LIN
Successful / attempted lumbar puncture	 P	Presence/absence	LO
Blood culture positive with a recognised pathogen (excluding skin commensal organisms)	W (among babies admitted to an NNU P	Presence/absence	LO

NNU=neonatal unit; NNRD= National Neonatal Research Database; LIN = Linear regression; LO = Logistic regression; ORD = Ordinal regression; PO/NBM= Poisson or negative binomial regression.

6.3 Subgroup analysis

A planned and powered subgroup of the primary maternal outcome will be conducted to compare rates separately for primiparous and multiparous women. The relationship between the proportion of women using a pool during labour, at individual sites and the incidence of adverse maternal and primary outcomes will be described and explored. A planned sub-group of the primary infant composite outcome will also be conducted to compare rates separately for infants born to primiparous and multiparous women. These pre-planned analyses will be conducted by the inclusion of appropriate interaction terms (waterbirth exposure x parity) in the regression models. Results will be presented using interaction coefficients, 95% CI and p-value.

6.4 Sensitivity analyses

For both maternal and infant primary outcomes a number of sensitivity analyses will be performed to assess the robustness of the results to factors which may introduce bias (i.e. definition of risk and the study populations, maternal characteristics associated with waterbirth, and fetal heart rate concerns).

6.4.1 Risk categorisation

To identify women with risk factors at the commencement of labour we will use both definitions of low-risk (as described in section 5.5.3), using a) a combination of risk factors described in the existing E3 fields and the midwives' assessment at pool entry and b) using the midwives' assessment at the time of pool entry alone. We will quantify agreement in risk categorisation by source.

6.4.2 Clinical need

The study will report outcomes for both study populations reflecting (a) 'pure' low-risk (an absence of risk factors inboth E3 and at popl entry) and (b) real life (risk described at the time of pol entry alone) (as described in section 5.5.6).

Primary analysis: (Group 1a+1b versus Group 2a +2b as the 'reflects real life' practice.

Sensitivity analysis: Group 1a (birth in pool+no clinical concerns) versus Group 2a (birth in /out of pool+no clinical concerns) as the 'pure' low-risk.

6.4.3 Propensity score analysis

Whether a woman who uses water immersion during labour remains in the pool for birth is likely to be influenced by their age, parity and other characteristics. This will result in imbalanced comparison groups. Incorporating propensity scores, i.e. the 'propensity' of a woman to choose a waterbirth, in the analysis is a way of controlling for this bias. Propensity score methods can examine, quantify and balance the recorded characteristics between treatment (therapy) and the control group. It can be easily implemented, and a large number of measurable covariates adjusted for. However, the ability to match within smaller areas may be restrictive and the algorithm may fail to find a control unless the matching is relaxed (e.g. a set limit or calliper is used). This will result in either a smaller overall sample size or imperfect balance. It also allows a more detailed examination of the impact of imbalanced comparison groups on the results. This method of matching results in better covariate balance and produces estimates with greater precision.

Measurable maternal characteristics associated with both waterbirth, and outcome will be pre-specified (e.g. age at gestation, parity). The balance of maternal characteristics (or degree of

bias) will be examined by exposure groups by calculating standardised differences for all variables, with a standardised difference of 10% or more to be indicative of imbalance. If they appear to be different, we will employ propensity score methods using logistic regression and a propensity score produced for all individuals to be used for matching purposes. Matching between treatment and controls will be done using a nearest neighbour (NN) method with a caliper (maximum permitted difference) of 0.2 of the standard deviation of the logit.[9] If too many controls are excluded, we will re-weight on the propensity score (using inverse probability weighting), so that no controls are excluded.

6.4.4 Instrumental variable analysis

Instrumental variables (IV) are factors associated with outcomes only via their association with exposure (in this case to birthing in water) and are independent of other factors associated with exposure. IVs can deal with the unobserved factors in selection bias and can add potential value to a study dealing with just observable factors. Such variables might include midwifery practice, or other factor that encapsulates unit culture. The capture of denominator data to provide information on the proportion of women using water for labour or birth at each unit, and the qualitative component of the study, will be used in this analysis.

6.5 Missing data

We will use multiple imputation methods (using the mi command in Stata) if data are found to be missing (completely) at random (likely to be only applicable where data is truly missing. To assess the effect of missing data on the results of the primary analysis, a sensitivity analysis is planned using multiple imputation techniques to impute missing data for each of the potential confounders included in the adjusted regression models, under the assumption that the data were missing at random. This assumes that the reason data are missing is not dependent on the value of the missing data if it were known. Missing outcome data would not be imputed since we cannot assume that these data are missing at random.

6.6 Bias

There is a potential for reporting bias of the risk categorisation at pool entry collected by midwives after site opening, as this will usually be recorded after the outcome of the baby/mother was known. To examine this bias we will examine trends in the incidence of overall risk and by categories over the study period and by the data sources (E3 existing fields and midwives' entry) to detect any increases caused my 'diagnostic drift'.

6.7 Exploratory

Several exploratory analyses will be conducted:

- We will examine the impact of the COVID-19 pandemic on the rates of pool use, waterbirths and other procedures that might have been altered by the pandemic (such as the rate of women under obstetric care, inductions, use of syntocinon etc) by examining trends overall and by sites.

[9] Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Statistics in medicine 2009;28:3083-107.

- We will examine the trends in antibiotic use in neonates, and whether change in trends can be attributed to a change in use of guidelines (from NICE to sepsis calculator). We will also examine the association with the factors associated with rates of antibiotic use.
- What are the factors associated with rates of pool use in individual maternity units?
- What are the maternal and site characteristics for pool use in low-risk women?
- The women classified as high-risk (Group 4) who used a pool during labour will be characterised by whether they gave birth in the pool or not and examine outcomes.

7. Guidelines

The reporting of findings will be in accordance with the STROBE[10] and RECORD[11] recommendations for reporting observational studies using routinely collected data.

8. Software

Statistical analysis will be performed in Stata (version 16 or higher).

[10] von Elm E AD, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, for the STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies. PLoS Med 2007(4(10):e296).

[11] Benchimol EI SL, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM for the RECORD Working Committee. The Reporting of studies conducted using observational routinely collected health Data (RECORD) Statement PLoS Med 2015(Oct 6;12(10):e1001885).

Appendix 1. NICE Intrapartum Care Guidelines

Table 1 and 2 show extracts from NICE Guidance[2] providing medical conditions or situations in which there is increased risk for the woman or baby during or shortly after labour, where care in an obstetric unit would be expected to reduce this risk. The factors listed in appendix table 3 and 4 are not reasons in themselves for advising birth within an obstetric unit, but indicate that further consideration of birth setting may be required.

Table 1. Medical conditions indicating increased risk suggesting planned birth at an obstetric unit

Disease area	Medical condition
Cardiovascular	• Confirmed cardiac disease • Hypertensive disorders
Respiratory	• Asthma requiring an increase in treatment or hospital treatment • Cystic fibrosis
Haematological	• Haemoglobinopathies – sickle-cell disease, beta-thalassaemia major • History of thromboembolic disorders • Immune thrombocytopenia purpura or other platelet disorder or platelet count below 100×10^9/litre • Von Willebrand's disease • Bleeding disorder in the woman or unborn baby • Atypical antibodies which carry a risk of haemolytic disease of the newborn
Endocrine	• Hyperthyroidism • Diabetes
Infective	• Risk factors associated with group B streptococcus whereby antibiotics in labour would be recommended • Hepatitis B/C with abnormal liver function tests • Carrier of/infected with HIV • Toxoplasmosis – women receiving treatment • Current active infection of chicken pox/rubella/genital herpes in the woman or baby • Tuberculosis under treatment
Immune	• Systemic lupus erythematosus • Scleroderma
Renal	• Abnormal renal function • Renal disease requiring supervision by a renal specialist
Neurological	• Epilepsy • Myasthenia gravis • Previous cerebrovascular accident
Gastrointestinal	• Liver disease associated with current abnormal liver function tests
Psychiatric	• Psychiatric disorder requiring current inpatient care

Table 2. Other factors indicating increased risk suggesting planned birth at an obstetric unit

Factor	Additional information
Previous complications	• Unexplained stillbirth/neonatal death or previous death related to intrapartum difficulty • Previous baby with neonatal encephalopathy • Pre-eclampsia requiring preterm birth • Placental abruption with adverse outcome • Eclampsia • Uterine rupture • Primary postpartum haemorrhage requiring additional treatment or blood transfusion • Retained placenta requiring manual removal in theatre • Caesarean section • Shoulder dystocia
Current pregnancy	• Multiple birth • Placenta praevia • Pre-eclampsia or pregnancy-induced hypertension • Preterm labour or preterm prelabour rupture of membranes • Placental abruption • Anaemia – haemoglobin less than 85 g/litre at onset of labour • Confirmed intrauterine death • Induction of labour • Substance misuse • Alcohol dependency requiring assessment or treatment • Onset of gestational diabetes • Malpresentation – breech or transverse lie • BMI at booking of greater than 35 kg/m2 • Recurrent antepartum haemorrhage • Small for gestational age in this pregnancy (less than fifth centile or reduced growth velocity on ultrasound) • Abnormal fetal heart rate/doppler studies • Ultrasound diagnosis of oligo-/polyhydramnios • Cholestasis* • Labour outside of 37+0 and 41+6*
Previous gynaecological history	• Myomectomy • Hysterotomy

**Some additional conditions, not included in the NICE guidelines, have been identified that if present would be also regarded as contraindications to pool use in labour and therefore if present would classify the woman as 'high-risk'*

Table 3. Medical conditions indicating individual assessment when planning place of birth

Disease area	Medical condition
Cardiovascular	• Cardiac disease without intrapartum implications
Haematological	• Atypical antibodies not putting the baby at risk of haemolytic disease • Sickle-cell trait • Thalassaemia trait • Anaemia – haemoglobin 85–105 g/litre at onset of labour
Infective	• Hepatitis B/C with normal liver function tests
Immune	• Non-specific connective tissue disorders
Endocrine	• Unstable hypothyroidism such that a change in treatment is required
Skeletal/neurological	• Spinal abnormalities • Previous fractured pelvis • Neurological deficits

Table 4. Other factors indicating individual assessment when planning place of birth

Factor	Additional information
Previous complications	• Stillbirth/neonatal death with a known non-recurrent cause • Pre-eclampsia developing at term • Placental abruption with good outcome • History of previous baby more than 4.5 kg • Extensive vaginal, cervical, or third- or fourth-degree perineal trauma • Previous term baby with jaundice requiring exchange transfusion
Current pregnancy	• Antepartum bleeding of unknown origin (single episode after 24 weeks of gestation) • BMI at booking of 30–35 kg/m2 • Blood pressure of 140 mmHg systolic or 90 mmHg diastolic or more on 2 occasions • Clinical or ultrasound suspicion of macrosomia • Para 4 or more • Recreational drug use • Under current outpatient psychiatric care • Age over 35 at booking
Fetal indications	• Fetal abnormality
Previous gynaecological history	• Major gynaecological surgery • Cone biopsy or large loop excision of the transformation zone • Fibroids

Appendix 2. Wellbeing software fields for primary and secondary outcomes

Maternal outcomes

Outcome	Data source (E3/NNRD) R=retro P=prosp	E3/NNRD Field name	Population
Primary outcome			
Obstetric Anal Sphincter Injuries (OASI)	E3R/P	AnalgesiaPerineum PerinealRepair PerineumVaginalTears ConsentSuturing	All women
Secondary outcomes			
Intrapartum			
Shoulder dystocia	E3R/P	EpisiotomyReason ShoulderDystocia ShoulderDystociaHelp HeadDeliveredMode	All women
Required management of shoulder dystocia	E3R/P	In babies with shoulder dystocia: McRoberts ManoeuvresPerformed SuprapubicPressure EpisiotomyPerformed PosteriorArm WoodScrewManoeuvre AllFoursPosition OtherManoeuvres	In babies with sh. dystocia
Time from Head born to time of birth (the longer duration the worst outcome)	E3R/P	To be derived by E3: HeadDeliveriedToBirthDuration	All women
Management of the third stage of labour	E3 P E3 R/P	POOLThirdStageMgt/POOLPlacentaDelivered/ Intended PlacentadeliveredHow OxytocinDrug3rd Stage Analgesia3rdStage	All women with a pool birth

Outcome	Data source (E3/NNRD) R=retro P=prosp	E3/NNRD Field name	Population
Need and reason for obstetric involvement in woman's care including sepsis	E3 P E3R/P	At labour: POOLObstetricCare Postnatally: AnalgeisaPerineum AnaesProcedurePerformed AnaesthsiaAtCaesarean AnalgesiaDelivery DrugsPostDelivery IVTherapyPostDelivery LabourAugmented MLUTransferredOut MLUTransferReason MonitoringChangedInLabour PerineumVaginalTears PlaceOfBirth PlacentaDeliveredHow (MROP) PNT_OtherProbs POOLObstetricCare PostnatalProblems ProblemsIntrapartum ProblemsMaternal ProblemsPostDelivery ReasonForChangeAN ReasondelPlaceChange Transferred TransferHospital (variables to pick up sepsis) PostnatalProblems Problemspostdelivery	All women that used a pool All women

Outcome	Data source (E3/NNRD) R=retro P=prosp	E3/NNRD Field name	Population
		problemsintrapartum	
Maternal position during vaginal birth	E3R/P	DeliveryPosition Semi-recumbent Left lateral Squatting Kneeling All fours Lithotomy Other Birthing stool Standing	All women
Treatment for haemorrhage 1. was there a haemorrhage? (PPH defined as blood loss>500ml, >1,000ml) 2. treatment for haemorrhage (Massive obstetric haemorrhage >1500ml)	E3R/P	BloodLossAtDelivery +BloodLossAfterDelivery AnaesCriticalIncidents(>1L) ProblemsPostDelivery 3rd stage drugs: PlacentadeliveredHow OxytocinDrug3rd Stage IVTherapyPostDelivery	All women
		3rdstage fluids: BloodTransfusion MOHcause MOHManagement MOHOperativeIntervention MOHBloodProductsInfused PNT_BloodTransfusion	
Incidence of perineal and other genital trauma	E3R/P	PerineumVaginalTears PerinealRepair	All women

Outcome	Data source (E3/NNRD) R=retro P=prosp	E3/NNRD Field name	Population
		Anagesia3rdstage	
Management of perineal and other genital trauma		PerinealRepair: Interrupted (labial lacerations only) Interrupted 1 layer repair Interrupted 2 layer repair Continuous 1 layer repair Continous 2 layer repair End to end (3rd degree tear) Overlapping (3rd degree tear)	
Postnatal			
Duration of postnatal stay	E3R/P	PN_StayDuration	All women
Breast feeding initiation and continuation (at community discharge)	E3R/P	Fed1hour PNT_Feeding Method FeedingMethodDelivery BNT_FeedingMethod BNT_FeedingType BNT_Breastmilk48Hrs BreastFeedingAt10Days FDFeeding (final discharge)	All women
Higher level care (NB: many delivery suites provide a HDU care so may not say)	E3R/P	Postnatal problems Transferred (ITU/HDU/other->main recovery) PNT_Mode PNT_DischargeMethod AnaesCriticalIncidents	All women
Maternal readmission to hospital within seven days of birth	E3R/P	ReAdmission PNT_Reason PNT_RoutineCare	All women

Infant Outcomes

Outcome	Data source (E3/NNRD) R=retro P=prosp	E3/NNRD Field name	Population
Primary outcome			
Composite of 'adverse infant outcomes or treatment' to include:			
a) any neonatal unit admission requiring respiratory support	E3R/P NNRD	TransferToNN4B/BNT_Separation/ BNT_ReasonNICUAdmission/ BNT_LengthNICUAdmission/ BNT_Destination TimeBirthToResps Respsupportgiven/numberofrespdays/ Methods1-14	All babies
b) intravenous antibiotic administration within 48 hours of birth (with or without culture proven infection)	E3 P NNRD	POOLAntibioticCommenced POOLAntibioticDuration anti48given	All babies whose mother had a pool birth
c) intrapartum stillbirth or infant death prior to neonatal unit/postnatal ward discharge	E3 NNRD	Outcome/ PbRComplications/ StillbirthClassification Death	All babies
Secondary outcomes			
Timing of cord clamping	E3R/P NNRD	CordClamping CordClamp TimeOfCordClamp	All babies
Apgar scores	E3R/P / NNRD	Apgar1MinuteNN4B_Value Apgar5Minutes_Value Apgar_1min Apgar_5min	All babies
Incidence of:			
NNU admissions requiring respiratory support		numberofadmissions Respsupportgiven	
Administration and duration of intravenous antibiotics	E3 P	POOLAntibioticsCommenced POOLAntibioticsDuration	All babies

Outcome	Data source (E3/NNRD) R=retro P=prosp	E3/NNRD Field name	Population
	NNRD	antiGivenIV/numberofantidays	
Cause of intrapartum stillbirth or all deaths prior to neonatal unit/postnatal ward discharge, neonatal deaths that occurred within seven days of birth on a neonatal unit/postnatal ward	E3R/P NNRD	Outcome (live-/stillbirth/early neonatal death) StillbirthClassification CauseofDeath1-3	All babies
Neonatal resuscitation	E3R/P NNDR	DrugsotherProcedures (intubation) DurationBirthToIntubation IntermitPosPresVenti DurationO2Intubation TimeBirthToResps Methods1-14	All babies
snapped umbilical cord prior to clamping	E3 P	CordSnap	All babies
skin to skin contact at birth	E3 R/P	SkinToSkinContact SkinToSkinDuration	All babies
first breastfeed within first hour	E3 R/P	Fed1Hour	All babies
culture proven infection	E3 P NNRD	POOLBloodCulture POOLCRPResult AnyGrowth	All babies given antibiotics
brachial plexus injury	E3 R/P NNRD	BirthInjurySuspected brachialplexus_injury	All babies
treatment for jaundice	E3 R/P NNRD	BNT_JaundiceTreatment BNT_Admitreason BNT_ProblemsPriorDischarge JaundiceTreatmentGiven	All babies
readmission to hospital within seven days of birth	E3 R/P NNRD	BNT_Admitreason BNT_ActionTaken readmission	All babies
Therapeutic hypothermia	NNRD	thGiven	All babies
Neonatal unit admissions	NNRD	numberofadmissions	All babies

Outcome	Data source (E3/NNRD) R=retro P=prosp	E3/NNRD Field name	Population
Respiratory support (same as primary)	NNRD	Respsupportgiven	All babies
Confirmed neonatal sepsis			
Highest CRP results	E3 P	POOLCRPResult	All babies given antibiotics
Successful / attempted lumbar puncture	E3 P	POOLBabyLumbarPunc	All babies given antibiotics
Blood culture positive with a recognised pathogen (excluding skin commensal organisms)	E3 P NNRD	POOLBloodCulture	All babies given antibiotics
Delivery of placenta in or out of water Third stage management	E3 P E3 R/P	POOLPlacentaDelivered PlacentaDeliveredHow	All women with a pool birth