The WILL Trial - Summary

(When to Induce Labour to Limit risk in pregnancy hypertension – a multicentre, randomised controlled trial)

WILL aims to address optimal timing of delivery for women with chronic or gestational hypertension who reach term gestational age and are otherwise well. We will investigate the clinical effectiveness and cost-effectiveness of two timing of delivery approaches, to provide data for women (to make informed choices about their care based on maternal and perinatal risk) and the NHS (to plan services).

This UK-wide multi-centre randomised controlled trial will run in ≈85 NHS consultant-led maternity units. WILL is NIHR-funded and will be adopted on portfolio.

Inclusion criteria	Exclusion criteria
● Maternal age ≥16 years; ● Diagnosis of chronic or gestational hypertension; ● Singleton pregnancy; ● Live fetus; ● Gestational age of 36^{+0} to 37^{+6} weeks; and ● Able to give documented informed consent to participate	● Contraindication to either one of the trial arms (e.g., evidence of pre-eclampsia); ● Severe hypertension [i.e., blood pressure (BP) ≥160mmHg systolic or ≥110mmHg diastolic] until BP falls below this level (i.e., it is 'controlled'); ● Major fetal anomaly anticipated to require neonatal unit admission ● Participation in another timing of delivery trial NOTE: Neither maternal co-morbidities (e.g., diabetes) nor fetal size will be exclusion criteria

Ideally, women will learn about WILL early in pregnancy, but eligibility will not be confirmed until 36^{+0}-37^{+6} weeks to minimise enrolment of women who may develop an indication for delivery (e.g., pre-eclampsia) or go into spontaneous labour prior to 38^{+0-3} weeks, the planned timing of delivery in the intervention arm.

At 36^{+0} to 37^{+6} weeks, ideally at their routine antenatal visit, women will be assessed for eligibility by the research midwife. The research midwife or medically-qualified member of the obstetric team will obtain informed consent (remote or in person, as per locally accepted practice). Following consent, the research midwife will collect women's baseline data.

If women are at 37^{+0-6} weeks at consent, they will be randomised (1:1 allocation, minimised by centre, hypertension type [chronic or gestational], and prior Caesarean) to one of the two timing of delivery approaches (as below). If, however, women are at 36^{+0-6} weeks at consent, the research midwife will re-contact them at 37^{+0-6} weeks, by phone or in person, to confirm that women remain 'well' (and ensure that they do not need to be reassessed by their care provider for an indication for delivery) and then randomise them in WILL. This is to minimise the number of women who may deliver spontaneously or develop an indication for caregiver-initiated delivery before 38^{+0-3} weeks, the planned timing of delivery in the intervention arm. As such, the trial will consent ≈1,317 pregnant women with chronic or gestational hypertension, in order to randomise 1,080 women.

Interventions: Women will be randomised to one of two timing of delivery approaches:

(i) Planned early term delivery at 38^{+0} to 38^{+3} weeks by labour induction (local protocol) or elective Caesarean (if previously indicated); or

(ii) Usual care at term, in accordance with the routine practice at individual sites, with maternal and fetal monitoring (local protocol), awaiting spontaneous labour or delivery indicated by clinical need (e.g., refractory severe hypertension or pre-eclampsia).

Outcomes (measured until hospital discharge or 28 days of life, whichever is earlier):

Maternal co-primary outcome: This is a composite of 'poor maternal outcome' until primary hospital discharge home or 28 days after birth (whichever is earlier) and includes:

- Systolic BP ≥160mmHg or diastolic BP ≥110mmHg; or
- Maternal death; or
- Maternal morbidity (as a composite of end-organ dysfunction defined by international consensus)

Neonatal co-primary outcome: Neonatal care unit admission for ≥ 4 hours

Key secondary outcome: Caesarean delivery

Support: Although study participants will follow local care pathways for Usual Care , research midwife support will be provided to approach, recruit, consent and support follow-up of women in the study. WILL has been adopted

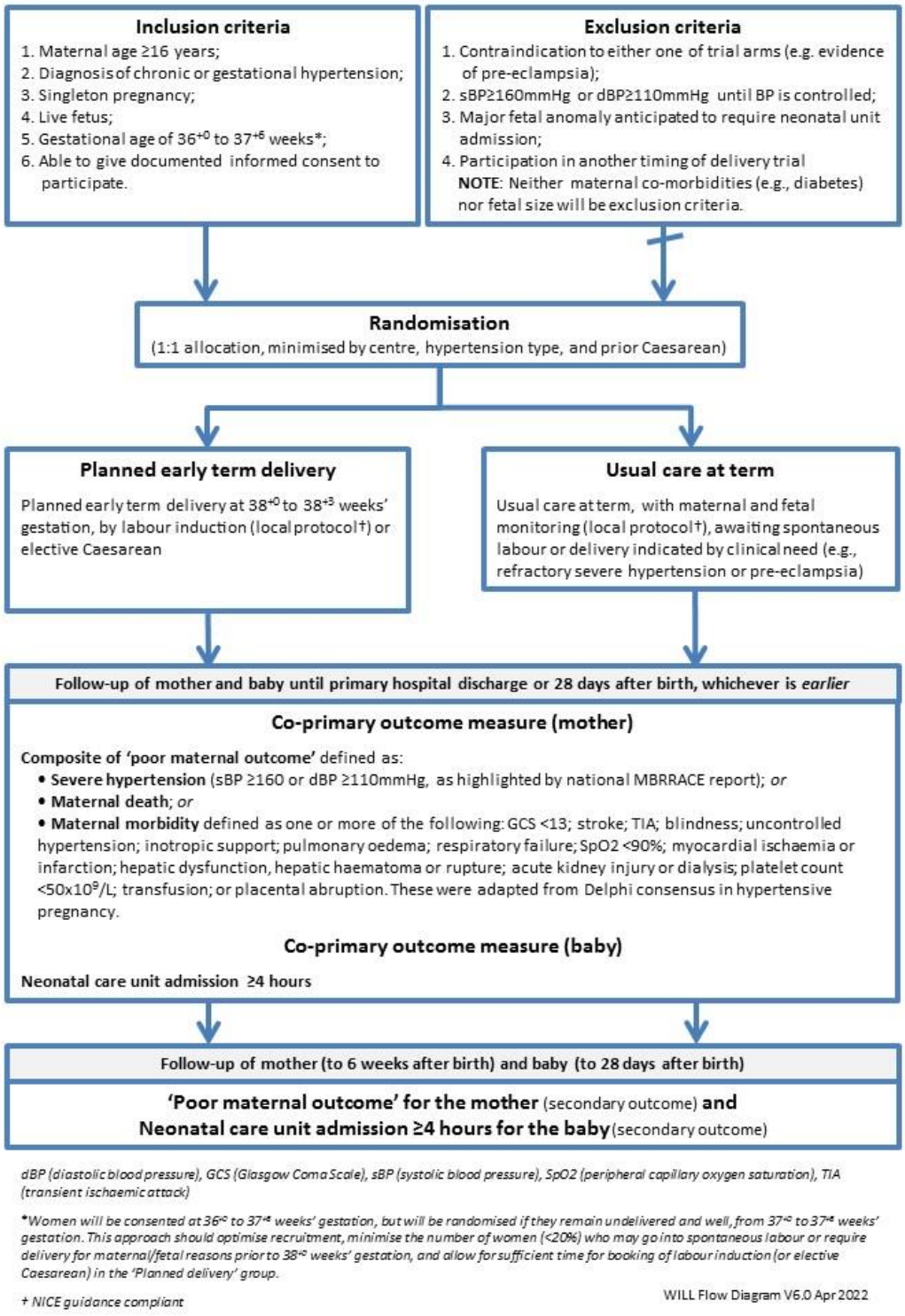
The WILL Trial - Summary

(When to Induce Labour to Limit risk in pregnancy hypertension – a multicentre, randomised controlled trial)

onto the NIHR portfolio, so CLRN network support is available. In addition, each centre will receive £300 per woman randomised.

If you are interested in WILL, please contact the WILL trial team on 0121 4159109 or at WILL@trials.bham.ac.uk
Thank you!

WILL Trial Schema



dBP (diastolic blood pressure), GCS (Glasgow Coma Scale), sBP (systolic blood pressure), SpO2 (peripheral capillary oxygen saturation), TIA (transient ischaemic attack)

**Women will be consented at 36+0 to 37+6 weeks' gestation, but will be randomised if they remain undelivered and well, from 37+0 to 37+6 weeks' gestation. This approach should optimise recruitment, minimise the number of women (<20%) who may go into spontaneous labour or require delivery for maternal/fetal reasons prior to 38+0 weeks' gestation, and allow for sufficient time for booking of labour induction (or elective Caesarean) in the 'Planned delivery' group.*

+ NICE guidance compliant

WILL Flow Diagram V6.0 Apr 2022