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Abstract:

Introduction: Maternal obesity increases the risk of multiple maternal and infant pregnancy complications, such as gestational diabetes and preeclampsia. Current UK guidelines use body mass index (BMI) to identify which women require additional care due to increased risk of pregnancy complications. However, BMI may not accurately predict which women will develop complications during pregnancy as it does not determine amount and distribution of adipose tissue. Some adiposity measures (e.g. waist circumference, ultrasound measures of abdominal visceral fat) can better identify where body fat is stored, which may be useful in predicting those women who need additional care.

Methods and analysis: This prospective cohort study aims to evaluate the prognostic performance of adiposity measures (either alone or in combination with other adiposity, socio-demographic or clinical measures) to estimate risk of adverse pregnancy outcomes. Pregnant women (n=1400) will be recruited at their first trimester ultrasound scan at Newcastle upon Tyne NHS Foundation Trust (NUTH),

UK. Early pregnancy adiposity measures and clinical and socio-demographic data will be collected. Routine data on maternal and infant pregnancy outcomes will be collected from routine hospital records. Regression methods will be used to compare the different adiposity measures with BMI in terms of their ability to predict pregnancy complications. If no individual measure performs better than BMI, multi-variable models will be developed and evaluated to identify the most parsimonious model. The apparent performance of the developed model will be summarised using calibration, discrimination and internal validation analyses.

Ethics and dissemination: This cohort study has been registered with ISRCTN (ISRCTN82185177). Ethical favourable opinion has been obtained from the North East: Newcastle & North Tyneside 1 Research Ethics Committee (REC reference: 22/NE/0035). Planned dissemination includes peer-reviewed publications and additional dissemination appropriate to target audiences, including policy briefs for policymakers, media/social-media coverage for public, and conferences for research

Strengths and limitations of this study

- This research will address the current evidence gap on whether adiposity measures are more accurate than BMI at predicting risk of pregnancy complications, either on their own or combined with other measures.
- This prospective cohort includes the collection of multiple measures of adiposity and pregnancy outcomes, which will enable direct comparison of measures and an exploration of differences in risk prediction across a range of maternal and infant outcomes.
- Extensive patient, public and stakeholder involvement has been carried out at all stages of the study design to improve research quality and strengthen its relevance and impact on maternity services.
- This is a cohort study from a single NHS Trust in the North East of England, UK, and therefore findings may not be directly generalisable to other populations. We will validate the findings of this study in new populations in a subsequent validation study.

Introduction

In England, 21% of women have pre-pregnancy obesity (BMI≥30.0kg/m^2) which equates to approximately 189,000 women per year based on current birth rates [1, 2]. A further 28% have an overweight BMI (25.0-29.9kg/m^2) which is approximately 245,500 women/year [1, 2]. Maternal obesity increases the risk of adverse pregnancy outcomes, including gestational diabetes (GDM), preeclampsia, large- and small-for-gestational-age (LGA/SGA) baby, and pre- and post-term delivery [3-6]. Additionally, women with obesity, and their children, are more likely to develop obesity and diabetes in the longer-term [3, 4, 7].

UK guidelines use early pregnancy BMI as a proxy measure for pre-pregnancy BMI to identify women who have obesity and to allocate additional antenatal care. This includes consultant-led obstetric and anaesthetic care, additional screening and monitoring such as screening for GDM and growth scans, and delivery in a high-dependency unit [8, 9]. Implementation of obesity guidance is a challenge to maternity services due to the high prevalence of maternal obesity, and associated costs [2, 10, 11]. A UK study identified that 22% of NHS Trusts were not adhering to the GDM screening guidelines for women with obesity, and key barriers to adherence were lack of capacity, resource and funding given the high prevalence of maternal obesity [12]. A recent systematic review identified 13 studies exploring the economic costs of maternal obesity [13], including five from the UK [10, 14-17]. The review found that average incremental costs of obesity ranged from €191 to €16,046, with higher costs among studies that included both neonatal and maternal care costs compared to those only reporting either maternal or neonatal costs (€8,964 and €1,612 respectively).

Identifying which women require additional care due to increased risk based on BMI may not be an efficient use of NHS resources. Many women who have an obese BMI do not develop any pregnancy complications and therefore do not require care offered. A multicentre study among 5,628 women from the UK, Ireland, New Zealand and Australia reported that 47% of pregnant women with an obese BMI had an uncomplicated pregnancy (53% developed complications), whereas 42% of women with an overweight BMI developed pregnancy complications (58% had uncomplicated pregnancies) [18]. In the NHS context, based on current birth rates

and maternal obesity prevalence, this prevalence of uncomplicated pregnancies would translate to approximately 87,000 women with an obese BMI each year who are not at increased risk of complications, yet receive additional care. The prevalence of women with an overweight BMI who do develop complications (that are usually associated with obesity) equates to approximately 103,000 women/year who would benefit from additional care but are not eligible based on their BMI. The similarity in numbers of women with an obese BMI who receive care but do not need it, and women with an overweight BMI who require additional care but do not receive it, suggests that more accurate targeting would have minimal net impact on the total cost of providing care but would improve pregnancy outcomes for women and their babies.

One potential reason for the inability of BMI to accurately determine which women will develop complications in pregnancy relates to the high variation in individual phenotype. This makes BMI a poor predictor of adiposity-level and risk, especially among women and some ethnic groups [19]. A meta-analysis of studies in non-pregnant populations shows that using obese BMI criteria only identifies 50% of adults with excess adiposity, as BMI cannot distinguish between fat mass and lean mass, whereas measures of body fat distribution can better distinguish individuals' mortality and cardiometabolic risk [20, 21]. This proportion is similar to that observed for women who do not have an obese BMI in pregnancy yet develop complications; these women may have excess adiposity not identified by BMI.

Failure to accurately predict which women are at risk of adverse pregnancy outcomes results in harm for the mothers and babies and increases healthcare costs. Furthermore, inaccurate risk communication can increase anxiety and distress for women [22]. There is an urgent need to identify whether there are measures of adiposity with greater sensitivity and specificity than BMI to inform targeted antenatal care, to improve health of women and babies, and make a better use of NHS resources. This prospective cohort study will measure adiposity in early pregnancy to explore the ability of these measures to predict adverse pregnancy outcomes. A range of potential measures exist which use anthropometry (e.g., waist circumference, neck circumference, skinfold thickness), imaging such as ultrasound or MRI scans (e.g., to measure subcutaneous and visceral fat) and bioelectrical

impedance (e.g., to measure body fat). However, some measures such as MRI scans and bioelectrical impedance are impractical for implementation into routine pregnancy care. Therefore, this study will focus on adiposity measurements that are feasible to implement in routine NHS maternity care.

Aim and objectives

The aim of this cohort study is to evaluate the prognostic performance of single adiposity measures or a multivariable model to estimate risk of adverse pregnancy outcomes (i.e., a risk prediction development study).

The objectives of this prognostic factor and model developmental study are:

1. To identify the prognostic value of single adiposity measures for predicting adverse maternal, fetal and neonatal outcomes (for each outcome of interest separately, and as a composite outcome).
2. To develop a prognostic model to investigate the effect of including multiple adiposity, socio-demographic, and clinical predictors on the accuracy of predicting outcomes.
3. To test the predictive performance of the prognostic measures/models using calibration, discrimination, and internal validation techniques.

Methods and analysis

Study design and setting

This is a prospective observational cohort study in pregnant women. The setting is the maternity unit at The Newcastle upon Tyne Hospitals NHS Foundation Trust (NUTH) where women attend for their 1st trimester ultrasound dating scan conducted at 11^{+2} to 14^{+1} weeks' gestation.

Study participants

Pregnant women are recruited at their dating scan appointment, starting from April 2022, and we will continue recruitment until sample size achieved. Baseline adiposity measures and other potential predictor variables of interest for a multi-variable model (including clinical and socio-demographic data) will be collected from women at this time, or from routine hospital records. Pregnancy outcomes will be collected from routine hospital records after delivery.

Inclusion and exclusion criteria

Inclusion criteria are women with a singleton pregnancy, ≥18 years of age, attending their dating scan between 11^{+2} to 14^{+1} weeks gestation, with a planned delivery at the recruiting NHS Trust. Women will be excluded if they are unable/unwilling to give informed consent to participate, have a miscarriage prior to the dating scan, have an Early Pregnancy Assessment Clinic or accident and emergency visit relating to their pregnancy with a recorded adverse outcome (e.g., miscarriage), or are identified as having twin or higher order pregnancy at the time of the dating scan.

Recruitment procedure

The recruitment procedure is embedded into routine processes and care pathways as much as possible. The process of contacting women for study recruitment is detailed in Figure 1. This involves the clinical teams sending a study letter to women referred to the maternity unit for their dating scan. The letter will also be added to the patient app Badger Notes which has a notification system to alert users to the letter (see Supplemental material 1). The clinical teams will phone the women to book their routine dating scan appointment and discuss the SHAPES study to enquire whether they might be interested in taking part. Those interested will be booked into the research clinic for their dating scan and will be sent the detailed participant information sheet (Supplement material 2). Women will be asked to provide written informed consent (Supplement material 3) on the day of their scan appointment. Additionally, some women may be approached upon arrival for their routine scan appointment with an offer to participate in this study and the informed consent process will be followed. Women will be offered three printed pictures of their baby from their scan appointment with a framed mount as a thank you gift for taking part in the study. They can also opt into taking part in a prize draw to win one of 40 available £100 gift vouchers. Finally, we will also promote the study via a website (https://research.ncl.ac.uk/shapes/) and social media (the Newcastle Maternity Voices Partnership Facebook page and Connie e-midwife website) to provide an additional opportunity for any eligible women to enquire about the research directly. Any women who do not provide informed consent on the day of their scan appointment will have their routine dating scan carried out, but no additional measurements for the SHAPES cohort study.

Figure 1. Study recruitment procedure

Footnote: NUTH - Newcastle Hospitals NHS Foundation Trust

Sample size

A sample of 1400 women will be recruited to the study. The sample size was based (at the time of grant application) on the 'rule of thumb' that 10 events (cases of the outcome) were required for each variable included in a multi-variable model to predict an outcome. However, recent developments in prognostic model research allowed us to confirm the above sample [23-25]. The sample size calculation is based on a maximum of 7 candidate variables that are associated with both maternal obesity and adverse pregnancy outcomes (Supplemental material 4) and the least common pregnancy outcome, which is preeclampsia (estimated prevalence of approximately 5-6% of pregnancies in the UK) [26]. This number of candidate variables is similar to previously published validated prognostic models in pregnancy including between 1 and 7 predictor variables [27-30]. Targeting a shrinkage factor of ≤10% and C-index equal to 80%, we would need a minimum sample of 980 participants for a new model development for pre-eclampsia. Given that other outcomes are more prevalent compared to pre-eclampsia, they would require sample sizes smaller lower than the above figure.

Data collection

Participants' dating scans will be performed by a qualified trained sonographer. Once viability of the pregnancy and normal fetal anatomy is confirmed, the additional ultrasound adiposity measures needed for the study will be performed by the study sonographer. The remaining data collection will be performed by a trained member of the research team.

The methods of adiposity measurement are detailed in Table 1. Ultrasound scans of subcutaneous and visceral abdominal fat volume will be performed using a GE E8 ultrasound machine (GE Healthcare Austria, GmbH & Co OG) with 2.3-8.4 MHz curvilinear probe. Methods described by Martin *et al.* [31] will be used to obtain the measurement. Ultrasound settings and patient position will be standardised to ensure consistency of the procedure. Further, image capture will be standardised for breathing movements (on expiration) and bladder filling. Midline transverse section

of the maternal abdomen will be obtained approximately 1cm superior to the umbilicus to allow visualisation of the transverse section of the abdominal aorta at the far field of the screen. The mean of three consecutive measurements will be employed in the analysis. In a small sub-set of participants, measurements will be repeated by a second operator to assess inter-rater reliability of the ultrasound technique. In addition to the above measurements of SAT and VAT, an alternative method of measuring these by ultrasound will be deployed to establish optimal methods for future implementation. SAT and VAT will be measured at the sagittal plane of xiphisternum as described by Cremona *et al* [32]. All anthropometry measurements will be taken directly on the skin (unless otherwise specified in Table 1) on the right side of the body unless impracticable due to injury, in which case the left side may be used. All anthropometric measurements will be taken by individuals who have received anthropometry training following the measurement protocols detailed by the International Society for the Advancement of Kinanthropometry [33]. Measurements will be taken in duplicate, and a third measurement taken if the difference between the first two measures is greater than 5% for skinfolds or 1% for all other measures. If two measures are taken, the mean value will be used in data analysis. If three measures taken, the median value will be used. Adverse outcomes of interest are shown in Table 2.

Table 1: Methods of adiposity measurement

Adiposity measure	**Measurement**
Subcutaneous Adipose Tissue[1]	Midline transverse section of the maternal abdomen, approximately 1 cm above the umbilicus from outer border of the subcutaneous fat layer to the outer border of rectus abdominus at the level of linea alba
Visceral Adipose Tissue[1]	Midline transverse section of the maternal abdomen, approximately 1 cm above the umbilicus from the inner border of rectus abdominus at the level of linea alba to the anterior wall of the aorta

Pre-peritoneal Subcutaneous Adipose Tissue [1]	Sagittal plane of xiphisternum from the lower border of the cutaneous layer to the upper border of the linea alba
Pre-peritoneal Visceral Adipose Tissue [1]	Sagittal plane of xiphisternum from the lower border of linea alba to the upper border of the liver capsule
Waist circumference[2]	Narrowest point of the abdomen between the lower costal (10th rib) border and the top of the iliac crest, perpendicular to the long axis of the trunk, at the end of normal expiration and with the abdominal muscles relaxed, to the nearest 0.1cm
Hip circumference[2]	Greatest posterior protuberance of the buttocks, perpendicular to the long axis of the trunk, with the gluteal muscles relaxed and the feet together, over light clothing and to the nearest 0.1cm
Height[2]	To the nearest 0.1cm with shoes removed and the participant's head positioned in the Frankfort plane
Weight[2]	In light clothing to the nearest 100g
Neck circumference	Immediately superior to the thyroid cartilage and perpendicularly to the long axis of the neck with the head in the Frankfort plane, to the nearest 0.1cm
Mid upper arm circumference	Midpoint of the upper arm between the acromiale and radiale, perpendicular to the long axis of the arm, to the nearest 0.1cm
Skinfold thickness[3]	Subscapular, triceps, biceps, iliac crest and supraspinale measured using Harpenden skinfold callipers, to the nearest 0.1mm

[1] Total adipose tissue will be calculated as a sum of subcutaneous and visceral adipose tissue

[2] Waist to hip ratio, waist to height ratio, BMI, Body adiposity index, A Body Shape Index (ABSI), Hip Index, Weight-Adjusted Waist Index, Body Roundness Index, Total abdominal fat, Abdominal Volume Index, Conicity Index, estimated total body fat, Relative fat Mass, CUN-BAE and body fat percentage will be calculated from these measurements.

[3] Sum of skinfolds will be calculated using 5 skinfold measurements

Table 2: Pregnancy outcomes for the SHAPES cohort

Outcomes	**Definition**
Maternal outcomes	

Outcomes	Definition
Gestational diabetes	Fasting plasma glucose level of ≥ 5.6 mmol/litre or 2-hour plasma glucose level of ≥7.8 mmol/litre
Gestational hypertension	Blood pressure ≥140/90 mmHg on two occasions at least 4 hours apart after 20 weeks' gestation
Preeclampsia	New onset of hypertension (>140 mmHg systolic or >90 mmHg diastolic) after 20 weeks of pregnancy with a new onset of proteinuria or/and maternal organ dysfunction or/and uteroplacental dysfunction. Early onset defined as onset of PE before 34 weeks gestation.
Induction of labour	Non-surgical treatment to induce the labour
Caesarean section	Surgical delivery of baby (emergency or elective)
Instrumental delivery	Assisted birth when forceps or a ventouse suction cup is applied
Retained placenta	As reported in medical records.
Maternal infection	As reported in medical records.
Postpartum haemorrhage (PPH)	3rd stage of labour and immediate postpartum period, measured in ml blood loss
Maternal length of stay in hospital	From admission date for any stay resulting in delivery to date of discharge
Infant outcomes	
Fetal growth	Measured at 2nd and 3rd trimester scans, including: 2nd trimester scan: Fetal head circumference; Fetal abdominal circumference; Fetal Femur Length; Estimated fetal weight Hadlock 3rd trimester scan: abdominal circumference; Femur Length; Estimated fetal weight Hadlock; Umbilical artery PI; End Diastolic flow; Amniotic Fluid Index
Pre-term birth	Birth before 37 weeks gestation
Late-term birth	Pregnancy that extends over 41 weeks gestation
Large for gestational age	birth weight above the 90th centile for gestational age and sex on INTERGROWTH chart

Outcomes	Definition
Small for gestational age	Birth weight below the 10th centile for gestational age and sex on INTERGROWTH chart [34]
Apgar score	1 and 5 minutes
Neonatal jaundice	As reported in medical records
Neonatal respiratory distress (requiring resuscitation)	Any of the following: Cords visualised meconium seen; Cord visualised no meconium; Facial air; Facial oxygen; Mucus extraction or suction; Positive pressure by bag or mask; Positive pressure by endotracheal tube
Feeding method	First feed: Artficial; Breast mother; Breast donor; Breast and artificial; No feed given Feed method at discharge: breastfeeding or artificial feed or both breast and artificial
Infant admission to specialist care	admission to neonatal special care baby unit (SCBU) or intensive care unit (NICU), high-dependency care, transitional care; length of stay if admitted

[1] Note this outcome can only be determined for those women who have had an oral glucose tolerance test (OGTT)

A number of socio-demographic and clinical variables associated with adverse pregnancy outcomes will be collected, as well as data to inform health economics analysis (e.g., place of delivery, length of inpatient stay, maternal medications use) and any reason for loss to follow up (e.g., late miscarriage, stillbirth, or participant moving to another area) (Supplemental material 4).

Data management

Participant identifiable information will be handled in line with GDPR 2018 principles. Initial data collection and storage will be via REDcap, a password-protected database. Data will be stored on the NHS secure server under Caldicott approval until recruitment is complete. At the end of the recruitment period, data will be anonymised using a unique identifier for each participant. Following completion of all follow-up data collection, anonymised electronic research data will be transferred to a Newcastle University secure server for analysis. No personal identifying information will be presented in the study outputs.

Analysis

The aim of the analysis is to explore if any single adiposity measure taken in this study performs better than BMI in terms of predicting women who develop an adverse pregnancy outcome. Each adiposity measure will be assessed individually and compared with BMI. Where possible, secondary sub-group analysis will be carried out for different ethnic groups. If no individual measure performs better than BMI, multiple logistic regression model(s) will be used for the analysis of each outcome separately. Wherever possible, we will retain continuous candidate predictors in their continuous form to avoid statistical power loss [35]. Nonlinear trends in continuous predictors will be explored using either fractional polynomials or restricted cubic splines.

The apparent performance of the developed model(s) will be summarised using calibration, discrimination and internal validation analyses [36]. Calibration determines performance in terms of the agreement between the probability of developing the outcome as estimated by the measure/model, and the observed outcome frequencies. Discrimination is the measure of the model's ability to distinguish between individuals who develop the outcome or not (i.e., a higher probability assigned to the individual who develops the outcome compared with an individual who does not. This will be assessed using the c-index (equivalent to the area under the receiver operating characteristic [AUROC] curve). Any missing values will be assumed to be missing at random (MAR) and multiple imputation (MI) will be implemented using 20 imputations [37]. Calibration and discrimination of the developed model(s) will be summarised in the development datasets (averaged over imputation datasets). Calibration will also be assessed graphically [38].

The model(s) will be internally validated using bootstrap re-sampling method in order to quantify the degree of optimism due to overfitting [39, 40] and to derive optimism-adjusted indices of discrimination (c index) and calibration (calibration slope). Two hundred bootstrap samples will be used [40, 41]. Optimism is expected when measures/models are applied to the same dataset used for development, as they have been developed to achieve the best fit for that specific dataset (i.e., overfitting). Statistical techniques (e.g., bootstrapping) can quantify the potential for overfitting,

and provide adjustment estimates (e.g., shrinkage factor) to reflect the prognostic performance in a new dataset/population.

Patient, Public, and Stakeholder Involvement

Extensive patient, public, and stakeholder involvement has been carried out for this research. Pregnant and postnatal women, clinical stakeholders (obstetricians, midwives, sonographers) and the NIHR Research Design Service North East and North Cumbria consumer panel were involved in the development of the proposed research funding application, protocol, and in planning how to embed PPI into this research.

PPI consultations were carried out with pregnant and postnatal women attending a community group. Discussion topics included: acceptability and timing of adiposity measurements; reviewing the plain English and PPI sections of the funding application; discussing how to communicate research to pregnant women and wider public; future PPI involvement in the research; the process of recruitment involving sending letters and follow up phone calls; the provision of thank you gifts to research participants; reviewing the PIS, recruitment letters and social media advertisements. PPI members strongly thought this research was a priority and we addressed issues raised during these discussions by amending our planned research methods, such as the recruitment strategy. We have planned consultations with pregnant and postnatal women to be embedded throughout the research, as well as having PPI representatives on the steering group and as a co-investigator (JS).

Key discussion points with clinical stakeholders included considering the effect of existing guideline interventions for women with a BMI≥30kg/m^2 as women will continue to receive this routine care during the research time period; recruitment and measurement logistics in the routine antenatal scan clinics; equipment and training required for sonographers to carry out the additional ultrasound measurements; and processes for recruitment. Clinical stakeholders will continue to be involved in the steering group.

Ethics and dissemination

This is a low risk, observational study. This study has been reviewed and given a favourable opinion by the North East - Newcastle & North Tyneside 1 Research Ethics Sub-Committee and the Health Research Authority. Caldicott and local R&D approvals will be in place before the study begins. The study sponsor is Newcastle upon Tyne Hospitals NHS Foundation Trust.

The SHAPES study is part of a wider NIHR Advanced Fellowship research programme. The planned research programme includes validating the results of the SHAPES cohort study in a subsequent study, using individual participant data meta-analysis methods. An economic evaluation of implementing an alternative approach to risk prediction into routine NHS maternity care is also planned. All research will be published in peer-reviewed journals. Further dissemination will be audience appropriate, for example utilising research briefs, policy briefs, media coverage and stakeholder and participant communication to achieve this goal. The target audiences for this work are health professionals and their affiliated organisations, pregnant women and their families, maternity managers and commissioners of services, national and international policy makers, wider public, third sector, and other researchers.

Authors' contributions: NH and LV developed the concept for this research and secured funding. All authors contributed to the development of the protocol and ethics application. RV, VM and RT developed the clinical implementation of the research, including the process of recruitment and logistics of measurements being carried out in routine clinics. TB and DT provided statistical methods input. GN and NH drafted this manuscript and all authors contributed to reviewing and editing.

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Competing interests statement: Investigators confirm that there are no conflicts of interest for the research study.

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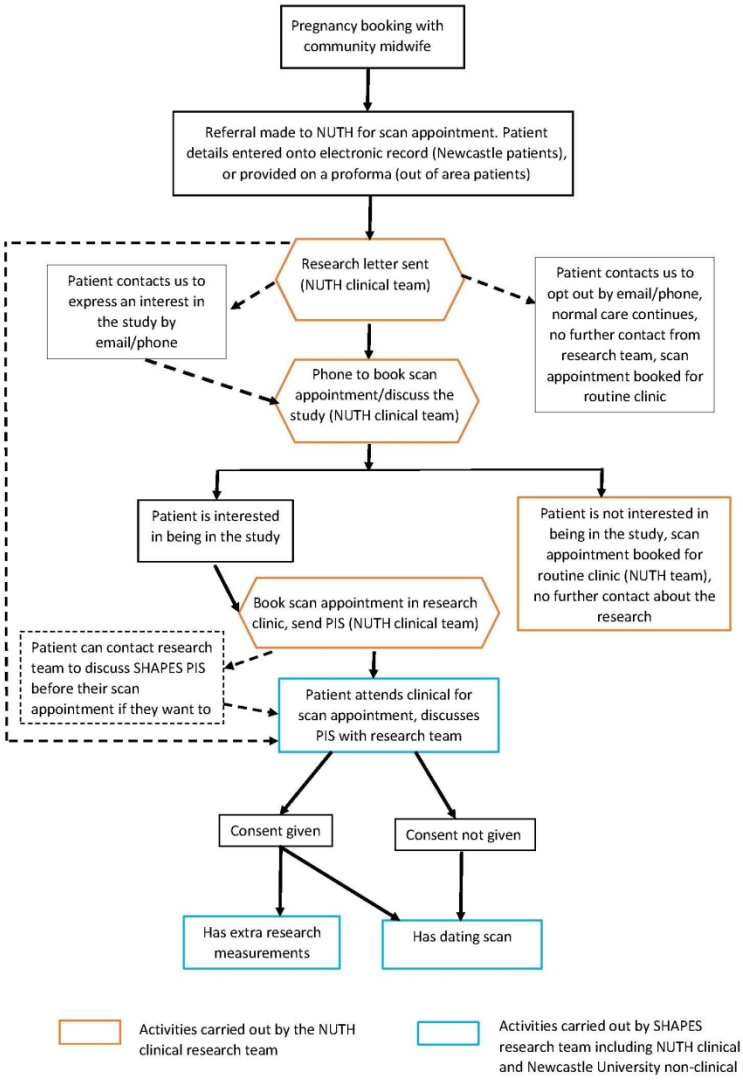

Figure 1. Study recruitment procedure

210x297mm (200 x 200 DPI)

Supplement material

1. Research Information Letter [1]

About the SHAPES research

A pregnant woman's Body Mass Index (also known as BMI) is used to identify which women might need extra care in pregnancy. Currently, women with a high BMI get extra care. However, BMI might not be the best measure to use and women's body shape in early pregnancy might be better. SHAPES will explore if other measurements, such as waist size or ultrasound scans, can be used to identify which women would benefit most from extra care during pregnancy. We need 1400 women with a whole range of BMIs to take part.

A member of the clinical team at NuTH might discuss this research with you over the phone if they call to book your routine 12-week scan appointment, or in the waiting room when attending for your scan appointment. If you are interested in taking part in this research, you will receive more detailed written information about the study to read and discuss with the research team. All the extra body shape measurements will be done at your 12-weeks scan appointment, which will take about an extra 45 minutes. As a thank you for your time, you will receive 3 photos of your baby from your 12-week scan, and you can be entered into a prize draw to win £100 shopping vouchers.

We only have a limited number of research appointments available each week, so unfortunately, we can't offer them to everyone. This means you may not be contacted about the research. If you think you might be interested in taking part, you can contact us directly. If you do not want anyone to approach you about this research, please let us know and we won't contact you.

Contact details: email: nuth.rhnresearch@nhs.net phone: 0191 2820362

For more information about this study, please visit our website: http://research.ncl.ac.uk/shapes/

Yours sincerely

Victoria Murtha, Principal Investigator for the SHAPES Study, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust

[1] This letter goes out to women alongside a generic letter from NUTH about research in maternity services, alongside summaries of other research projects active at the same time as SHAPES.

2. Participant Information Sheet (PIS)

Study of **h**ow **a**diposity in **p**regnancy has an **e**ffect on outcome**s**: the SHAPES study

Participant Information Sheet

Research Centre: The Newcastle Upon Tyne Hospitals NHS Foundation Trust

Chief Investigator: Nicola Heslehurst, Newcastle University

Principal Investigator: Victoria Murtha, Newcastle upon Tyne NHS Foundation Trust, Reproductive Health Research Team, The Royal Victoria Infirmary (RVI), 0191 2820362, nuth.rhnresearch@nhs.net

We would like to invite you to take part in a research study. Before you decide if you want to take part it is important that you understand what it will involve. Please take time to read this document and discuss it with others if you wish. You will have the opportunity to discuss the research with a member of the team when you attend for your 12-week scan appointment and we encourage you to do this if there is anything you are unsure of. If you have received this information sheet before your scan appointment, you can contact us directly if you would like to discuss anything in advance.

Part one of this document tells you about the purpose of the study and what would happen if you decided to take part. Part two provides information about optional extras, which are extra parts of this research that you can choose whether or not you want to take part in. Part three gives more details about the conduct of the research. Further contact details are on the last page of this document.

Part One

What is the purpose of the research? This research will explore body shape in early pregnancy and how it impacts on the health of women and babies. The NHS uses Body Mass Index (BMI) to identify who might need extra care in pregnancy. However, there may be more accurate measures than BMI to understand who would most benefit from extra pregnancy care. We will look at body shape in early pregnancy, and need women with a whole range of BMIs to take part. This research will inform how maternity services provide care to improve health of women and babies.

Why have I been invited? The study is being carried out at the RVI. We are inviting pregnant women attending this hospital for a 12-week scan, and aim to include 1400 women in this study.

What will happen to me if I take part? A member of the research team will discuss the research with you at your 12-week scan appointment. If you decide to take part, you will be asked to sign a consent form. We will take some extra body shape measurements on the same day as your scan

appointment. The sonographer who is doing your 12-week scan will take some extra ultrasound measurements. A female researcher will then take all the extra measurements in a private room. These will include your waist size, hip size, upper arm size, neck size, skinfold measurements of fat stored underneath the skin, height and weight. We will need to draw some lines on your arms, stomach and back using an erasable pen. It would be helpful if you could wear a loose-fitting top and lightweight clothing on the day. Most of the measurements will be taken using a tape measure. The skinfold measurements will use callipers to compress the skin, but this should not cause any pain. You will also be asked to fill in a short questionnaire to get some extra information about you, for example your age, ethnic group and postcode. We will review your routine maternity notes after you have had your baby so that we can get information about your pregnancy, for example, how you delivered your baby. You don't need to do anything else for this research after your 12-week scan appointment.

Will I learn more about my own body shape measurements or health? No. We don't yet know which body shape measurements are most accurate, so we can't give you any feedback on this.

What will happen to the results of the research study? The results from this study will be used to see how well body shape measurements relate to health during pregnancy. This will give us a better idea of which women and babies would benefit the most from extra care during pregnancy. The results will be published in a scientific journal so that other researchers and health professionals can learn from this research. You would not be identified in any results we present or publish. If you would like to receive a summary of results from the study, then we can share these with you.

What are the possible benefits and disadvantages of taking part? Your hospital ultrasound scan appointment will take up to 45 minutes longer than normal. There are no direct benefits for you during this pregnancy but taking part in this research could help to improve care of for women and their babies during pregnancy in the future. To say thank you for taking part you will receive a photograph mount with three printed pictures of your baby from your 12-week scan which will be given to you on the day of your scan appointment. You can also take part in a research prize draw which will be drawn at the end of the research. There are 40 prizes of £100 shopping vouchers to be won.

Do I have to take part? No. Participation is voluntary, and it is up to you to decide if you want to participate in the study. If you do not want to take part, you do not have to give a reason and your care will not be affected in any way. If you have received this document before your scan appointment and you decide that you don't want to take part in the study, you can either contact us to let us know before attending for your appointment or turn up and let us know on the day. Your scan appointment will go ahead as planned whether you decide to take part in this research or not.

What if I change my mind? You are free to withdraw from the study at any time, without giving a reason. If you change your mind, your care will not be affected in any way. If you want to withdraw from the study, please use the contact details on page 1 of this document.

Part Two: Optional Extras[2]

There are two optional extras for this research. You can still take part in the research without agreeing to either of these optional extras, or you can choose to agree to one or both of them.

SHAPES Study Interviews: You will be asked by the research team if you are happy to share your contact details with the research team at Newcastle University for a second study related to SHAPES. The second study involves being interviewed about your experiences of having the extra body shape measurements taken. If you agree to share your contact details now, this does not mean that you are agreeing to be interviewed, you are only agreeing to share your contact details with the research team. Not all women who share their details will be contacted as there will be 1400 women in SHAPES and only around 30 women will be interviewed. If you are contacted about the interview study, you will receive detailed written information and have the opportunity to discuss with the researchers before deciding whether to take part. If you don't want to take part, you do not have to give a reason and your care won't be affected in any way.

Future research about long-term health and well-being of women and their children: We would like to explore whether body shape in early pregnancy is linked to the future health and well-being of women and their children. An example of the type of research question we would be asking would be "can waist size measured at 12-weeks in pregnancy identify which women or children develop diabetes later in life?" If pregnancy measurements are useful, then we could plan ways to support women and children after pregnancy to try and improve long-term health and well-being.

To do this future research, we would need your consent to store your NHS number, name and date of birth, and your baby's NHS number and date of birth, linked to your SHAPES Study ID number. This is needed so that we can link the SHAPES data with routinely collected health data in the future, through organisations such as NHS Digital, hospital attendance data and GP records. For example, we could link to medical records to see if you or your child has been diagnosed with diabetes at any point after pregnancy. This extra research will only involve accessing routine electronic data and not any further contact with you. Any researcher who wants to access your health records can only do so if you consent to the use of your data in this way, and will follow best ethical and legal practice.

Part Three

Will my taking part in the study be kept confidential? Yes. Newcastle upon Tyne Hospitals NHS Foundation Trust, based in the United Kingdom, is the sponsor for this study and will act as the data controller for it. This means they are responsible for looking after your information and using it properly. Newcastle upon Tyne Hospitals NHS Foundation Trust will keep identifiable information about you for 5 years after the study has finished. Newcastle upon Tyne Hospitals NHS Foundation Trust will collect information from you and/or your medical records for this research study in

[2] Women in the SHAPES study can choose to consent to any combination of the optional extras, or none of them, and can still take part in SHAPES

accordance with our instructions. Only trained clinical-research team members will have access to your information.

Your rights to access, change, or move your information is limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personal identifiable information possible.

Individuals from Newcastle upon Tyne Hospitals NHS Foundation Trust (NuTH) and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The research team will pass these details to individuals at NuTH along with the information collected from you and/or your medical records upon request for audit purposes. The only people in NuTH who will have access to information that identifies you will be people who need to contact you to discuss this study or audit the data collection process. People outside the NuTH will have no access to your identifiable information and will not be able to access your medical notes, find out your name, NHS number or contact details.

If you give consent to participate in the study, we would use non-identifiable personal information (through allocating a study ID number) to analyse the data and report the findings. Any paper documents will be stored in a locked fire-resistant cupboard at the RVI. To allow us to analyse the anonymised data it will be transferred to a secure server on the Newcastle University system and stored in accordance with the regulations of the Data Protection Act 2018 and the Newcastle upon Tyne Hospitals NHS Foundation Trust Caldicott guidelines. You can find out more about how we use your information at:

- www.hra.nhs.uk/information-about-patients/
- https://newcastlejro.com/research/new-study/data-security
- Email the NUTH Data Protection Officer, Richard Oliver, richard.oliver2@nhs.net

Future research: If you consent to us keeping your data for future research, it will be stored on a secure server at Newcastle University. Newcastle University will be the data controller for the future research. All data protection regulations will be followed. Even if you agree to us storing this data, we will still need to get ethical approval to access your data again for future research. This would be to make sure we are using the data in the way we have told you about in this document, and that you have consented to. If you consent to us storing your data, we will not share it with anyone else or use it for any other purpose than described in this document. If you consent to us storing this data for future research, you are free to withdraw at any time, without giving a reason. Any information already collected can be destroyed if you wish. If you change your mind, your care will not be affected in any

way. To withdraw from this future research, please contact the chief investigator (contact details on the last page of this document).

What will happen to information collected about me for the research study? The information we collect during the study will be analysed (or processed) to enable us to explore if body shape measurements in early pregnancy relate to the health of women and babies.

Who is organising and funding the research? This project is funded by the Department of Health via the National Institute for Health Research. It is being led by Dr Nicola Heslehurst who is a researcher at Newcastle University.

Who has reviewed the study? This study has been reviewed and given a favourable opinion by North East - Newcastle & North Tyneside 1 Research Ethics Sub-Committee. The study design has been reviewed by Sponsor (NuTH). Members of the public were involved in review of a scope (lay summary), design and incentives for this research.

Extra Contact Details

Where can I get further information about the study? If you have any questions or concerns about participating in the study please contact the clinical lead for this research at the RVI (Victoria Murtha, 0191 2820362, nuth.rhnresearch@nhs.net), or the Chief Investigator from Newcastle University (Nicola Heslehurst, 0191 2083823, nicola.heslehurst@ncl.ac.uk).

What if there is a problem? If you are not satisfied with any aspect of the way you have been approached or treated during the course of this study, you should first speak to the research team (please see contact details on page 1) who will do their best to answer your questions. If you remain unhappy and wish to complain formally, the normal National Health Service complaints mechanisms are available to you: please ask to speak to the complaints manager for the Hospital.

If you have any concerns about how you are treated in relation to this research study, you can raise these with the Patient Advice and Liaison Service (PALS). This service is confidential and can be contacted on Freephone: 0800 032 0202.

Alternatively, if you wish to make a formal complaint you can contact the Patient Relations Department, Tel: 0191 2231382 or 0191 2231454, Email: nuth.patient.relations@nhs.net Address: Patient Relations Department, Newcastle upon Tyne Hospitals NHS Foundation Trust

Thank you for taking the time to read this participant information sheet.

3. Inform consent

Participant Identifica

CONSENT FORM (SHAPES Study)

Study of **h**ow **a**diposity in **p**regnancy has an **e**ffect on outcome**s**

Chief Investigator: Nicola Heslehurst

Please initial box

1. I confirm that I have read the information sheet dated 08/02/2022 (version 2.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of my medical notes and data collected during this study may be looked at by individuals from the Newcastle upon Tyne Hospitals NHS Foundation Trust or relevant regulatory bodies where relevant to my taking part in this research (for example, for the purpose of audit of this research project). I give permission for these individuals to have access to my records. ☐
4. I agree for my information, gathered for this study, to be stored on a secure database for analysis on a Newcastle University server anonymously. ☐
5. I agree to take part in the above study. ☐

Name of participant	Date	Signature
Name of person taking consent	Date	Signature

Please tick the relevant box and provide contact details below if you would like to:

a) take part in the prize draw ☐
b) receive a summary of results for the SHAPES study ☐

e-mail:

Telephone number:

Address:

4. Data items

Data item	Source		
	Measured for research	Routine data: electronic records	Routine data: from paper-based notes
Questionnaire at research visit			
Age at booking*	x		
Gravidity	x		
Parity*	x		
Ethnic group*	x		
Postcode*	x		
Smoking status (in the past 12 months and current smoking)*	x		
Alcohol intake (before pregnancy and current intake)*	x		
Substance use (before pregnancy)	x		
History of bariatric surgery (date and type)	x		
Medical record review at research visit			
Gestational age at research visit		x	x
Blood pressure at booking (systolic and diastolic)*		x	x
Previous caesarean delivery		x	x
Previous macrosomia		x	x
Diabetes history		x	x
Family history of diabetes		x	x
Previous spontaneous preterm birth or mid trimester loss between 16+0 and 34+0 weeks gestation		x	x
Cervical trauma		x	x
Cervical length < 25 mm		x	x
Family history of preeclampsia		x	x
Essential hypertension		x	x
Previous pregnancy hypertension		x	x
Chronic renal disease		x	x
Autoimmune disease		x	x
Last pregnancy >10 years ago		x	x
Previous low birth weight <10%		x	x
Previous still birth		x	x
Previous neonatal death within 4 weeks of life		x	x
Ultrasound and anthropometry measurements at research visit			
Subcutaneous fat	x		
Visceral fat	x		
Pre-peritoneal VAT	x		
Pre-peritoneal SAT	x		
Height at research visit	x		
Weight at research visit	x		
Waist circumference	x		
Hip circumference	x		
Neck circumference	x		
Mid upper arm circumference	x		
Skinfold thicknesses (subscapular, triceps, biceps, iliac crest, supraspinale)	x		
Follow up data linkage			
Congenital anomaly		x	
Reason for outcome data not being available		x	
Number of antenatal scans (in antenatal clinic and fetal medicine)		x	

Data item	Source		
	Measured for research	Routine data: electronic records	Routine data: from paper-based notes
2nd trimester fetal growth (gestation at scan; fetal head circumference; abdominal circumference; femur length; estimated fetal weight)		x	
3rd Trimester fetal growth (gestation at scan; abdominal circumference; femur length; estimated fetal weight; umbilical artery PI; end diastolic flow; deepest pool)		x	
Hospital admissions in antenatal period		x	
Number antenatal clinic appointments (antenatal clinic, fetal medicine and maternity assessment unit)		x	
Infant date of birth or end of pregnancy		x	
Baby sex		x	
Viability (Live birth, still birth, late miscarriage 12-24 weeks)		x	
Neonatal death within 28 days of delivery (and date)		x	
Baby exam colour		x	
Apgar scores at 1 and 5 minutes		x	
Respiratory distress/resuscitation		x	
Feeding method (first feed and at discharge)		x	
Gestation at delivery		x	
Birthweight and percentile		x	
Induction of labour (and reason)		x	
Caesarean delivery (elective or emergency and reason)		x	
Instrumental delivery (and type)		x	
Place of delivery		x	
Water birth		x	
Maternal death (and date)		x	
Maternal folic acid supplementation		x	
Gestational diabetes diagnosis (and gestational age)			
Oral glucose tolerance test (OGTT test (fasting and 2 hour blood glucose)		x	
Preeclampsia (PE) diagnosis (and gestation)		x	
Pregnancy induced hypertension (PIH) diagnosis (and gestation); if yes (stillbirth, proteinuria, birthweight <3%, Abnormal umbilical artery Doppler waveform analysis, Renal insufficiency, Liver involvement, Haematological complications, Neurological complications)		x	
Manual removal of placenta		x	
Maternal infection during pregnancy		x	
Total blood loss 3rd stage and immediate postpartum		x	
Maternal length of stay in hospital		x	
Admission to neonatal intensive, high-dependency, special or transitional care (and length of stay)		x	
Antenatal and discharge medications (and description)		x	

* *A-priori* socio-demographic and clinical candidate predictor variables

BMJ Open

Study of How Adiposity in Pregnancy has an Effect on outcomeS (SHAPES): protocol for a prospective cohort study

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Study of How Adiposity in Pregnancy has an Effect on outcomeS (SHAPES): protocol for a prospective cohort study

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Abstract

Introduction: Maternal obesity increases the risk of multiple maternal and infant pregnancy complications, such as gestational diabetes and preeclampsia. Current UK guidelines use body mass index (BMI) to identify which women require additional care due to increased risk of complications. However, BMI may not accurately predict which women will develop complications during pregnancy as it does not determine amount and distribution of adipose tissue. Some adiposity measures (e.g. waist circumference, ultrasound measures of abdominal visceral fat) can better identify where body fat is stored, which may be useful in predicting those women who need additional care.

Methods and analysis: This prospective cohort study (SHAPES) aims to evaluate the prognostic performance of adiposity measures (either alone or in combination with other adiposity, socio-demographic or clinical measures) to estimate risk of adverse pregnancy outcomes. Pregnant women (n=1400) will be recruited at their

first trimester ultrasound scan (11^{+2}-14^{+1} weeks') at Newcastle upon Tyne NHS Foundation Trust, UK. Early pregnancy adiposity measures and clinical and socio-demographic data will be collected. Routine data on maternal and infant pregnancy outcomes will be collected from routine hospital records. Regression methods will be used to compare the different adiposity measures with BMI in terms of their ability to predict pregnancy complications. If no individual measure performs better than BMI, multi-variable models will be developed and evaluated to identify the most parsimonious model. The apparent performance of the developed model will be summarised using calibration, discrimination and internal validation analyses.

Ethics and dissemination: Ethical favourable opinion has been obtained from the North East: Newcastle & North Tyneside 1 Research Ethics Committee (REC reference: 22/NE/0035). All participants provide informed consent to take part in SHAPES. Planned dissemination includes peer-reviewed publications and additional dissemination appropriate to target audiences, including policy briefs for policymakers, media/social-media coverage for public, and conferences for research

Study registration: ISRCTN82185177.

Strengths and limitations of this study

- This research will address the current evidence gap on whether adiposity measures are more accurate than BMI at predicting risk of pregnancy complications, either on their own or combined with other measures.
- This prospective cohort includes the collection of multiple measures of adiposity and pregnancy outcomes, which will enable direct comparison of measures and an exploration of differences in risk prediction across a range of maternal and infant outcomes.
- Extensive patient, public and stakeholder involvement has been carried out at all stages of the study design to improve research quality and strengthen its relevance and impact on maternity services.
- This cohort study is from a single NHS Trust in the North East of England, UK, and may not be generalisable to other population; therefore, we will validate the findings in new populations in a subsequent validation study.
- There are considerations that need to be factored into any policy change recommendations, such as the costs and benefits of implementing adiposity

measures or more complex risk predictions models compared with BMI; these will be explored in a subsequent health economics study.

Introduction

In England and Wales, 22.4% of women have pre-pregnancy obesity (BMI≥30.0kg/m^2) which equates to approximately 185,000 women per year based on estimated pregnancy rates (approximately 825,000) [1, 2]. A further 28.5% have an overweight BMI (25.0-29.9kg/m^2) which is approximately 235,000 women/year [1, 2]. Maternal obesity increases the risk of adverse pregnancy outcomes, including gestational diabetes (GDM), preeclampsia, large- and small-for-gestational-age (LGA/SGA) baby, and pre- and post-term delivery [3-6]. Additionally, women with obesity, and their children, are more likely to develop obesity and diabetes in the longer-term [3, 4, 7].

UK guidelines use early pregnancy BMI measured by their GP or midwife in the 1st trimester as a proxy measure for pre-pregnancy BMI to identify women who have obesity and to allocate additional antenatal care. This includes consultant-led obstetric and anaesthetic care, additional screening and monitoring such as screening for GDM and growth scans, and delivery in a high-dependency unit [8, 9]. Implementation of obesity guidance is a challenge to maternity services due to the high prevalence of maternal obesity, and associated costs [10-12]. A UK study identified that 22% of NHS Trusts were not adhering to the GDM screening guidelines for women with obesity, and key barriers to adherence were lack of capacity, resource and funding given the high prevalence of maternal obesity [13]. A recent systematic review identified 13 studies exploring the economic costs of maternal obesity [14], including five from the UK [11, 15-18]. The review found that average incremental costs of obesity ranged from €191 to €16,046, with higher costs among studies that included both neonatal and maternal care costs compared to those only reporting either maternal or neonatal costs (€8,964 and €1,612 respectively).

Identifying which women require additional care due to increased risk based on BMI may not be an efficient use of NHS resources. Many women who have an obese

BMI do not develop any pregnancy complications and therefore do not require care offered. A multicentre study among 5,628 women from the UK, Ireland, New Zealand and Australia reported that 47% of pregnant women with an obese BMI had an uncomplicated pregnancy (defined a normotensive pregnancy, >37 weeks gestation, live birth, not small for gestational age, and no other significant pregnancy complications) and 53% developed complications [19]. Pregnancy complications also occurred in other BMI groups: 42% of women with an overweight BMI, 33% of women with a recommended BMI and 38% of women with an underweight BMI [19]. In the NHS context, based on current conception rates and maternal obesity prevalence, this prevalence of uncomplicated pregnancies would translate to approximately 87,000 women with an obese BMI each year who are not at increased risk of complications, yet receive additional care. The prevalence of women with an overweight BMI who do develop complications (that are usually associated with obesity) equates to approximately 136,000 women/year who would benefit from additional care but are not eligible based on their BMI. The similarity in numbers of women with an obese BMI who receive care but do not need it, and women with an overweight BMI who require additional care but do not receive it, suggests that more accurate targeting would have minimal net impact on the total cost of providing care but would improve pregnancy outcomes for women and their babies.

One potential reason for the inability of BMI to accurately determine which women will develop complications in pregnancy relates to the high variation in individual phenotype [20]. This makes BMI a poor predictor of adiposity-level and risk, especially among women and some ethnic groups [21]. A meta-analysis of studies in non-pregnant populations shows that using obese BMI criteria only identifies 50% of adults with excess adiposity, as BMI cannot distinguish between fat mass and lean mass, whereas measures of body fat distribution can better distinguish individuals' mortality and cardiometabolic risk [22, 23]. This proportion is similar to that observed for women who do not have an obese BMI in pregnancy yet develop complications; these women may have excess adiposity not identified by BMI. Two recent systematic reviews and meta-analysis identified 70 observational studies reporting associations between maternal early-pregnancy adiposity and maternal health outcomes [5] and 34 reporting infant outcomes [6]. However, a limitation of the existing evidence-base is the focus on single or few measures of adiposity and/or

pregnancy outcomes within each dataset. This makes it challenging to compare the usefulness of different adiposity measurements for predicating the range of pregnancy outcomes usually associated with obesity. A more comprehensive cohort study including multiple measures and outcomes would enable these direct comparisons between adiposity measures, and with BMI, I the same population of women.

Failure to accurately predict which women are at risk of adverse pregnancy outcomes may result in harm for the mothers and babies and increase healthcare costs. Furthermore, inaccurate risk communication can increase anxiety and distress for women [24]. There is an urgent need to identify whether there are measures of adiposity with greater sensitivity and specificity than BMI to inform targeted antenatal care, to improve health of women and babies, and make a better use of NHS resources. This prospective cohort study will measure adiposity in early pregnancy to explore the ability of these measures to predict adverse pregnancy outcomes. A range of potential measures exist which use anthropometry (e.g., waist circumference, neck circumference, skinfold thickness), imaging such as ultrasound or MRI scans (e.g., to measure subcutaneous and visceral fat) and bioelectrical impedance (e.g., to measure body fat). However, some measures such as MRI scans and bioelectrical impedance are impractical for implementation into routine pregnancy care due to costs and stringent measurement protocols. Therefore, this study will focus on adiposity measurements that are feasible to implement in routine NHS maternity care.

Aim and objectives

The aim of this cohort study is to evaluate the prognostic performance of single adiposity measures or a multivariable model to estimate risk of adverse pregnancy outcomes (i.e., a risk prediction development study).

The objectives of this prognostic factor and model developmental study are:

1. To identify the prognostic value of single adiposity measures for predicting adverse maternal, fetal and neonatal outcomes (for each outcome of interest separately, and as a composite outcome).

2. To develop a prognostic model to investigate the effect of including multiple adiposity, socio-demographic, and clinical predictors on the accuracy of predicting outcomes.
3. To test the predictive performance of the prognostic measures/models using calibration, discrimination, and internal validation techniques.

Methods and analysis

Study design and setting

This is a prospective observational cohort study in pregnant women. The setting is the maternity unit at The Newcastle upon Tyne Hospitals NHS Foundation Trust (NUTH) where women attend for their 1st trimester ultrasound dating scan conducted at 11^{+2} to 14^{+1} weeks' gestation.

Study participants

Pregnant women are recruited at their dating scan appointment, starting from April 2022, and we will continue recruitment until sample size achieved. Baseline adiposity measures and other potential predictor variables of interest for a multi-variable model (including clinical and socio-demographic data) will be collected from women at this time, or from routine hospital records. Pregnancy outcomes will be collected from routine hospital records after delivery.

Inclusion and exclusion criteria

Inclusion criteria are women with a singleton pregnancy, ≥18 years of age, attending their dating scan between 11^{+2} to 14^{+1} weeks gestation, with a planned delivery at the recruiting NHS Trust. Women will be excluded if they are unable/unwilling to give informed consent to participate, have a miscarriage prior to the dating scan, have an Early Pregnancy Assessment Clinic or accident and emergency visit relating to their pregnancy with a recorded adverse outcome (e.g., miscarriage), or are identified as having twin or higher order pregnancy at the time of the dating scan. Due to small numbers of women with twin or higher order pregnancy and different levels of risk to singletons, the study is not powered for this population.

Recruitment procedure

The recruitment procedure is embedded into routine processes and care pathways as much as possible. The process of contacting women for study recruitment is detailed in Figure 1. This involves the clinical teams sending a study letter to women referred to the maternity unit for their dating scan (either by post, email or the e-patient record App Badger Notes which has a notification system to alert users to the letter) (see Supplemental material 1). The reproductive health clinical research team (including clinical trial associates, midwives, nurses and radiographers) will phone the women to book their routine dating scan appointment and discuss the SHAPES study to enquire whether they might be interested in taking part, using a script to ensure uniformed information provision. Those interested will be booked into the research clinic for their dating scan and will be sent the detailed participant information sheet (Supplement material 2). Women will be asked to provide written informed consent (Supplement material 3) on the day of their scan appointment, following their dating scan being completed and checks for eligibility (i.e., singleton viable pregnancy within the required gestation). Additionally, some women may be approached upon arrival for their routine scan appointment with an offer to participate in this study and the informed consent process will be followed. Women will be offered three printed pictures of their baby from their scan appointment with a framed mount as a thank you gift for taking part in the study. They can also opt into taking part in a prize draw to win one of 40 available £100 gift vouchers. Finally, we will also promote the study via a website (https://research.ncl.ac.uk/shapes/) and social media (the Newcastle Maternity Voices Partnership Facebook page and Connie e-midwife website) to provide an additional opportunity for any eligible women to enquire about the research directly. Any women who do not provide informed consent on the day of their scan appointment will have their routine dating scan carried out, but no additional measurements for the SHAPES cohort study.

We will continuously monitor the recruitment of SHAPES participants in relation to how representative they are of the background maternity population in relation to maternal BMI, age, ethnic group and deprivation. If there are any concerns relating to the recruitment strategy resulting in a biased sample, we will explore alternative strategies with the PPI group.

Sample size

A sample of 1400 women will be recruited to the study. The sample size was based (at the time of grant application) on the 'rule of thumb' that 10 events (cases of the outcome) were required for each variable included in a multi-variable model to predict an outcome. However, recent developments in prognostic model research allowed us to confirm the above sample [25-27]. The sample size calculation is based on a maximum of 7 candidate variables that are associated with both maternal obesity and adverse pregnancy outcomes (Supplemental material 4) and the least common pregnancy outcome, which is preeclampsia (estimated prevalence of approximately 5-6% of pregnancies in the UK at the time of developing the protocol) [28]. This number of candidate variables is similar to previously published validated prognostic models in pregnancy including between 1 and 7 predictor variables [29-32]. Targeting a shrinkage factor of ≤10% and C-index equal to 80%, we would need a minimum sample of 980 participants for a new model development for pre-eclampsia. Given that other outcomes are more prevalent compared to pre-eclampsia, they would require sample sizes lower than the above figure.

Data collection

Participants' dating scans will be performed by qualified trained research sonographers who are part of the usual clinical care team. Once viability of the pregnancy and normal fetal anatomy is confirmed, the additional ultrasound adiposity measures needed for the study will be performed by the study sonographer. The remaining data collection will be performed by a trained member of the research team.

The methods of adiposity measurement are detailed in Table 1. Ultrasound scans of subcutaneous and visceral abdominal fat volume will be performed using a GE E8 ultrasound machine (GE Healthcare Austria, GmbH & Co OG) with 2.3-8.4 MHz curvilinear probe. Methods described by Martin *et al.* [33] will be used to obtain the measurement. Ultrasound settings and patient position will be standardised to ensure consistency of the procedure. Further, image capture will be standardised for breathing movements (on expiration) and bladder filling. Midline transverse section of the maternal abdomen will be obtained approximately 1cm superior to the umbilicus to allow visualisation of the transverse section of the abdominal aorta at

the far field of the screen. The mean of three consecutive measurements will be employed in the analysis. In addition to the above measurements of subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT), an alternative method of measuring these by ultrasound will be deployed to establish optimal methods for future implementation. SAT and VAT will be measured at the sagittal plane of xiphisternum as described by Cremona *et al* [34]. All study sonographers will receive bespoke theoretical and practical training developed locally based on the described methodological literature before data collection commences. In a small sub-set of participants (n=25), paired and blinded measurements will be repeated by a second operator. Agreement between sonographer measurements will be assessed by calculating intra-class correlation coefficients and Bland Altman plots will be constructed for each measurement types for trends.

All anthropometry measurements will be taken directly on the skin (unless otherwise specified in Table 1) on the right side of the body unless impracticable due to injury, in which case the left side may be used. All anthropometric measurements will be taken by individuals who have received anthropometry training following the measurement protocols detailed by the International Society for the Advancement of Kinanthropometry (ISAK) [35] by an ISAK level 3 instructor anthropometrist. Inter-rater reliability will be estimated following ISAK recommendations for calculating technical error of measurements and intraclass correlation coefficients. Measurements will be taken in duplicate, and a third measurement taken if the difference between the first two measures is greater than 5% for skinfolds or 1% for all other measures. If two measures are taken, the mean value will be used in data analysis. If three measures taken, the median value will be used.

Adverse outcomes of interest are shown in Table 2 and will be extracted from routine electronic patient medical records. Quality checks will include interrogating the data for missing, unrealistic or inconsistent data, and the clinical research team will resolve these through full medical record review. Adverse outcomes were selected based on maternal obesity evidence-base of risks, and two systematic reviews exploring associations between maternal adiposity and health outcomes [5, 6], and

reviewing what data were routinely recorded in maternity patient records. Additional outcome measures considered important for clinical practice and for patients were suggested and included by the external steering group consisting of PPIE members, academics and clinical (midwifery, obstetrics, sonography) representatives.

Table 1. Methods of adiposity measurement

Adiposity measure	**Measurement**
Subcutaneous Adipose Tissue[1]	Midline transverse section of the maternal abdomen, approximately 1 cm above the umbilicus from outer border of the subcutaneous fat layer to the outer border of rectus abdominus at the level of linea alba
Visceral Adipose Tissue[1]	Midline transverse section of the maternal abdomen, approximately 1 cm above the umbilicus from the inner border of rectus abdominus at the level of linea alba to the anterior wall of the aorta
Pre-peritoneal Subcutaneous Adipose Tissue [1]	Sagittal plane of xiphisternum from the lower border of the cutaneous layer to the upper border of the linea alba
Pre-peritoneal Visceral Adipose Tissue [1]	Sagittal plane of xiphisternum from the lower border of linea alba to the upper border of the liver capsule
Waist circumference[2]	Narrowest point of the abdomen between the lower costal (10th rib) border and the top of the iliac crest, perpendicular to the long axis of the trunk, at the end of normal expiration and with the abdominal muscles relaxed, to the nearest 0.1cm
Hip circumference[2]	Greatest posterior protuberance of the buttocks, perpendicular to the long axis of the trunk, with the gluteal muscles relaxed and the feet together, over light clothing and to the nearest 0.1cm
Height[2]	To the nearest 0.1cm with shoes removed and the participant's head positioned in the Frankfort plane
Weight[2]	In light clothing to the nearest 100g

Neck circumference	Immediately superior to the thyroid cartilage and perpendicularly to the long axis of the neck with the head in the Frankfort plane, to the nearest 0.1cm
Mid upper arm circumference	Midpoint of the upper arm between the acromiale and radiale, perpendicular to the long axis of the arm, to the nearest 0.1cm
Skinfold thickness[3]	Subscapular, triceps, biceps, iliac crest and supraspinale measured using Harpenden skinfold callipers, to the nearest 0.1mm

[1] Total adipose tissue will be calculated as a sum of subcutaneous and visceral adipose tissue.

[2] Waist to hip ratio, waist to height ratio, BMI, Body adiposity index, A Body Shape Index (ABSI), Hip Index, Weight-Adjusted Waist Index, Body Roundness Index, Total abdominal fat, Abdominal Volume Index, Conicity Index, estimated total body fat, Relative fat Mass, Clínica Universidad de Navarra-Body Adiposity Estimator (CUN-BAE) and body fat percentage will be calculated from these measurements.

[3] Sum of skinfolds will be calculated using 5 skinfold measurements.

Table 2. Pregnancy outcomes for the SHAPES cohort

Outcomes	**Definition**
Maternal outcomes	
Gestational diabetes[1]	Fasting plasma glucose level of ≥ 5.6 mmol/litre or 2-hour plasma glucose level of ≥7.8 mmol/litre
Gestational hypertension	Blood pressure ≥140/90 mmHg on two occasions at least 4 hours apart after 20 weeks' gestation
Preeclampsia	New onset of hypertension (>140 mmHg systolic or >90 mmHg diastolic) after 20 weeks of pregnancy with a new onset of proteinuria or/and maternal organ dysfunction or/and uteroplacental dysfunction. Early onset defined as onset of PE before 34 weeks gestation.
Induction of labour	Non-surgical treatment to induce the labour
Caesarean section	Surgical delivery of baby (emergency or elective)
Instrumental delivery	Assisted birth when forceps or a ventouse suction cup is applied
Retained placenta	As reported in medical records.

Outcomes	Definition
Maternal infection	As reported in medical records.
Postpartum haemorrhage (PPH)	3rd stage of labour and immediate postpartum period, measured in ml blood loss
Maternal length of stay in hospital	From admission date for any stay resulting in delivery to date of discharge
Infant outcomes	
Fetal growth	Measured at 2nd and 3rd trimester scans, including: 2nd trimester scan: Fetal head circumference; Fetal abdominal circumference; Fetal Femur Length; Estimated fetal weight Hadlock 3rd trimester scan: abdominal circumference; Femur Length; Estimated fetal weight Hadlock; Umbilical artery PI; End Diastolic flow; Amniotic Fluid Index
Pre-term birth	Birth before 37 weeks gestation
Late-term birth	Pregnancy that extends over 41 weeks gestation
Large for gestational age	birth weight above the 90th centile for gestational age and sex on INTERGROWTH chart
Small for gestational age	Birth weight below the 10th centile for gestational age and sex on INTERGROWTH chart [36]
Apgar score	1 and 5 minutes
Neonatal jaundice	As reported in medical records
Neonatal respiratory distress (requiring resuscitation)	Any of the following: Cords visualised meconium seen; Cord visualised no meconium; Facial air; Facial oxygen; Mucus extraction or suction; Positive pressure by bag or mask; Positive pressure by endotracheal tube
Feeding method	First feed: Artficial; Breast mother; Breast donor; Breast and artificial; No feed given Feed method at discharge: breastfeeding or artificial feed or both breast and artificial
Infant admission to specialist care	admission to neonatal special care baby unit (SCBU) or intensive care unit (NICU), high-dependency care, transitional care; length of stay if admitted

[1] Note this outcome can only be determined for those women who have had an oral glucose tolerance test (OGTT).

A number of socio-demographic and clinical variables associated with adverse pregnancy outcomes will be collected, as well as data to inform subsequent health economics analysis (e.g., place of delivery, length of inpatient stay, maternal medications use) and any reason for loss to follow up (e.g., late miscarriage, stillbirth, or participant moving to another area) (Supplemental material 4).

Data management

Participant identifiable information will be handled in line with GDPR 2018 principles. Initial data collection and storage will be via REDCap, a password-protected database. Data will be stored on the NHS secure server under Caldicott approval until recruitment is complete. At the end of the recruitment period, data will be anonymised using a unique identifier for each participant. Following completion of all follow-up data collection, anonymised electronic research data will be transferred to a Newcastle University secure server for analysis. If a participant is withdrawn from the study, the data collected up to that point will be kept to compare the characteristics of withdrawals to non-withdrawals, but not further analysis will be conducted. No personal identifying information will be presented in the study outputs.

Analysis

The aim of the analysis is to explore if any single adiposity measure taken in this study performs better than BMI in terms of predicting women who develop an adverse pregnancy outcome. Each adiposity measure will be assessed individually and compared with BMI (i.e. unadjusted model(s). Where possible, secondary sub-group analysis will be carried out for different ethnic groups. If no individual measure performs better than BMI (i.e. current practice), we will build multiple logistic regression model(s) by adding all the pre-specified predictors/covariates for the analysis of each outcome separately (i.e. the adjusted model). A backward selection method will be used to eliminate unimportant predictors/covariates. A backward elimination may lead to a more parsimonious model which is therefore easier to implement in clinical practice than a full model. We will compare these models to the unadjusted BMI model to identify which has the best predictive performance

measures. Wherever possible, we will retain continuous candidate predictors in their continuous form to avoid statistical power loss [37]. In case a linear association between a continuous predictor and the outcome is doubtful, we will explore flexible parametrisation of the predictor to study non-linear associations. To this end, fractional polynomials and restricted cubic splines will be used, and we will select the one giving best fit (using appropriate statistical measures) [37].

The apparent performance of the developed model(s) will be summarised using calibration, discrimination and internal validation analyses [38]. Calibration determines performance in terms of the agreement between the probability of developing the outcome as estimated by the measure/model, and the observed outcome frequencies. Discrimination is the measure of the model's ability to distinguish between individuals who develop the outcome or not (i.e., a higher probability assigned to the individual who develops the outcome compared with an individual who does not. This will be assessed using the c-index (equivalent to the area under the receiver operating characteristic [AUROC] curve). Any missing values will be assumed to be missing at random (MAR) and multiple imputation (MI) will be implemented using 20 imputations [39]. Calibration and discrimination of the developed model(s) will be summarised in the development datasets (averaged over imputation datasets). Calibration will also be assessed graphically [40].

The model(s) will be internally validated using bootstrap re-sampling method in order to quantify the degree of optimism due to overfitting [41, 42] and to derive optimism-adjusted indices of discrimination (c index) and calibration (calibration slope). Two hundred bootstrap samples will be used [42, 43]. Optimism is expected when measures/models are applied to the same dataset used for development, as they have been developed to achieve the best fit for that specific dataset (i.e., overfitting). Statistical techniques (e.g., bootstrapping) can quantify the potential for overfitting, and provide adjustment estimates (e.g., shrinkage factor) to reflect the prognostic performance in a new dataset/population.

Patient, public, and stakeholder Involvement

Extensive patient, public, and stakeholder involvement has been carried out for this research. Pregnant and postnatal women, clinical stakeholders (obstetricians,

midwives, sonographers) and the NIHR Research Design Service North East and North Cumbria consumer panel were involved in the development of the proposed research funding application, protocol, and in planning how to embed PPI into this research.

PPI consultations were carried out with pregnant and postnatal women attending a community group. Discussion topics included: acceptability and timing of adiposity measurements; reviewing the plain English and PPI sections of the funding application; discussing how to communicate research to pregnant women and wider public; future PPI involvement in the research; the process of recruitment involving sending letters and follow up phone calls; the provision of thank you gifts to research participants and decision to include a prize draw; reviewing the PIS, recruitment letters and social media advertisements. PPI members strongly thought this research was a priority and we addressed issues raised during these discussions by amending our planned research methods, such as the recruitment strategy. We have planned consultations with pregnant and postnatal women to be embedded throughout the research, as well as having PPI representatives on the steering group and as a co-investigator (JS).

Key discussion points with clinical stakeholders included considering the effect of existing guideline interventions for women with a BMI≥30kg/m^2 as women will continue to receive this routine care during the research time period; recruitment and measurement logistics in the routine antenatal scan clinics; equipment and training required for sonographers to carry out the additional ultrasound measurements; and processes for recruitment. Clinical stakeholders will continue to be involved in the steering group.

Ethics and dissemination

This is a low risk, observational study. This study has been reviewed and given a favourable opinion by the North East - Newcastle & North Tyneside 1 Research Ethics Sub-Committee and the Health Research Authority. Caldicott and local R&D approvals will be in place before the study begins. The study sponsor is Newcastle upon Tyne Hospitals NHS Foundation Trust. All SHAPES participants will be required to give informed consent before taking part in the research. Potential

participants will receive a copy of the participant information sheet and consent form, and these will be discussed with a member of the research team when they attend for their dating scan appointment (Figure 1). Those consenting to participate in SHAPES will have their routine dating scan and SHAPES additional measurements carried out at their appointment. Those not consenting at this stage will have their routine dating scan and no further measurements.

The SHAPES study is part of a wider NIHR Advanced Fellowship research programme. The planned research programme includes validating the results of the SHAPES cohort study in a subsequent study, using individual participant data (IPD) meta-analysis methods. We have identified eligible studies for the IPD study in two systematic reviews [5, 6] as well as a search for registered cohort studies as described in the PROSPERO registration [44], and invited authors to join an international IPD collaboration. An economic evaluation of implementing an alternative approach to risk prediction into routine NHS maternity care is also planned. A decision model approach will be used and the data required for the model will come from the SHAPES study (e.g. the performance of the risk prediction approaches), expert opinion (e.g. costs of using the risk prediction tools) and from the literature (e.g. relating to potential implications for longer term maternal and infant outcomes). The analysis will compare the costs of changing routine practice to implement adiposity measures/risk prediction models if they are shown to be better at predicting risk than current practice using BMI, and the cost implications of changes to health outcomes following changes in the targeting of antenatal care. In this study, we can also explore the health economics implications of implementation of more complex versus simpler risk prediction models. The findings of this will also be used to help inform policy recommendations. All research will be published in peer-reviewed journals and reported using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [45] and the Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) guidelines [46]. Further dissemination will be audience appropriate, for example utilising research briefs, policy briefs, media coverage and stakeholder and participant communication to achieve this goal. The target audiences for this work are health professionals and their affiliated organisations, pregnant women and their families, maternity managers and commissioners of

services, national and international policy makers, wider public, third sector, and other researchers.

Contributors: NH and LV developed the concept for this research and secured funding. All authors contributed to the development of the protocol and ethics application. RV, VM and RT developed the clinical implementation of the research, including the process of recruitment and logistics of measurements being carried out in routine clinics. TB and DT provided statistical methods input. GN and NH drafted this manuscript and all authors contributed to reviewing and editing.

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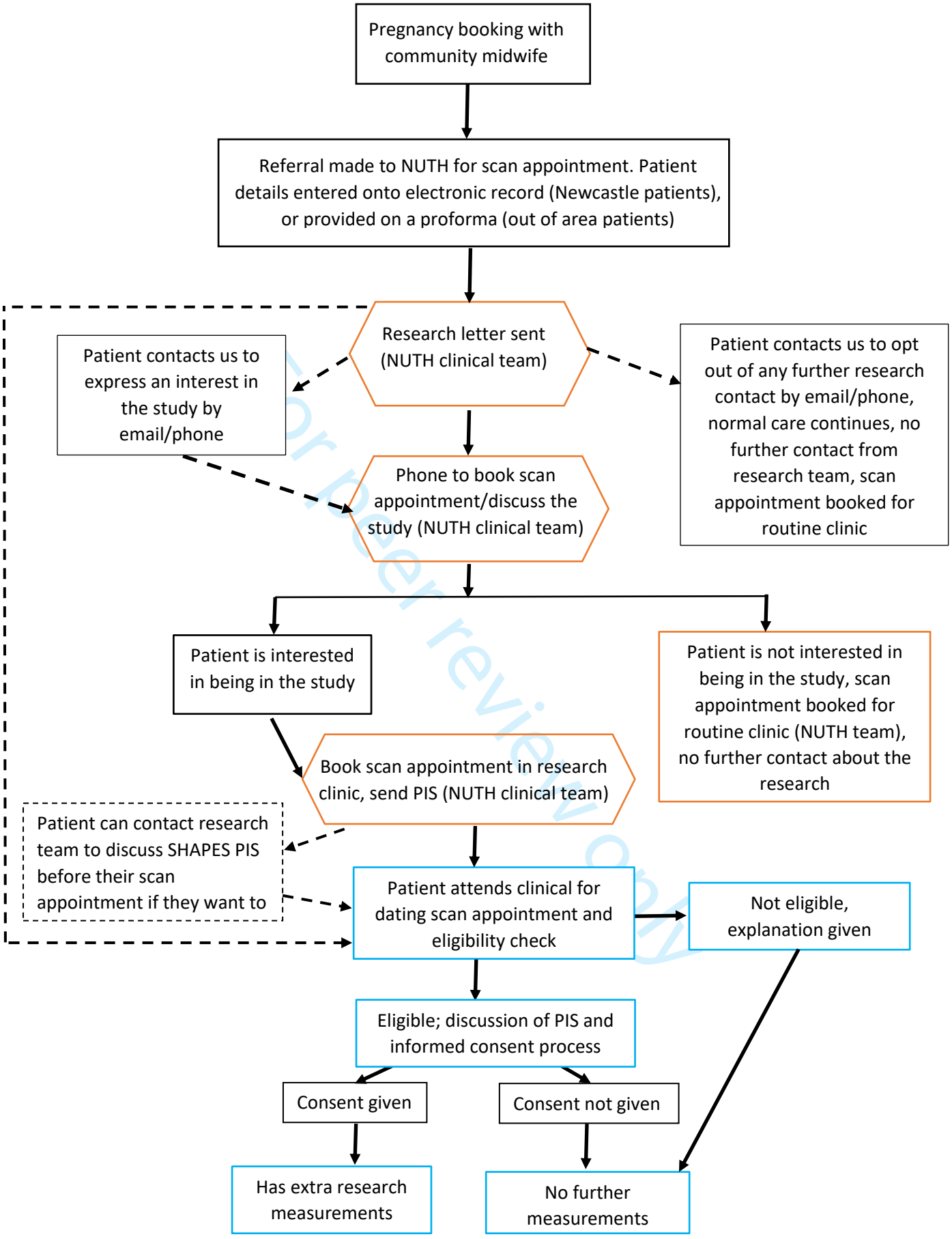
Figures title and legend

Figure 1. Study recruitment procedure

NUTH: Newcastle Hospitals NHS Foundation Trust



Supplement material

1. Research Information Letter [1]

SHAPES

About the SHAPES research

A pregnant woman's Body Mass Index (also known as BMI) is used to identify which women might need extra care in pregnancy. Currently, women with a high BMI get extra care. However, BMI might not be the best measure to use and women's body shape in early pregnancy might be better. SHAPES will explore if other measurements, such as waist size or ultrasound scans, can be used to identify which women would benefit most from extra care during pregnancy. We need 1400 women with a whole range of BMIs to take part.

A member of the clinical team at NuTH might discuss this research with you over the phone if they call to book your routine 12-week scan appointment, or in the waiting room when attending for your scan appointment. If you are interested in taking part in this research, you will receive more detailed written information about the study to read and discuss with the research team. All the extra body shape measurements will be done at your 12-weeks scan appointment, which will take about an extra 45 minutes. As a thank you for your time, you will receive 3 photos of your baby from your 12-week scan, and you can be entered into a prize draw to win £100 shopping vouchers.

We only have a limited number of research appointments available each week, so unfortunately, we can't offer them to everyone. This means you may not be contacted about the research. If you think you might be interested in taking part, you can contact us directly. If you do not want anyone to approach you about this research, please let us know and we won't contact you.

Contact details: email: nuth.rhnresearch@nhs.net phone: 0191 2820362

For more information about this study, please visit our website: http://research.ncl.ac.uk/shapes/

Yours sincerely

Victoria Murtha, Principal Investigator for the SHAPES Study, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust

[1] This letter goes out to women alongside a generic letter from NUTH about research in maternity services, alongside summaries of other research projects active at the same time as SHAPES.

2. Participant Information Sheet (PIS)

Study of **h**ow **a**diposity in **p**regnancy has an **e**ffect on outcome**s**: the SHAPES study

Participant Information Sheet

Research Centre: The Newcastle Upon Tyne Hospitals NHS Foundation Trust

Chief Investigator: Nicola Heslehurst, Newcastle University

Principal Investigator: Victoria Murtha, Newcastle upon Tyne NHS Foundation Trust, Reproductive Health Research Team, The Royal Victoria Infirmary (RVI), 0191 2820362, nuth.rhnresearch@nhs.net

We would like to invite you to take part in a research study. Before you decide if you want to take part it is important that you understand what it will involve. Please take time to read this document and discuss it with others if you wish. You will have the opportunity to discuss the research with a member of the team when you attend for your 12-week scan appointment and we encourage you to do this if there is anything you are unsure of. If you have received this information sheet before your scan appointment, you can contact us directly if you would like to discuss anything in advance.

Part one of this document tells you about the purpose of the study and what would happen if you decided to take part. Part two provides information about optional extras, which are extra parts of this research that you can choose whether or not you want to take part in. Part three gives more details about the conduct of the research. Further contact details are on the last page of this document.

Part One

What is the purpose of the research? This research will explore body shape in early pregnancy and how it impacts on the health of women and babies. The NHS uses Body Mass Index (BMI) to identify who might need extra care in pregnancy. However, there may be more accurate measures than BMI to understand who would most benefit from extra pregnancy care. We will look at body shape in early pregnancy, and need women with a whole range of BMIs to take part. This research will inform how maternity services provide care to improve health of women and babies.

Why have I been invited? The study is being carried out at the RVI. We are inviting pregnant women attending this hospital for a 12-week scan, and aim to include 1400 women in this study.

What will happen to me if I take part? A member of the research team will discuss the research with you at your 12-week scan appointment. If you decide to take part, you will be asked to sign a consent form. We will take some extra body shape measurements on the same day as your scan

appointment. The sonographer who is doing your 12-week scan will take some extra ultrasound measurements. A female researcher will then take all the extra measurements in a private room. These will include your waist size, hip size, upper arm size, neck size, skinfold measurements of fat stored underneath the skin, height and weight. We will need to draw some lines on your arms, stomach and back using an erasable pen. It would be helpful if you could wear a loose-fitting top and lightweight clothing on the day. Most of the measurements will be taken using a tape measure. The skinfold measurements will use callipers to compress the skin, but this should not cause any pain. You will also be asked to fill in a short questionnaire to get some extra information about you, for example your age, ethnic group and postcode. We will review your routine maternity notes after you have had your baby so that we can get information about your pregnancy, for example, how you delivered your baby. You don't need to do anything else for this research after your 12-week scan appointment.

Will I learn more about my own body shape measurements or health? No. We don't yet know which body shape measurements are most accurate, so we can't give you any feedback on this.

What will happen to the results of the research study? The results from this study will be used to see how well body shape measurements relate to health during pregnancy. This will give us a better idea of which women and babies would benefit the most from extra care during pregnancy. The results will be published in a scientific journal so that other researchers and health professionals can learn from this research. You would not be identified in any results we present or publish. If you would like to receive a summary of results from the study, then we can share these with you.

What are the possible benefits and disadvantages of taking part? Your hospital ultrasound scan appointment will take up to 45 minutes longer than normal. There are no direct benefits for you during this pregnancy but taking part in this research could help to improve care of for women and their babies during pregnancy in the future. To say thank you for taking part you will receive a photograph mount with three printed pictures of your baby from your 12-week scan which will be given to you on the day of your scan appointment. You can also take part in a research prize draw which will be drawn at the end of the research. There are 40 prizes of £100 shopping vouchers to be won.

Do I have to take part? No. Participation is voluntary, and it is up to you to decide if you want to participate in the study. If you do not want to take part, you do not have to give a reason and your care will not be affected in any way. If you have received this document before your scan appointment and you decide that you don't want to take part in the study, you can either contact us to let us know before attending for your appointment or turn up and let us know on the day. Your scan appointment will go ahead as planned whether you decide to take part in this research or not.

What if I change my mind? You are free to withdraw from the study at any time, without giving a reason. If you change your mind, your care will not be affected in any way. If you want to withdraw from the study, please use the contact details on page 1 of this document.

Part Two: Optional Extras[2]

There are two optional extras for this research. You can still take part in the research without agreeing to either of these optional extras, or you can choose to agree to one or both of them.

SHAPES Study Interviews: You will be asked by the research team if you are happy to share your contact details with the research team at Newcastle University for a second study related to SHAPES. The second study involves being interviewed about your experiences of having the extra body shape measurements taken. If you agree to share your contact details now, this does not mean that you are agreeing to be interviewed, you are only agreeing to share your contact details with the research team. Not all women who share their details will be contacted as there will be 1400 women in SHAPES and only around 30 women will be interviewed. If you are contacted about the interview study, you will receive detailed written information and have the opportunity to discuss with the researchers before deciding whether to take part. If you don't want to take part, you do not have to give a reason and your care won't be affected in any way.

Future research about long-term health and well-being of women and their children: We would like to explore whether body shape in early pregnancy is linked to the future health and well-being of women and their children. An example of the type of research question we would be asking would be "can waist size measured at 12-weeks in pregnancy identify which women or children develop diabetes later in life?" If pregnancy measurements are useful, then we could plan ways to support women and children after pregnancy to try and improve long-term health and well-being.

To do this future research, we would need your consent to store your NHS number, name and date of birth, and your baby's NHS number and date of birth, linked to your SHAPES Study ID number. This is needed so that we can link the SHAPES data with routinely collected health data in the future, through organisations such as NHS Digital, hospital attendance data and GP records. For example, we could link to medical records to see if you or your child has been diagnosed with diabetes at any point after pregnancy. This extra research will only involve accessing routine electronic data and not any further contact with you. Any researcher who wants to access your health records can only do so if you consent to the use of your data in this way, and will follow best ethical and legal practice.

Part Three

Will my taking part in the study be kept confidential? Yes. Newcastle upon Tyne Hospitals NHS Foundation Trust, based in the United Kingdom, is the sponsor for this study and will act as the data controller for it. This means they are responsible for looking after your information and using it properly. Newcastle upon Tyne Hospitals NHS Foundation Trust will keep identifiable information about you for 5 years after the study has finished. Newcastle upon Tyne Hospitals NHS Foundation Trust will collect information from you and/or your medical records for this research study in

[2] Women in the SHAPES study can choose to consent to any combination of the optional extras, or none of them, and can still take part in SHAPES

accordance with our instructions. Only trained clinical-research team members will have access to your information.

Your rights to access, change, or move your information is limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personal identifiable information possible.

Individuals from Newcastle upon Tyne Hospitals NHS Foundation Trust (NuTH) and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The research team will pass these details to individuals at NuTH along with the information collected from you and/or your medical records upon request for audit purposes. The only people in NuTH who will have access to information that identifies you will be people who need to contact you to discuss this study or audit the data collection process. People outside the NuTH will have no access to your identifiable information and will not be able to access your medical notes, find out your name, NHS number or contact details.

If you give consent to participate in the study, we would use non-identifiable personal information (through allocating a study ID number) to analyse the data and report the findings. Any paper documents will be stored in a locked fire-resistant cupboard at the RVI. To allow us to analyse the anonymised data it will be transferred to a secure server on the Newcastle University system and stored in accordance with the regulations of the Data Protection Act 2018 and the Newcastle upon Tyne Hospitals NHS Foundation Trust Caldicott guidelines. You can find out more about how we use your information at:

- www.hra.nhs.uk/information-about-patients/
- https://newcastlejro.com/research/new-study/data-security
- Email the NUTH Data Protection Officer, Richard Oliver, richard.oliver2@nhs.net

Future research: If you consent to us keeping your data for future research, it will be stored on a secure server at Newcastle University. Newcastle University will be the data controller for the future research. All data protection regulations will be followed. Even if you agree to us storing this data, we will still need to get ethical approval to access your data again for future research. This would be to make sure we are using the data in the way we have told you about in this document, and that you have consented to. If you consent to us storing your data, we will not share it with anyone else or use it for any other purpose than described in this document. If you consent to us storing this data for future research, you are free to withdraw at any time, without giving a reason. Any information already collected can be destroyed if you wish. If you change your mind, your care will not be affected in any

way. To withdraw from this future research, please contact the chief investigator (contact details on the last page of this document).

What will happen to information collected about me for the research study? The information we collect during the study will be analysed (or processed) to enable us to explore if body shape measurements in early pregnancy relate to the health of women and babies.

Who is organising and funding the research? This project is funded by the Department of Health via the National Institute for Health Research. It is being led by Dr Nicola Heslehurst who is a researcher at Newcastle University.

Who has reviewed the study? This study has been reviewed and given a favourable opinion by North East - Newcastle & North Tyneside 1 Research Ethics Sub-Committee. The study design has been reviewed by Sponsor (NuTH). Members of the public were involved in review of a scope (lay summary), design and incentives for this research.

Extra Contact Details

Where can I get further information about the study? If you have any questions or concerns about participating in the study please contact the clinical lead for this research at the RVI (Victoria Murtha, 0191 2820362, nuth.rhnresearch@nhs.net), or the Chief Investigator from Newcastle University (Nicola Heslehurst, 0191 2083823, nicola.heslehurst@ncl.ac.uk).

What if there is a problem? If you are not satisfied with any aspect of the way you have been approached or treated during the course of this study, you should first speak to the research team (please see contact details on page 1) who will do their best to answer your questions. If you remain unhappy and wish to complain formally, the normal National Health Service complaints mechanisms are available to you: please ask to speak to the complaints manager for the Hospital.

If you have any concerns about how you are treated in relation to this research study, you can raise these with the Patient Advice and Liaison Service (PALS). This service is confidential and can be contacted on Freephone: 0800 032 0202.

Alternatively, if you wish to make a formal complaint you can contact the Patient Relations Department, Tel: 0191 2231382 or 0191 2231454, Email: nuth.patient.relations@nhs.net Address: Patient Relations Department, Newcastle upon Tyne Hospitals NHS Foundation Trust

Thank you for taking the time to read this participant information sheet.

3. Inform consent

Participant Identifica

CONSENT FORM (SHAPES Study)

Study of **h**ow **a**diposity in **p**regnancy has an **e**ffect on outcome**s**

Chief Investigator: Nicola Heslehurst Please initial box

1. I confirm that I have read the information sheet dated 08/02/2022 (version 2.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of my medical notes and data collected during this study may be looked at by individuals from the Newcastle upon Tyne Hospitals NHS Foundation Trust or relevant regulatory bodies where relevant to my taking part in this research (for example, for the purpose of audit of this research project). I give permission for these individuals to have access to my records. ☐
4. I agree for my information, gathered for this study, to be stored on a secure database for analysis on a Newcastle University server anonymously. ☐
5. I agree to take part in the above study. ☐

Name of participant	Date	Signature
Name of person taking consent	Date	Signature

Please tick the relevant box and provide contact details below if you would like to:

a) take part in the prize draw ☐
b) receive a summary of results for the SHAPES study ☐

e-mail:

Telephone number:

Address:

4. Data items

Data item	Source		
	Measured for research during the research visit	Routine data: electronic records	Routine data: from paper-based notes
Questionnaire at research visit			
Age at booking*	x		
Gravidity	x		
Parity*	x		
Ethnic group*	x		
Postcode (linked with Index of Multiple Deprivation)*	x		
Smoking status (in the past 12 months and current smoking)*	x		
Alcohol intake (before pregnancy and current intake)*	x		
Substance use (before pregnancy)	x		
History of bariatric surgery (date and type)	x		
Medical record review at research visit			
Gestational age at research visit		x	x
Blood pressure at booking (systolic and diastolic)*		x	x
Previous caesarean delivery		x	x
Previous macrosomia		x	x
Diabetes history		x	x
Family history of diabetes		x	x
Previous spontaneous preterm birth or mid trimester loss between 16+0 and 34+0 weeks gestation		x	x
Cervical trauma		x	x
Cervical length < 25 mm		x	x
Family history of preeclampsia		x	x
Essential hypertension		x	x
Previous pregnancy hypertension		x	x
Chronic renal disease		x	x
Autoimmune disease		x	x
Last pregnancy >10 years ago		x	x
Previous low birth weight <10%		x	x
Previous still birth		x	x
Previous neonatal death within 4 weeks of life		x	x
Ultrasound and anthropometry measurements at research visit			
Subcutaneous fat	x		
Visceral fat	x		
Pre-peritoneal VAT	x		
Pre-peritoneal SAT	x		
Height at research visit	x		
Weight at research visit	x		
Waist circumference	x		
Hip circumference	x		
Neck circumference	x		
Mid upper arm circumference	x		
Skinfold thicknesses (subscapular, triceps, biceps, iliac crest, supraspinale)	x		
Follow up data linkage			
Congenital anomaly		x	
Reason for outcome data not being available		x	

Data item	Source		
	Measured for research during the research visit	Routine data: electronic records	Routine data: from paper-based notes
Number of antenatal scans (in antenatal clinic and fetal medicine)		x	
2nd trimester fetal growth (gestation at scan; fetal head circumference; abdominal circumference; femur length; estimated fetal weight)		x	
3rd Trimester fetal growth (gestation at scan; abdominal circumference; femur length; estimated fetal weight; umbilical artery PI; end diastolic flow; deepest pool)		x	
Hospital admissions in antenatal period		x	
Number antenatal clinic appointments (antenatal clinic, fetal medicine and maternity assessment unit)		x	
Infant date of birth or end of pregnancy		x	
Baby sex		x	
Viability (Live birth, still birth, late miscarriage 12-24 weeks)		x	
Neonatal death within 28 days of delivery (and date)		x	
Baby exam colour		x	
Apgar scores at 1 and 5 minutes		x	
Respiratory distress/resuscitation		x	
Feeding method (first feed and at discharge)		x	
Gestation at delivery		x	
Birthweight and percentile		x	
Induction of labour (and reason)		x	
Caesarean delivery (elective or emergency and reason)		x	
Instrumental delivery (and type)		x	
Place of delivery		x	
Water birth		x	
Maternal death (and date)		x	
Maternal folic acid supplementation		x	
Gestational diabetes diagnosis (and gestational age)			
Oral glucose tolerance test (OGTT test (fasting and 2 hour blood glucose)		x	
Preeclampsia (PE) diagnosis (and gestation)		x	
Pregnancy induced hypertension (PIH) diagnosis (and gestation); if yes (stillbirth, proteinuria, birthweight <3%, Abnormal umbilical artery Doppler waveform analysis, Renal insufficiency, Liver involvement, Haematological complications, Neurological complications)		x	
Manual removal of placenta		x	
Maternal infection during pregnancy		x	
Total blood loss 3rd stage and immediate postpartum		x	
Maternal length of stay in hospital		x	
Admission to neonatal intensive, high-dependency, special or transitional care (and length of stay)		x	
Antenatal and discharge medications (and description)		x	

* *A-priori* socio-demographic and clinical candidate predictor variables

Note: the full data dictionaory for SHAPES is available on request