SHAPES

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

Full Title:	Study of How Adiposity in Pregnancy has an Effect on outcomeS (SHAPES): a cohort study
Short Title:	SHAPES Cohort Study
Funders:	NIHR Career Development (Advanced) Fellowship CDF-2018-11-ST2-011
Sponsor:	Newcastle upon Tyne Hospitals NHS Foundation Trust
Sponsor reference number:	08964
IRAS reference number:	302444
Protocol version:	3.5

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: Date:

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Name (please print):

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Position:

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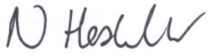
Chief Investigator:

Signature:  Date:

01/12/2022

Name:
Dr Nicola Heslehurst

Position:
Senior Lecturer in Maternal Nutrition
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1. Contents

2. Contact Details

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Clinical Trial Assistant (CTA): Gayle Gills

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Co-Investigators:

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* Denotes members of the Project Management Group

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Study Steering Group:

Chair:

Dr Vikki Smith, Clinical Academic Midwife Sonographer, RVI, NUTH; Senor Lecturer in Midwifery, Northumbria University, vikki.smith@northumbria.ac.uk

Newcastle University/NUTH:

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External:

Janine Smith, Patient and Public Involvement Representative, Parent Support Worker, hello@janine-smith.com

Two PPI representatives (pregnant women or new mums) will be invited to all steering group meetings (see section 10).

Prof Marian Knight, Professor of Maternal and Child Population Health, Oxford University, marian.knight@npeu.ox.ac.uk

Sponsor:

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Funders:

National Institute for Health Research (NIHR) Academy, academy@nihr.ac.uk

3. Glossary of Abbreviations

Abbreviation	Definition
ABSI	A Body Shape Index
BMI	Body Mass Index
CTA	Clinical Trial Assistant
GDM	Gestational Diabetes Mellitus
ISAK	International Society for the Advancement of Kinanthropometry
LGA	Large for Gestational Age
NHS	National Health Service
NICU	Neonatal Intensive Care Unit
NIHR	National Institute for Health Research
NUTH	Newcastle upon Tyne Hospitals NHS Foundation Trust
PI	Principal Investigator
RVI	Royal Victoria Infirmary
SAT	Subcutaneous Adipose Tissue
SCBU	Special Care Baby Unit
SGA	Small for Gestational Age
SHAPES	Study of How Adiposity in Pregnancy has an Effect on outcomeS
TAT	Total Adipose Tissue
VAT	Visceral Adipose Tissue

4. Responsibilities

Sponsor: NUTH NHS Foundation Trust

Funder: National Institute for Health Research (NIHR): award ID CDF-2018-11-ST2-011

Project Management and Oversight:

The study will be conducted in accordance with the Research Governance Framework for Health and Social Care. The Project Management Group (section 1) will meet every two months to review progress, but there will be opportunity to meet more frequently should issues or unforeseen concerns arise. The CI (Dr Nicola Heslehurst), PI (Victoria Murtha) and study research associate (Dr Giang Nguyen) will meet monthly.

The day-to-day management of the study will be led by Dr Nicola Heslehurst, supported by Dr Giang Nguyen.

Victoria Murtha is the PI at NUTH. The PI will have overall responsibility for the conduct of the study at NUTH.

A steering group has been established to provide oversight of the study and will meet twice a year as a minimum.

The following functions falling under the responsibility of the sponsor will be delegated to Dr Nicola Heslehurst [Chief Investigator]:

- Ethics Committee Opinion (including application for research ethics committee favourable opinion, notification of protocol amendments and end of study, site specific assessment & local approval)
- R&D Approval (including application for global checks, via NIHR CSP)
- Good Clinical Practice (including GCP arrangements, data monitoring, emergency & safety procedures)
- Administration of funding for the study

Study conduct at site, PI responsibilities:

- Daily management of their research at their site.
- Ensure Trust-wide Policies and Standard Operating Procedures (SOPs) and/or study-specific SOPs are followed.

- Ensure that the necessary approvals for their research are in place prior to the research commencing including but not limited to:
    - A favourable opinion from a Research Ethics Committee
    - NHS Capacity and Capability from Trust Research & Development (R&D) (NJRO)
    - Approvals from relevant regulatory bodies (e.g. MHRA, NIGB, ARSAC)
- Ensure all essential documents are maintained for their research in the form on an Investigator Site File (ISF)/ Project file.
- Ensure research is conducted in accordance with the approved protocol (unless an Urgent Safety Measure (USM) is required) and that appropriate systems are in place to guarantee version control of documentation e.g. Protocol/abstract, to ensure researchers are working to the correct and most recent version.
- Ensure that each member of their research team is qualified by education, training and experience for their role in the study.
- Research conducted in the Trust (with the exception of those studies involving staff only), the research team should be trained in the principles of GCP. This training must be updated at least every 3 years but should be pragmatic to the study. The Trust agrees to follow the MHRA/HRA joint statement for GCP training. www.hra.nhs.uk/about-us/news-updates/updated-guidance-good-clinical-practice-gcp-training/
- Ensure that, as applicable, arrangements (including staff training and competence) are in place for obtaining informed consent from research participants before research activity is undertaken.
- Ensure that amendments to the protocol or other study documentation are submitted to Trust R&D for review to confirm that there are no changes to Confirmation and Capacity status of the research. Amendments must also be submitted to the REC and Regulatory Authorities for approval as applicable.
- Protect the integrity and confidentiality of research data.
- Abide by all appropriate legislation in relation to patient data, including but not limited to:
    - Data Protection Act 2018
    - Mental Capacity Act 2005

- Ensure all the necessary employment contracts, honorary research contracts or other access arrangements are in place for all research staff before the study commences.
- Ensure that an appropriate CI/PI is named on the study at all time. In cases where an Investigator will be absence from employment (sick leave/maternity) or leaves their position and interim or new CI/PI must be nominated and approved by R&D.
- Ensure that all employment contracts remain active throughout the study. Where an employee is working under the research passport scheme, continuous access must be maintained and renewal applications should be received by R&D three (3) months in advance of expiry.
- Where clinical duties are undertaken by an Investigator and/or delegated to others within the research team, the Investigator must ensure that all Trust mandatory clinical training is undertaken and a record is maintained within the site file.
- Ensure that all clinical staff have the applicable registrations and licences to practice for the duration of the study, including any revalidation requirements.
- Ensure that students and inexperienced researchers involved in the study have adequate supervision. Supervision should be documented.
- Ensure where appropriate that relevant healthcare professionals (e.g. GPs) are informed of their patients' participation in research.
- Provide access to all study documents, devices and equipment as required for monitoring, auditing and inspection purposes.
- Discuss with their employing organisation any arrangements that need to be put in place to ensure effective exploitation of intellectual property (IP).
- Ensure appropriate archiving of their investigator site file/project file at the end of a study.
- Notify Trust R&D, REC and Regulatory Authorities as appropriate of changing timelines on a study and of the end of a study.

Funder's responsibilities:

The funders have no role or responsibility for the study design, conduct, data analysis and interpretation, manuscript writing, and dissemination of results. The funders do not control the final decision regarding any of these aspects of the study.

The Chief Investigator will submit annual reports to the funders on the research progress and any changes made compared with the funding application.

Sponsors responsibilities:

The sponsor has overall responsibility for the research, including:

- identifying and addressing poorly designed or planned research and poor-quality research proposals, protocols or applications and ensuring that research proposals and protocols:
    a. take into account systematic reviews of relevant existing research evidence and other relevant research in progress,
    b. make appropriate use of patient, service user and public involvement and
    c. are scientifically sound, safe, ethical, legal and feasible and remain so for the duration of the research, taking account of developments while the research is ongoing
- satisfying itself that the investigators, research team and research sites are suitable
- ensuring that roles and responsibilities of the parties involved in the research and any delegation by the sponsor of its tasks are agreed and documented
- ensuring adequate provision is made for insurance or indemnity to cover liabilities which may arise in relation to the design, management and conduct of the research project
- ensuring appropriate arrangements are made for making information about the research publicly available before it starts (unless a deferral is agreed by or on behalf of the research ethics committee)
- agreeing appropriate arrangements for making data and tissue accessible, with adequate consent and privacy safeguards, in a timely manner after it has finished
- ensuring arrangements for information about the findings of the research to be made available, including, where appropriate, to participants

- ensuring that, where expected or required, the research has approval from a research ethics committee (Whether outright or following a provisional opinion, resubmission or appeal) and any other relevant approval bodies before it begins
- verifying that regulatory and practical arrangements are in place, before permitting the research to begin in a safe and timely manner
- putting and keeping in place arrangements for adequate finance and management of the research project, including its competent risk management and data management
- ensuring that effective procedures and arrangements are kept in place and adhered to for reporting (e.g. progress reports, safety reports) and for monitoring the research, including its conduct and the ongoing suitability of the approved proposal or protocol in light of adverse events or other developments.

Patient and Public Involvement in the protocol design:

Pregnant and postnatal women and the 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 future PPI activities as part of this research. A detailed overview of the patient and public involvement is provided in section 10 of the protocol.

5. Protocol Summary

Short title:	*SHAPES Cohort Study*
Protocol version:	*1.0*
Protocol date:	*05/05/2017*
Chief investigator:	*Dr Nicola Heslehurst*
Sponsor:	*NUTH NHS Trust*
Funder:	*NIHR*
Study design:	*Prospective Cohort*
Research question:	*Are there alternative adiposity measures to BMI which better predict adverse pregnancy outcomes?*
Study aim:	*To evaluate the prognostic performance of single adiposity measures or a multivariable model to estimate risk of adverse pregnancy outcomes.*
Study objectives:	*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*

Adiposity exposure measures:	*Subcutaneous abdominal fat; Visceral abdominal fat; Waist circumference; Hip circumference; Height; Weight; Neck circumference; Mid upper arm circumference; Skinfold thicknesses.*
Outcomes:	*Gestational diabetes* *Gestational hypertension* *Preeclampsia* *Retained placenta* *Haemorrhage* *Maternal infection* *Metabolic syndrome* *Pre-term birth* *Late-term birth* *Induction of labour* *Caesarean section* *Instrumental delivery* *Fetal growth* *Large for gestational age* *Small for gestational age* *Apgar scores* *Jaundice* *Respiratory distress* *Feeding method* *Admission to neonatal special care baby unit (SCBU) or intensive care unit (NICU), high-dependency care, transitional care*

Number of study sites:	*One*
Study population/size:	1400 pregnant women
Study duration:	*Four years*

6. Background

In England, 21% (~189,000/year) of women have pre-pregnancy obesity (BMI≥30.0kg/m^2) and a further 28% (~245,500/year) have an overweight BMI (25.0-29.9kg/m^2) (1, 2). There is strong evidence of significantly increased risk of adverse outcomes associated with overweight and obesity including maternal and perinatal mortality, gestational diabetes (GDM), preeclampsia, large/small-for-gestational-age (LGA/SGA), pre-/post-term births, and long-term obesity and diabetes development among women and offspring (3, 4).

UK guidelines use early pregnancy BMI (as a proxy measure for pre-pregnancy BMI) to identify obesity and allocate high-risk care, including consultant-led obstetric and anaesthetic care, additional screening, monitoring, and delivery in high-dependency unit (5-8). Implementation of maternal obesity guidance is a daily challenge to health services due to high prevalence and associated costs which are significantly increased for women who have obesity (e.g. 39% increased costs in Wales in 2011/12) (2, 9-12). Identifying women who should receive high-risk care on the basis of BMI wastes NHS resources as many women who have obesity do not have any pregnancy complications and therefore do not require the high-risk care offered. A multicentre study reported that 47% of pregnant women with obesity had an uncomplicated pregnancy, whereas 42% of women with an overweight BMI developed pregnancy complications and could have benefited from additional care which they are not currently offered due to their BMI being below the “high-risk” cut off (13).

In the NHS context, the prevalence of uncomplicated pregnancies amongst women with obesity means that ~87,000 obese women/year unnecessarily receive high-risk care. The prevalence of women with an overweight BMI who develop complications usually associated with obesity means that ~103,000 women are high-risk/year and are not allocated to high-risk care based on their BMI not meeting the required criteria. The similarity in numbers of women who receive unnecessary high-risk care and those who require, but do not receive, high-risk care strongly suggests that more accurate targeting would have minimal net impact on health service costs.

There is a high variation in individual phenotype makes BMI a poor predictor of adiposity-level and risk, especially among women and some ethnic groups (14). 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 distinguish individuals' mortality and cardiometabolic risk (15, 16).

Failure to predict pregnancy risk results in harm for mother and child and increases healthcare costs. Furthermore, inaccurate risk communication can increase anxiety and distress, as well as waste care. There is an urgent need to identify measures of adiposity-related risk with greater sensitivity and specificity than BMI to inform targeted high-risk care to improve health of women and offspring and reduce waste of NHS resources.

This prospective cohort study will measure alternative (to BMI) indicators of obesity/adiposity in pregnant women to explore the ability of these markers to predict adverse pregnancy outcomes. A range of alternative adiposity measures exist, which can be assessed using a number of different anthropometric measures (for example, waist circumference, neck circumference) or ultrasound/MRI scans (for example to identify abdominal subcutaneous and visceral fat volumes). Some of these measures (e.g. MRI scans) are costly and impractical for implementation into routine pregnancy care. This study will focus on the measurement of indicators of obesity that it would be feasible to implement in routine NHS maternity care.

This study is one part of a larger body of work that seeks to address the question of if there are more cost-effective adiposity measures than BMI to allocate high-risk care in pregnancy.

7. Research question, aim and objectives

Are there alternative adiposity measures to BMI which better predict adverse pregnancy outcomes?

Aim

To evaluate the prognostic performance of single adiposity measures or a multivariable model to estimate risk of adverse pregnancy outcomes.

Objectives

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.

8. Plan of investigation

a. Design

Prospective cohort study. Pregnant women will be recruited at 11^{+2} to 14^{+1} weeks' gestation (dating scan). 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 hospital records. Data on outcome of pregnancy will be collected from hospital records after delivery.

b. Population

Pregnant women attending the Royal Victoria Infirmary (RVI), Newcastle upon Tyne NHS Trust (NUTH) for a 1st trimester scan (conducted at 11^{+2} to 14^{+1} weeks' gestation; hereafter referred to as the "12-week scan").

c. Inclusion and exclusion criteria

Inclusion criteria

- Singleton pregnancy (women who consent to participate but who are subsequently found to have a multiple pregnancy will be excluded)
- ≥ 18 years of age

- Approximately 12 weeks' gestation (11^{+2} to 14^{+1} weeks)
- Planned delivery at NUTH

Exclusion criteria

- Unable/unwilling to give informed consent to participate
- Women with a miscarriage prior to the 12-week scan, or threatened miscarriage identified on the patient's records as a visit to the Early Pregnancy Assessment Clinic (EPAC) or A&E relating to their pregnancy with an adverse outcome, will be excluded.
- Women having twins (or higher order pregnancy) - we will not know whether women have a multiple pregnancy until their 12 week scan appointment (after consent). Any women identified as having a multiple pregnancy at the 12-week scan will be excluded. They will still receive the thank you gift of pregnancy photographs.

d. Recruitment procedure

The recruitment procedure has been embedded into routine processes and care pathways as much as possible. The process of contacting women for study recruitment is detailed in Appendix 1. This process involves the clinical teams sending a letter to women who are referred to the RVI for their 12-week scan with some brief details about maternity research at the Trust, and the SHAPES study. The clinical teams will phone the women to book their routine 12-week scan appointment. While on the phone, the clinical team will discuss the SHAPES study and enquire whether they might be interested in taking part. Women who are potentially interested in taking part will be assigned to the research sonographer scan list for their 12-week scan which is embedded within the routine antenatal scan clinic. Women who are not interested in taking part at this stage will be have their 12-week scan appointment booked onto the routine (non-research) scan list.

Letter: All women who are referred to NUTH for maternity care are sent a standard letter describing research being carried out in the trust maternity services. A brief introduction to the SHAPES cohort study will be added to this letter during the recruitment period, and will be sent to women before they have had their 12-week

scan booked. The letter will explain to the women that a member of the clinical team might contact them by telephone prior to their 12-week scan appointment date being confirmed, or they might be approached in the clinic when waiting for their 12-week scan, to discuss the research. The letter will indicate that as additional adiposity measurements for the study will be taken, their appointment will be approximately 45 minutes longer. The letter will be sent by the clinical team that normally has access to the patient details. Not all women who are sent the letter will be contacted to be offered to take part in the research due to the limited number of scan slots we have available; therefore once all slots are filled, any remaining women on the scan referral list will have their scan appointment booked onto the routine lists and the research will not be discussed with them by the clinical team.

This process may exclude some women who are interested in taking part who would not get the opportunity. Therefore the letter will state that women can contact the clinical research team directly to discuss the research. The women can also let the clinical team know if they do not want to be contacted to discuss this research over the phone or while attending their scan appointment. If they do this, the clinical team will book their 12-week scan appointment without further mention of the SHAPES study.

NuTH is preparing to transition to the new digital patient records system using Badgernet and the associated patient app Badger Notes. At their booking appointment, women will be asked if they are happy to install the Badger Notes app. For women who want to use the app, their midwife will support them to install this during their booking appointment. Within in the app, there is a function for the Trust to add documents directly and to notify women that they have a new message/document. We will add the initial research letter to the app and use the notification system rather than sending out hard copies of the letter through the post when the Trust has fully transitioned to this new system. We expect that 90% of women will choose to use the app based on feedback from other NHS trusts currently using this system, and that 10% will decline. To be inclusive, and being aware of digital exclusion, we will continue to send the postal letters to any women who do not sign up to use the app.

Telephone calls: The lists of women who are referred to the RVI for a 12-week scan appointment and are due to have their appointment made will be accessed by the clinical team. The team will phone women in chronological order from this list to book their 12-week scan appointment. During this phone call, they will discuss the research and ask whether they might be interested in taking part. Women who indicate that they might be interested in taking part will be offered an appointment for their 12-week scan in one of our research clinics which are embedded within the routine antenatal scan clinics. They will receive a copy of the detailed PIS in advance of the appointment, and will have the opportunity to discuss the study with a member of the research team on the day of their appointment, and can choose to contact us directly in advance of their appointment, before deciding whether or not they wish to participate. Women who decide to participate will be asked to provide written informed consent on the day of their scan appointment. Women who decide not to participate will have their 12-week scan appointment as planned, with no further contact relating to this research.

Approaching women in the scan clinic: Some women do not attend their routine healthcare appointments for various reasons, including scan appointments. A woman who has expressed an interest in the study by phone and has been allocated to the research scan clinic may not attend on the day. In this situation, we have an agreement with the clinical team that we will fill that scan slot with another patient who has attended the routine clinic that day and is waiting for their 12-week scan (e.g. to help clear any backlog of patients waiting due to the clinics over-running or staff absence etc). Any women who have not already declined to take part or discuss this research will be approached upon arrival for their appointment with an offer to participate in this study. These women should have already received the letter informing them about the study before coming to the scan clinic, but not had a discussion on the phone or received the PIS. The research team will share the PIS and have a discussion with them to see if they are interested in taking part in the study. If they are, then the informed consent process will be implemented. If they decline to participate, their 12-week scan will be carried out as planned without any further contact relating to this research.

Other recruitment methods: In addition, we plan to promote the study via social media, giving women who are interested in taking part the opportunity to contact the research team. We have developed a poster and a social media advertisement poster for SHAPES and we will approach the Newcastle Maternity Voices Partnership (www.newcastle-hospitals.nhs.uk/services/maternity/maternity-voices-partnership/) to share this on their Facebook page as well as share on Connie e-midwife website.

Optional extras: The PIS and consent forms include details of additional stages of research that the women in the SHAPES study can participate in. They can choose to consent to any combination of the optional extras, or none of them, and can still take part in SHAPES.

i. *SHAPES Study Interviews*: a planned future study linked to SHAPES is to explore women's experiences of having the additional adiposity measurements taken during their scan appointment. This qualitative research would be carried out as part of a PhD student project (Susan Lennie, co-investigator for the SHAPES study) and will be subject to a different ethics application, with its own protocol and study documents. When recruiting for the shapes study, women will also be informed about the option to take part in this second qualitative study. At this stage, we would only be getting consent to share their details with the research team at Newcastle University who may (or may not) contact them for interview. The reason for not contacting some women is due to the sample size required for the qualitative study being substantially smaller than the SHAPES Cohort Study (approximately 30 women).

ii. *Future research about long-term health and well-being of women and their children:* the SHAPES study will provide a unique cohort dataset in the UK, prospectively collecting early pregnancy adiposity measures which are not part of routine care and therefore not available for analysis using routine datasets.

There is a strong evidence base from non-pregnant populations demonstrating the importance of body fat distribution for predicting cardio-

metabolic risk (described in the background to this protocol, section 6). Therefore, the SHAPES study provides a unique opportunity for future research to explore whether early pregnancy adiposity measures can predict which women go on to develop disease later in life (e.g. type 2 diabetes, cardiovascular disease). There is also a strong evidence base relating to fetal origins of disease and maternal obesity. A recent meta-analysis demonstrated that children of women who start pregnancy with an obese BMI have a 264% increased risk of developing obesity themselves (17). They are also have a significantly increased risk of developing type 2 diabetes (18). Potential mechanisms relate to epigenetic processes in utero, including alterations in DNA methylation and the gut microbiome (19), suggesting that maternal adiposity might have a role to play. However, there is no existing dataset available exploring whether maternal body fat distribution, rather than BMI, can predict which children are at increased risk.

If early pregnancy measures of adiposity were implemented into routine antenatal care, and these measures have strong predictive value for future health of women and/or their children, then these could be utilised for public health screening. Routine maternity measurements could identify which women and babies would benefit most from preventative intervention, and targeted support could start in the postnatal period.

The potential use of early pregnancy adiposity measures in predicting risk for women and babies is hypothetical, based on a wealth of evidence from non-pregnant populations, and would need to be tested. For example, the SHAPES data could be linked with routine health datasets (e.g. NHS Digital) to explore whether early pregnancy adiposity measures predicted women of children who develop type 2 diabetes. No further contact with women or their children for data collection would be required.

We are also asking women who consent to be part of the SHAPES cohort study to also consent to the long term storage of their SHAPES study ID linked with identifiable data for future research (see section 9 for details on

data storage). Any future studies using the SHAPES data would need their own ethics approvals.

e. Sample size

A sample of 1400 women will be recruited to the study. The sample size was based (at the time of grant application and original protocol development) 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 (20, 21). However, recent developments in prognostic model research have allowed us to confirm the above sample is sufficient for this study (22). The sample size calculation is based on a maximum of 7 variables being included in the model based on previously published validated prognostic models in pregnancy including between 1 and 7 predictor variables (23, 24, 25) and the least common pregnancy outcome, which is preeclampsia (estimated prevalence of approximately 5-6% of pregnancies in the UK) (26). 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 than pre-eclampsia, they would require sample sizes smaller than the above figure.

f. Data collection

Following informed consent, participants' 12-week scans will be performed by the study 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. After ultrasound and any other clinical procedures are completed, the rest of the data collection will be performed by a female member of the research team, in a private room. Any women who do not consent to participating in the research will still have their 12-week scan carried out as planned, but no further measurements specific to the research will be taken.

Adiposity measures

The following ultrasound and anthropometry measurements will be taken.

Ultrasound scans:

- *Subcutaneous abdominal fat volume*
- *Visceral abdominal fat volume*
- *Total abdominal fat*

Measurements of subcutaneous and visceral fat will be performed by trained operators (sonographer) using a GE E8 ultrasound machine with 2-5 MHz curvilinear probe. Methods described by Martin *et al.* (27) will be used to obtain the measurement. Ultrasound settings and patient position will be standardised to insure 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 1 cm above the umbilicus to allow visualisation of transvers section of the abdominal aorta at the far field of the screen.

- Subcutaneous fat (SAT) measurement will be obtained from outer border of the subcutaneous fat layer to the outer border of rectus abdominus at the level of linea alba.
- Visceral fat (VAT) measurement will be obtained from the inner border of rectus abdominus at the level of linea alba to the anterior wall of the aorta.
- Total abdominal fat (TAT) will be calculated as a sum of SAT and VAT.

Three consecutive measurements will be performed and average of three will be employed in the predictive model. In a small sub-set of participants, measurement 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* (28).

Anthropometry:

- Waist circumference, measured at the 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 0.1 centimetre.
- Hip circumference, measured at the 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 0.1 centimetre.
- Height will be measured to the nearest 0.1 centimetre with shoes removed and the participant's head positioned in the Frankfort plane.
- Weight will be measured, in light clothing to the nearest 100g.
- Neck circumference, measured 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 0.1 centimetre.
- Mid upper arm circumference, measured at the midpoint of the upper arm between the acromiale and radiale, perpendicular to the long axis of the arm, to the nearest 0.1 centimetre.
- Skinfold thicknesses (subscapular, triceps, biceps, iliac crest and supraspinale) measured using Harpenden skinfold callipers. Sum of skinfolds will be calculated using these measurements.
- 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, Abdominal Volume Index, Conicity Index, Estimated Total Body Fat, Relative Fat Mass, CUN-BAE and body fat percentage will be calculated from these measurements. If any additional composite adiposity measures/indices become available in the literature that can be calculated by the data we have collected then we will explore whether to include these in our analysis.
- Self-reported body shape using a visual scale for body shapes

Measurements will be taken, directly on the skin unless otherwise specified above, 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 ISAK training (https://www.isak.global/). Measurements will be taken

in duplicate, and a third measurement undertaken if the difference between the first two measures is greater than 5% for skinfolds or 1% for 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.

Other predictor variables

A number of other variables that have previously been reported to be associated with pregnancy outcome will be collected by questionnaire or from routine records:

a. Socio-demographic:
    a. maternal age
    b. parity
    c. ethnic group
    d. Index of Multiple Deprivation score (derived from postcode)
b. Clinical:
    a. This pregnancy/booking data (e.g. blood pressure, smoking, alcohol consumption)
    b. Past obstetric history (previous gestational diabetes (GDM), pregnancy hypertension, caesarean section, macrosomia)
    c. Other medical history (pre-existing type 1/type 2 diabetes, hypertension, bariatric surgery)
    d. Family history of diabetes

The table provided in Appendix 2 indicates which additional predictor variables are available from routine records and which will be collected by questionnaire during the 12-week scan appointment. A member of the research team will be available to answer any queries that the participants have related to the completion of the questionnaire.

Outcomes

Adverse outcomes of interest are:

- Gestational diabetes; defined as fasting plasma glucose level of ≥ 5.6 mmol/litre or 2 hour plasma glucose level of ≥7.8 mmol/litre

- Gestational hypertension; defined as blood pressure ≥140/90 mmHg on two occasions at least 4 hours apart after 20 weeks' gestation
- Preeclampsia; defined as a 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.
- Metabolic syndrome: diagnosed using 3 of the following measures: overweight/obese BMI or high waist circumference, elevated triglycerides, high blood pressure that's consistently 140/90mmHg or higher, insulin resistance.
- Pre-term birth; defined as birth before 37 weeks gestation
- Late-term birth; defined as pregnancy that extends over 41 weeks gestation
- Induction of labour; defined as non-surgical treatment to induce the labour.
- Caesarean section; defined as surgical delivery of baby (emergency or elective)
- Instrumental delivery; defined as an assisted birth when forceps or a ventouse suction cup is applied
- Retained placenta: as reported in medical records.
- Haemorrhage: 3rd stage of labour and immediate postpartum period, measured in ml blood loss; as reported in medical records.
- Maternal infection: as reported in medical records.
- 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; as reported in medical records.
    - 3rd trimester scan: abdominal circumference; Femur Length; Estimated fetal weight Hadlock; Umbilical artery PI; End Diastolic flow; Amniotic Fluid Index; as reported in medical records.
- Large for gestational age; defined as birth weight above the 90th centile for gestational age and sex on INTERGROWTH chart.
- Small for gestational age; defined as birth weight below the 10th centile for gestational age and sex on INTERGROWTH chart.
- Apgar scores at 1 and 5 minutes (score 1-10); as reported in medical records.
- Jaundice: as reported in medical records.

- Respiratory distress (including requiring resuscitation): as reported in medical records.
- Feeding method (first feed and feed method at discharge): breastfeeding or artificial feed; as reported in medical records.
- Admission to neonatal special care baby unit (SCBU) or intensive care unit (NICU), high-dependency care, transitional care; as reported in medical records.

In addition, information on any reason for loss to follow up (e.g. late miscarriage, stillbirth, or participant moving to another area) will be sought from medical records in order to account for missing outcome data.

g. 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 at high-risk of an adverse pregnancy outcome. Each adiposity measure will be assessed individually. If no one measure performs better than BMI, multiple logistic regression models will be used for the analysis of each outcome separately. There won't be any variable selection since our predictors are already fixed. Wherever possible, we will retain continuous candidate predictors in their continuous form to avoid statistical power loss (29). Nonlinear trend in continuous predictors will be explored using either fractional polynomials or restricted cubic splines.

The apparent performance of the developed model will be summarised using calibration, discrimination and internal validation analyses (30). 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 (31). Calibration and discrimination of the developed model(s) will be summarised in the datasets

(averaged over imputation datasets). Calibration will also be assessed graphically (32).

The model will be internally validated using bootstrap re-sampling method in order to quantify the degree of optimism due to overfitting (33, 34) and to derive optimism-adjusted indices of discrimination (c index) and calibration (calibration slope) (35). Two hundred bootstrap samples will be used (36). 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.

9. Data storage and management

Data handling, record keeping and access to data

Participant identifiable information will be handled in line with GDPR 2018 principles. Initial data collection and storage will be via Redcap and data will be stored on the NUTH secure server under Caldicott approval until recruitment is complete. At the end of the recruitment period data will be anonymised. All participants will be given a unique identifier to facilitate this. Following completion of all follow up data collection (i.e. from routine maternity records), 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.

The clinical research team and local R&D monitors may require access to the participants' clinical notes; participants will be informed of this in the participant information sheet, and permission to do so will be obtained as part of the consent process.

Archiving

For women who have consented to the SHAPES study, data will be stored securely with restricted access for a period of 5 years after the end of the study. Any

identifiable data will be stored by NUTH, and anonymised research data stored by Newcastle University on a secure server.

Future research: long-term follow-up

Additional consent will also be sought from participants to store their data for future long-term follow up studies. These future studies will explore the association between early pregnancy adiposity and future health-related risks (e.g. for metabolic abnormalities) in women and their offspring. To facilitate linkage of participants' data to other relevant routine datasets in the future (e.g. NHS Digital data), a file containing the 'key' to enable anonymised data to be linked to personal identifiers (i.e. maternal name, date of birth and NHS number, and baby's date of birth and NHS number) will be stored in a separate folder on a Newcastle University secure server, for the participants who consent to this. Access to the separate folder will be restricted to the study's Chief Investigator. Ethical approval will be sought for any future research using this data.

Data Controller

NUTH will be the data controller for the identifiable data collected for the SHAPES Cohort study. For SHAPES participants who consent to the long-term follow up study, Newcastle University will be the data controller (appendix 3).

10. Patient, Public, and Stakeholder Involvement

Pregnant and postnatal women (from here on referred to as mums), clinical stakeholders (obstetricians, midwives, sonographers) and the Research Design Service North East (RDS NE) consumer panel were involved in the development of the proposed research funding application, protocol, and in planning future PPI activities as part of this research.

PPI for research design to date:

Five PPI consultations have been carried out with mums attending a community group (http://birthbabyandfamily.com) led by Janine Smith, a parent support

specialist. Discussions 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; and reviewing the recruitment letters to be sent in advance of making their 12-week scan appointment.

PPI members strongly thought this research was a priority. In addition to reviewing and changing the wording on documentation (PIS and recruitment letters), a summary of the additional issues raised and how we have addressed these (in italic) is provided below:

- Mums' felt the planned research was acceptable as they were used to having multiple measurements in pregnancy, although they thought that some women might be uncomfortable with certain adiposity measurements.
    - *We have specified in the PIS that the researcher taking measurements will be female.*
- Suggested strategies to increase recruitment included:
    - Informing women about the research before their scan appointment
        - *We have included information about SHAPES in a routine NUTH research letter which will be sent in advance of the scan appointment.*
    - Phoning women as part of the strategy (linked with previous suggestion) was discussed; women felt this would be acceptable as long as measures were put in place to avoid phoning women who had a miscarriage following the booking appointment
        - *We have included these steps in the recruitment process, including checking patient records for any reported miscarriage, or any warning signs of a threatened miscarriage such as bleeding or attendance at the Early Pregnancy Assessment Clinic (EPAC) or A&E relating to their pregnancy. We will screen the reports of any EPAC/A&E visits to check for adverse outcomes and will only follow up with women who have confirmation of no adverse outcomes or*

suspected adverse outcomes following assessment at the EPAC/A&E.

- Providing clear information on what the measurements involved, and that those measurements were one-off with no follow-up required.
    - *We have included this information in the PIS*.
- Partners/family members tend to be present at scans so privacy while having the extra measurements taken may be an issue.
    - *We have agreement form the clinical team to have a private room available for these measurements*. *The measurements will also be taken by a female researcher and this is described on the PIS.*
- Options for thank you gifts were discussed. We have the budget to give all women a £5 gift voucher, or photographs of the baby at the 12-week scan appointment plus entry to a prize drawer to win gift vouchers. The provision of photographs was considered an appropriate thank you gift as women would usually have to pay for these, and would be preferable and more meaningful than a £5 gift voucher. The value of a prize draw was also discussed, with women preferring multiple smaller value prizes (e.g. £100) than one or two large value prizes (e.g. £1000).
    - *We have included thank you gifts of mounted photographs from the 12-week scan appointment for all participants, and women can opt into the prize draw if they want to. There are 40 prizes of £100 vouchers in the draw.*

PPI model for the research:

Mums' discussed involvement on steering groups (i.e. PPI collaboration) versus having PPI consultation sessions for the research going forward. They discussed the challenge to PPI collaboration due to the transience of pregnancy versus the lengthy research process. For this reason, PPI consultations were preferable, and we have planned to use this approach throughout the research. However, mums also felt that collaboration would be possible if different PPI representatives could be involved throughout the research rather than having to commit to all of them, as continuity of mums sitting on a steering group was unlikely. It was suggested that non-health

professionals who work with mums (e.g. parent support specialists, breastfeeding peer supporters) could be involved on the steering group for continuity.

- *The PPI plan for this research is based on these discussions with mums. We have planned a series of consultations with mums/parents throughout the research. Janine Smith, a non-health professional parent support specialist, will sit on the steering group, and two mums will be invited to each steering group meeting (likely to be different women each meeting, to be supported by Janine).*

PPI training and development support:

We will carry out a PPI training and support needs assessment for PPI representatives attending steering group meetings. They will have access to Newcastle University PPI workshops, Peer to Peer online forum and annual meetings; buddies from the RDS NE consumer panel; online training (https://www.epaponline.org/); INVOLVE Public Information Pack and other guidance. Role descriptions will be developed with PPI members using INVOLVE recommendations (e.g. mentoring, continued involvement after the project). We will discuss the topics of steering group meetings at PPI consultation sessions in advance of the meetings so PPI perspectives can be represented by PPI members in attendance at the meetings. Steering group meeting preparation will include pre-meetings with PPI representatives; post-meeting debriefs; a glossary of terms relevant to the research; the steering group will be asked not to use jargon/acronyms; and regular PPI updates between steering group meetings. Mums' felt additional training wasn't required for consultation sessions, and that it was the researcher's responsibility to ensure these were delivered at the right level.

PPI contributions to the dissemination plan:

When discussing communication of research to pregnant women and the wider public, mums' stated their information sources were primarily non-NHS (e.g. pregnancy groups, social-media, bloggers), which has informed the dissemination strategy. Plain English writing will be required for patient and public dissemination. When reviewing the plain English summary of the proposed research for the funding

application, the RDS consumer panel and mums provided some similar and also some different feedback. The RDS consumer panel (not necessarily having recent experience with pregnancy) highlighted additional pregnancy-specific terminology that needed explaining, suggesting that mums are more familiar with pregnancy jargon. Therefore, other generalist PPI groups such as the RDS consumer panel will be consulted when developing written communication to ensure the messages are clear to the wider public.

Stakeholder involvement:

Clinical stakeholders were also involved in the development of the research. Key discussion points included considering the effect of existing guideline interventions for women with a BMI≥30kg/m^2 that women will continue to receive as part of routine care during the research time period; recruitment and measurement logistics in the routine antenatal scan clinics; equipment and training required for midwife sonographers to carry out the additional ultrasound measurements; and processes for recruitment relating to sending out letters and follow up phone calls. Clinical stakeholders will continue to be involved in the Project Management Group and Study Steering Group. Additional stakeholders including policy, practice and third sector organisations (e.g. NICE, Royal College of Midwives, Tommy's the Baby Charity, Association for the Study of Obesity, Royal College of Obstetricians and Gynaecologists) will also be invited onto the Study Steering Group.

11. Dissemination

The SHAPES study is part of an NIHR Advanced Fellowship research programme. The findings of this study, in terms of the variables with the best predictive power, will be validated in a subsequent study using individual participant data meta-analysis methods. An economic evaluation of implementing the alternative approach to risk prediction will also be conducted. All research will be published in peer reviewed journals.

Dissemination of the whole programme of work will focus on maximising its impact on the delivery of routine NHS care. Outputs will be target audience appropriate, for example utilising research briefs, policy briefs, media coverage and stakeholder and

participant communication to achieve this goal. The target audience for this work includes:

- health professionals/organisations (e.g. Royal College of Obstetricians and Gynaecologists, Royal College of Midwives)
- pregnant women and their families
- maternity managers and commissioners of services
- national and international policy makers and decision makers (e.g. NICE, CMO's, WHO)
- wider public and media
- third sector (e.g. Tommy's the Baby Charity, Association for the Study of Obesity)
- academics

12. Ethical considerations

This is a low risk, observational study. Caldicott, Research Ethics Committee and Health Research Authority Approval and will be in place before the study begins. The study sponsor is Newcastle upon Tyne Hospitals NHS Foundation Trust.

The main ethical issue for this study is that women will be asked to spend longer in the antenatal clinic (approximately an additional 45 minutes) when they attend for their routine 12-week scan. This is to allow study specific measurements and data collection to be completed. Participants will not be contacted again after this appointment as outcome data will be obtained from routine records, with participants' consent.

There is the potential for distress to be caused to women if we contact them to see if they would like to take part in the research and they have suffered a miscarriage between the time of their booking appointment and the time they are contacted by the clinical research team. To minimise this risk, the clinical teams will check electronic records for any indication that a miscarriage has occurred, or any warning signs that a miscarriage is likely. This will include any record of miscarriage, as well as checking for any attendance at the EPAC or A&E relating to their pregnancy. To be inclusive, if the reports of these clinical assessments are positive and there are no

potentially adverse outcomes reported, then we will contact these women. In cases where either a miscarriage or early warning signs of a miscarriage have been recorded, women will not be contacted about the study.

Only clinically qualified members of the research team will have access to patient records prior to obtaining informed consent to participate in the study.

13. Efforts to reduce bias

We will use standardised approaches to measurement of the adiposity exposure variables. All members of the research team taking the anthropometry measurements will be trained to the international gold standard for these measurements (ISAK). Ultrasound scan measurements will be taken by experienced pregnancy sonographers with training on the non-routine visceral and subcutaneous fat measurements delivered by RV.

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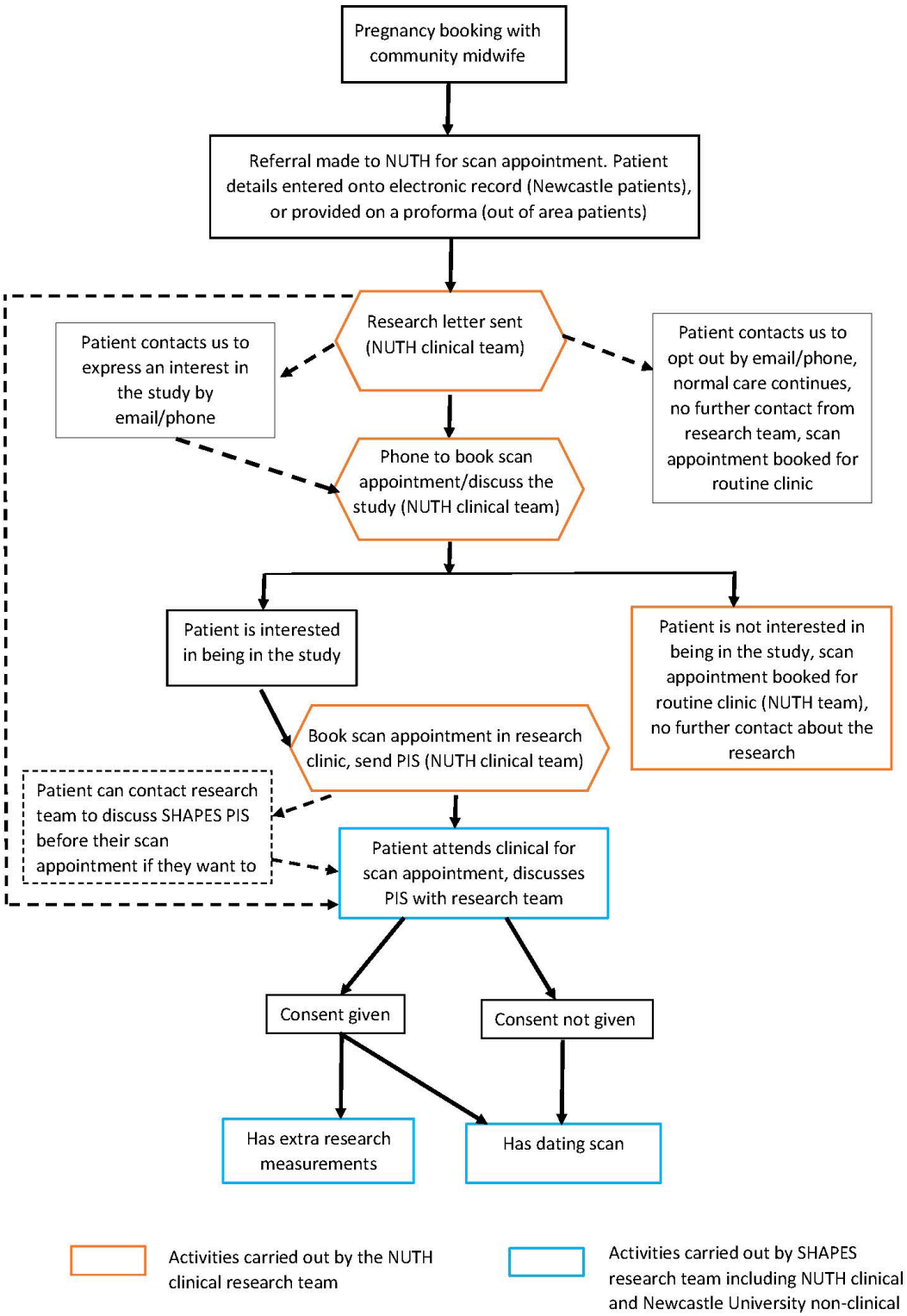
Appendix 1: Participant recruitment process



Appendix 2: Data items

Data item	Reason needed (if not predictor or outcome)	Source		
		Measured	Electronic records	From notes
Mother's NHS number	For data linkage		x	
Mother's name	For data linkage		x	
Mothers date of birth	For data linkage		x	
Maternal death	For data linkage/reason for missing outcome variables		x	
Infant date of birth	For data linkage		x	
Infant name if known	For data linkage		x	
Infant NHS number	For data linkage		x	
Predictor variables				
Height at research visit	n/a	X (12 weeks)	X (at booking)	x
Weight at research visit	n/a	X (12 weeks)	X (at booking)	x
Waist circumference	n/a	X (12 weeks)		
Hip circumference	n/a	X (12 weeks)		
Subcutaneous fat	n/a	X (12 weeks)		
Visceral fat	n/a	X (12 weeks)		
Pre-peritoneal VAT	n/a	X (12 weeks)		
Pre-peritoneal SAT	n/a	X (12 weeks)		
Neck circumference	n/a	X (12 weeks)		
Mid upper arm circumference	n/a	X (12 weeks)		
Skinfold thicknesses	n/a	X (12 weeks)		
Self-reported body image	n/a	X (12 weeks)		
Age at booking	n/a	x	x	x
Gravidity	n/a	x	x	x
Parity	n/a	x	x	x
Ethnic group	n/a	x	x	x
Postcode	To link to Index of Multiple Deprivation (IMD)	x	x	x
Blood pressure at booking systolic	n/a		x	x
Blood pressure at booking diastolic	n/a		x	x
Smoking status (in the past 12 months and current smoking)	n/a	x	x	x
Alcohol intake (before pregnancy and current intake)	n/a	x	x	x
Substance use (before pregnancy)	n/a	x	x	x
Previous C-section	n/a		x	x
Previous macrosomia	n/a		x	x
Diabetes history	n/a		x	x
Family history of diabetes	n/a		x	x
Previous spontaneous preterm birth or mid trimester loss between 16+0 and 34+0 weeks gestation	n/a		x	x
Cervical trauma	n/a		x	x
Cervical length < 25 mm	n/a		x	x
Family history of preeclampsia	n/a		x	x
Essential hypertension	n/a		x	x
Previous pregnancy hypertension	n/a		x	x
Chronic renal disease	n/a		x	x
Autoimmune disease	n/a		x	x
Last pregnancy >10 years ago	n/a		x	x
Previous low birth weight <10%	n/a		x	x

Data item	Reason needed (if not predictor or outcome)	Source		
		Measured	Electronic records	From notes
Previous still birth	n/a		x	x
Previous neonatal death within 4 weeks of life	n/a		x	x
Previous bariatric surgery	n/a	x	x	x
Congenital anomaly	n/a		x	x
Maternal folic acid supplementation	n/a		x	
Outcome measures				
Diagnosis of GDM from home glucose monitoring	GDM			>32 w
OGTT Fasting blood glucose	GDM		< 32 w	
OGTT fasting insulin	GDM/Metabolic Syndrome		< 32 w	
OGTT 1 hour post 75g glucose challenge glucose	GDM		< 32 w	
OGTT 2 hour post 75g glucose challenge glucose	GDM		< 32 w	
OGTT Triglycerides	Metabolic Syndrome		< 32 w	
Gestation at diagnosis of GDM/OGTT	GDM		Date of GDM diagnosis/OGTT Estimated delivery date (EDD)	
Pregnancy induced hypertension (PIH) diagnosis	n/a		x	
Preeclampsia (PE) diagnosis	n/a		x	
Gestation at onset of PIH/PE	PIH/PE		Date of PIH/PE diagnosis EDD	x
Gestation at delivery	Preterm/post term birth LGA/SGA		Date of delivery EDD	
Birthweight	LGA/SGA		x	
Sex of baby	LGA/SGA		x	
Induction of labour	Outcome on its own, plus link to gestation at delivery for spontaneous/ induced preterm		x	
Caesarean section (elective or emergency)	Outcome on its own, plus link to gestation at delivery for spontaneous/ induced preterm		x	
Instrumental delivery (ventouse or forceps)	n/a		x	
Place of delivery	Health economics analysis		x	
Water birth	Health economics analysis		x	
Professionals involved in antenatal care and during labour	Health economics analysis		x	
Retained placenta	n/a		x	
Haemorrhage	n/a		x	
Maternal infection	n/a		x	

Data item	Reason needed (if not predictor or outcome)	Source		
		Measured	Electronic records	From notes
2nd trimester fetal growth (Gestation at the time of 18+0- 20+6; Fetal head circumference; abdominal circumference; Femur Length; Estimated fetal weight)	n/a		x	
3rd Trimester fetal growth (Gestation at the 3rd trimester scan; abdominal circumference; Femur Length; estimated fetal weight; Umbilical artery PI; End Diastolic flow; Amniotic Fluid Index)	n/a		x	
Live birth, still birth, late miscarriage 12-24 weeks	Health economics analysis, Reasons for outcome data not being available		x	
Apgar scores at 1 and 5 minutes	n/a		x	
Jaundice	n/a		x	
Respiratory distress/resuscitation	n/a		x	
Feeding method (first feed and at discharge)	n/a		x	
Number of antenatal scans	Health economics analysis		x	
Hospital admissions in antenatal period	Health economics analysis		x	
Neonatal death within 28 days of delivery	Health economics analysis		x	
Admission to neonatal intensive, high-dependency, special or transitional care	n/a		x	
Maternal length of stay in hospital	Health economics analysis		x	
Maternal medications	Health economics analysis		x	
Other data				
Reasons for outcome data not being available	Data completeness		x	x

Appendix 3 Data Flow

	NUTH (clinical research team / REDCAP)	Newcastle University Secure Server
SHAPES Cohort Study	Consent form* Participant SHAPES ID numbers linked to patient identifiers* Questionnaire data collected at 12-week scan appointment* Adiposity measurements collected at 12-week scan appointment* Pregnancy outcome variables extracted from routine pregnancy data (electronic and hand-held notes)* - NUTH is the data controller	Anonymised questionnaire, adiposity and pregnancy outcome data (SHAPES Study ID number only, no other identifiers) - Newcastle University is the data processor
Optional extra**: Consent to be contacted for SHAPES interviews	Consent form*	Patient contact details*
Optional extra**: Long-term follow-up of SHAPES study	Consent form*	Participant SHAPES ID linked with woman's NHS number, name and DOB; baby's NHS number and DOB* - Newcastle University is the data controller and data processor

* Patient identifiable data

** Optional extra data for SHAPES participants who consent to these