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

STATISTICAL ANALYSIS PLAN (SAP)

Study Title:	Study of How Adiposity in Pregnancy has an Effect on outcomeS (SHAPES): a cohort study
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This statistical analysis plan (SAP) provides a framework and guidelines for the statistical analysis and reporting of the SHAPES cohort study. Any deviation from the methods outlined in this SAP will be documented in the Statistical End of Trial Report. Example Tables, Figures and Listings are for illustrative purposes only and are subject to change.

Revision history

Version	Date	Changes made	Justification for change	Timing of change
1.0	*23/06/2025*	First version	NA	NA

Abbreviations

ABBREVIATION	DEFINITION
ABSI	A Body Shape Index
A&E	Accident and Emergency
AUC-ROC	Area Under the Receiver Operating Characteristic
BAI	Body Adiposity Index
BIF	Bootstrap Inclusion Frequencies
BMI	Body Mass Index
C-index	Concordance index
CI	Chief Investigator
CUN-BAE	Clínica Universitaria de Navarra Body Adiposity Estimator
DBP	Diastolic Blood Pressure
EPAC	Early Pregnancy Assessment Clinic
GDM	Gestational Diabetes Mellitus
HEAP	Health Economics Analysis Plan
ICC	Intra-Class Correlation
IDA	Initial data analysis
IMD	Indices of Multiple Deprivation
IPD-MA	Individual Participant Data meta-analysis
IPD-MAP	IPD-MA Plan
IPW	Inverse Probability Weighting
ITT	Intention-to-treat
LASSO	Least Absolute Shrinkage and Selection Operator
LGA	Large for Gestational Age
MAR	missing at random
MCAR	missing completely at random
MNAR	missing not at random
MFP	Multivariate fractional polynomial
MICE	multiple imputation by chained equations
MROP	Retained placenta/Manual removal of placenta
NHS	National Health Service
NICU	Neonatal Intensive Care Unit
NIHR	National Institute for Health Research
NUTH	Newcastle upon Tyne Hospitals NHS Foundation Trust
OR	odds ratio
OGTT	Oral Glucose Tolerance Test

PE	**Preeclampsia**
PP	Per-protocol
PPIE	Patient and Public Involvement and Engagement
REC	Research Ethics Committee
RVI	Royal Victoria Infirmary
SAP	Statistical Analysis Plan
SAT	Subcutaneous Adipose Tissue
SBP	Systolic Blood Pressure
SCBU	Special Care Baby Unit
SD	Standard Deviation
SGA	Small for Gestational Age
SHAPES	Study of How Adiposity in Pregnancy has an Effect on outcomeS
TAT	Total Adipose Tissue
TRIPOD	Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis
VAT	Visceral Adipose Tissue

1. INTRODUCTION

1.1. STUDY BACKGROUND

Maternal obesity increases risk of pregnancy complications, including gestational diabetes (GDM), maternal/perinatal mortality, and longer-term obesity and type 2 diabetes for women and children. Obesity is usually defined as Body Mass Index (BMI) ≥30kg/m^2. With rising obesity rates, ~185,000 pregnancies/year in England and Wales are considered to have obesity-related increased risk of pregnancy complications and require "high risk" obstetric care. While BMI is routinely used to stratify risk and triage care, it is a poor predictor of individual risk, particularly among women and some ethnic groups, as it doesn't distinguish between fat and lean mass. Qualitative studies and SHAPES PPIE members describe that BMI is stigmatising, inaccurately classifies their health status, and want more accurate measures to inform pregnancy care. Measures of body fat amount and distribution (adiposity) may work better than BMI and be more acceptable to pregnant women/people. This prospective cohort study will measure adiposity indicators, including waist circumference and ultrasound assessments of abdominal visceral fat, during early pregnancy to evaluate their potential to predict adverse pregnancy outcomes.

1.2. STUDY OBJECTIVES

1.2.1. AIMS

This study aims 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).

1.2.2. PRIMARY OBJECTIVES

1. To evaluate the ability of subcutaneous abdominal fat to predict GDM compared to BMI.
2. To evaluate the ability of visceral abdominal fat to predict GDM compared to BMI.
3. To evaluate the ability of total abdominal fat to predict GDM compared to BMI.
4. To evaluate the ability of subcutaneous pre-peritoneal fat to predict GDM compared to BMI.
5. To evaluate the ability of visceral pre-peritoneal fat to predict GDM compared to BMI.
6. To evaluate the ability of total pre-peritoneal fat to predict GDM compared to BMI.
7. To evaluate the ability of waist circumference to predict GDM compared to BMI.
8. To evaluate the ability of neck circumference to predict GDM compared to BMI.
9. To evaluate the ability of mid upper arm circumference to predict GDM compared to BMI.

10. To evaluate the ability of individual and sum of skinfold thicknesses to predict GDM compared to BMI.
11. To evaluate the ability of waist to hip ratio to predict GDM compared to BMI.
12. To evaluate the ability of waist to height ratio to predict GDM compared to BMI.
13. To evaluate the ability of body adiposity index to predict GDM compared to BMI.
14. To evaluate the ability of a body shape index (ABSI) to predict GDM compared to BMI.
15. To evaluate the ability of hip index to predict GDM compared to BMI.
16. To evaluate the ability of weight-adjusted waist index to predict GDM compared to BMI.
17. To evaluate the ability of body roundness index to predict GDM compared to BMI.
18. To evaluate the ability of abdominal volume index to predict GDM compared to BMI.
19. To evaluate the ability of conicity index to predict gestational diabetes compared to BMI.
20. To evaluate the ability of estimated total body fat to predict GDM compared to BMI.
21. To evaluate the ability of relative fat mass to predict GDM compared to BMI.
22. To evaluate the ability of Clínica Universitaria de Navarra Body Adiposity Estimator (CUN-BAE) to predict GDM compared to BMI.
23. To evaluate the ability of body fat percentage to predict GDM compared to BMI.
24. To evaluate the ability of Subscapular/Triceps skinfold ratio to predict GDM compared to BMI.
25. To evaluate the ability of the combination of BMI and waist to height ratio (NICE guidance for non-pregnant populations 2022) to predict GDM compared to BMI.
26. To develop a prognostic model to investigate the effect of including multiple indicators (or measures) of adiposity on the accuracy of predicting GDM (a risk prediction model development study).
27. To develop a prognostic model to investigate the effect of including multiple indicators of adiposity, socio-demographic, and clinical predictors on the accuracy of predicting GDM (a risk prediction model development study).
28. To test the predictive performance of the prognostic measures/models to predict GDM using calibration, discrimination, and internal validation techniques.

1.2.3. **SECONDARY OBJECTIVES**

- To evaluate the ability of subcutaneous abdominal fat, visceral abdominal fat, waist circumference, hip circumference, neck circumference, mid upper arm circumference, skinfold thicknesses, waist to hip ratio, waist to height ratio, the combination of BMI and waist to hip ratio, 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, Subscapular/Triceps skinfold ratio, and body fat percentage to predict other outcomes including gestational hypertension, preeclampsia, retained placenta, haemorrhage, maternal infection, pre-term birth, late-term birth, induction of labour, caesarean delivery, instrumental delivery, birth weight, large for gestational age (LGA), small for gestational age (SGA), Apgar scores, respiratory distress, feeding method and admission to special care baby unit (SCBU) or neonatal intensive care unit (NICU) separately compared to BMI.

- To develop a prognostic model to investigate the effect of including multiple indicators of adiposity on the accuracy of predicting other outcomes (a risk prediction model development study).
- To develop a prognostic model to investigate the effect of including multiple indicators of adiposity, socio-demographic, and clinical predictors on the accuracy of predicting other outcomes (a risk prediction model development study).
- To test the predictive performance of the prognostic measures/models to predict other outcomes using calibration, discrimination, and internal validation techniques.

1.2.4. FURTHER OBJECTIVES

- To determine whether this study can contribute to a larger body of work exploring more cost-effective adiposity measures than BMI for allocating high-risk care during pregnancy.
- To provide results relating to adiposity and pregnancy outcomes that can be used in future data linkage research to explore the association between early pregnancy adiposity and future longer-term health-related risks (e.g. for metabolic abnormalities) in women and their children (subject to further funding).

1.2.5. FUTURE AIMS

To identify the prognostic value of adiposity measures for predicting adverse maternal, fetal, and neonatal outcomes as a composite outcome.

1.3. STUDY DESIGN

This prospective cohort study of 1,450 pregnant women recruited during their first-trimester ultrasound scan at Newcastle upon Tyne NHS Foundation Trust (NUTH), UK, will evaluate the prognostic performance of adiposity measures to estimate risk of adverse pregnancy outcomes, alone or combined with other factors. Early pregnancy adiposity, clinical, and socio-demographic data were collected, along with routine maternal and infant outcome data, to compare adiposity measures with BMI in predicting pregnancy complications.

The study protocol was approved by the North East: Newcastle & North Tyneside 1 Research Ethics Committee (REC reference: 22/NE/0035).

1.4. SAMPLE SIZE AND POWER

The sample size calculation was approached using two different methods at two stages of the study development. Initially, during the grant application and protocol development, we used the "rule of thumb" method, which assumes that 10 events per variable are required for each predictor included in a multivariable model. With 7 predictors and the lowest outcome prevalence (preeclampsia, with an estimated prevalence of 5–6% in the UK) [1], this method suggested a sample size of 1,400 participants was needed.

Subsequently, estimation methods were applied to confirm whether a sample size of 1,400 would be sufficient. Based on previously published and validated prognostic models in pregnancy [2-5], which include between 1 and 7 predictor variables, and focusing on the least common pregnancy outcome (preeclampsia), a sample size of at least 980 participants was calculated as necessary to develop a new model, targeting a shrinkage factor of ≤10% and a C-index of 80%.

Given that other outcomes are more prevalent than preeclampsia and would require smaller sample sizes, the initial target of 1,400 participants would ensure sufficient power and robust modelling across all outcomes. The recruitment target was increased to 1,450 to allow for loss to follow up due to miscarriage or termination of pregnancy, transfer of care to another maternity unit (meaning outcome data could not be retrieved from routine medical records), and withdrawal. However, we have since reviewed our approach and, in the SHAPES PMG meeting held on 19 May 2025, it was decided to include participants who transferred to other maternity units (n = 13) and treat them as missing data to be addressed through imputation. We also agreed to exclude participants who experienced miscarriage or termination of pregnancy outcomes (n = 18), as these outcomes were not originally planned for inclusion. In addition, we decided to exclude participants who withdrew from the study (n = 3), as no information was available for them.

1.5. STUDY POPULATION

In England, an estimated 21% of women have pre-pregnancy obesity according to their BMI (≥30.0kg/m^2) which equates to approximately 189,000 women per year based on current birth rates. A further 28% have an overweight BMI (25.0-29.9kg/m^2) which is approximately 245,500 women/year [6, 7]. Eligible pregnant women attending the Royal Victoria Infirmary (RVI), Newcastle upon Tyne NHS Hospitals Trust (NUTH) for their 12-week scan (11+2 to 14+1 weeks) were recruited starting in April 2022. Recruitment continued until the target sample size was reached. Women aged ≥18 with a singleton pregnancy, attending a dating scan at 11+2 to 14+1 weeks, and planning delivery at NUTH were eligible to participate in this study. Those unable/unwilling to consent, with a miscarriage before the scan, an Early Pregnancy Assessment Clinic (EPAC)/ Accident and Emergency (A&E) visit with an adverse pregnancy outcome, or a multiple pregnancy detected at the scan were not eligible to participate in the study.

At the time data were collected, a small proportion of participants (~1%), were found to have experienced a late miscarriage or termination of pregnancy. These participants were excluded as their pregnancy ended before any of the outcomes of interest for this study could develop. This outcome had not been accounted for in the original protocol, and a decision was later made to exclude these cases accordingly. However, this change was not incorporated into the protocol.

Section 8.c of the study protocol provides more detailed inclusion and exclusion criteria.

1.6. STATISTICAL ANALYSIS PLAN (SAP)

1.6.1. SAP OBJECTIVES

The objective of this SAP is to outline the statistical analyses required to address the objectives of the SHAPES Cohort Study. This SAP will primarily focus on risk prediction modelling for a range of maternal and infant outcomes. The analysis and reporting of the cost-effectiveness of using candidate adiposity measures/models—compared to BMI, the currently used predictor—for assessing risks of adverse pregnancy outcomes will be detailed separately in the SHAPES Health Economics Analysis Plan (HEAP). The candidate adiposity measures/models will be derived from the analyses conducted within this SAP. Additionally, the analysis and reporting related to the presentation and publication of the individual participant data meta-analysis (IPD-MA) for the SHAPES study will be outlined separately in the SHAPES IPD-MA Plan (IPD-MAP). For further details, please refer to the latest version of the SHAPES HEAP and SHAPES IPD-MAP.

The analyses specified in this SAP align with the intent of the protocol, as they compare various adiposity measures to BMI in terms of their ability to predict pregnancy complications. This SAP will focus on two steps. (1) Exploring 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. (2) Building and presentation of a prediction model containing risk factors of an adverse pregnancy outcome. The general considerations for creating these models are: (I) determine the prediction problem - defining predictors and outcome of interest, (II) code predictors, (III) specify a model, (IV) estimate model parameters, (V) evaluate the model, (VI) validate the model, and (VII) presentation of the model.

1.6.2. GENERAL PRINCIPLES

All relevant study data will be summarised overall, and where appropriate by adverse pregnancy outcome. The number of observations and number of missing values will be reported; continuous variables will be summarised using the mean, standard deviation (SD), median, quartiles and range; categorical variables will be summarised with frequencies and percentages.

1.6.3. CURRENT PROTOCOL

The current study protocol at the time of writing is version 6.0, dated 27/11/2023. Future amendments to the protocol will be reviewed for their impact on this SAP, which will be updated only if necessary. If no changes are required to this SAP following future amendments to the study protocol, this will be documented as part of the BRG Change Impact Assessment processes.

1.6.4. DEVIATIONS FROM THE PROTOCOL

For this study only major protocol deviations will be summarised in the statistical end of trial report. Major deviations will include participants found to be ineligible after recruitment. Protocol deviations will be provided in a line listing.

1.6.5. SOFTWARE

Analyses will be carried out using recognised statistical software packages, e.g. R v4.1.0, or later.

2. ANALYSIS

2.1. STUDY POPULATIONS

Intention-to-treat (ITT): This population consists of all participants for whom outcome data were intended to be collected. In this approach, it is assumed that all required outcome data have been successfully obtained. If some participants —those who moved out of the area— do not contribute data for the outcome of interest at the time of study (i.e., there are missing outcome data), data will be imputed. The availability of outcome data will be presented as described in Section 2.6.

The ITT analysis will be performed using the full dataset, including imputed values, to maintain the integrity of the planned analyses. All analyses will be conducted on the ITT population. A per-protocol (PP) analysis may be performed as a sensitivity analysis using only completed cases.

2.2. STUDY STATUS

At the time of writing, recruitment for the study has been completed (April 2022 to April 2024) and all pregnancies were complete (by November 2024), but the data cleaning and validation process is still ongoing.

2.3. INITIAL DATA ANALYSES

Initial data analysis (IDA) will be conducted after the completion of data collection but before formal statistical analyses. IDA will cover all elements of data cleaning and data quality assessment. All initial analysis will be performed independently of the analyses required to address the research questions by the Chief Investigator (CI). Aspects of the IDA will consist of checking for plausible values. Inconsistencies in the data include,

but are not limited to, incorrect data collection or measurement, measurements falling outside acceptable ranges, duplicate measurements, and protocol deviations. The following types of data checks will be undertaken: 1) variable level data checks where the ranges in measurements are examined for outliers and feasibility of values and missing data. 2) Participant level data checks where results for variables are compared to identify if any discrepancies (e.g. if there is a participant with a parity 0 but they have a record of previous GDM). All data queries will be investigated by the clinical research delivery team and missing data or data entry errors corrected prior to data preparation.

2.3.1. DATA PREPARATION

The processes required to derive outcome and predictor variables are shown here, along with how outcomes and predictors will be defined.

2.3.1.1. OUTCOMES

This study includes multiple endpoints/outcomes; however, the focus will be on objective, well-defined, and clinically significant outcomes that are not subject to interpretation. From a medical perspective, 'hard' endpoints are generally preferred. Hard endpoints provide clear, measurable events that indicate a definitive outcome, ensuring robust and reliable conclusions. A comprehensive list of all outcome variables used in the study, along with their definitions, derivation methods, units of measurement, and data types, is provided in the Appendix.

2.3.1.2. PREDICTORS

All anthropometry measurements were 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 were taken, the mean value will be used in data analysis. If three measures were taken, the median value will be used. Measurements of subcutaneous and visceral fat were performed by trained operators. Three consecutive measurements were performed and the average of the three will be employed in data analysis.

For a well-performing prediction model, strong predictors have to be present. The strength of a predictor depends on both its effect size (the strength of its association with the outcome) and its prevalence in the dataset. This means that a predictor's relevance is determined not only by its odds ratio (OR) but also by how frequently it appears in the data. Predictors should be well-defined and consistently measurable by any observer to ensure reliability and reproducibility. Intra-class correlation (ICC) will be used to evaluate the reliability of these predictors after removal of any obvious data entry errors. A comprehensive list of all predictor variables used in the study, along with their definitions, derivation methods, units of measurement, and data types, is provided in the Appendix.

2.4. CLINICAL CHARACTERISTICS OF PARTICIPANTS

Clinical characteristics of participants will be summarised for the ITT population. The following data will be summarised in descriptive analysis:

- Demographics
  - Age
  - Parity
  - Ethnic group
  - Indices of Multiple Deprivation (IMD)

- Medical History
  - Smoking status
  - Alcohol intake
  - Substance use
  - Blood pressure
  - Previous caesarean delivery
  - Previous macrosomia
  - Previous GDM
  - Previous bariatric surgery
  - Previous pregnancy hypertension
  - Diabetes history
  - Family history of diabetes
  - Previous spontaneous preterm birth or mid trimester loss
  - Cervical trauma
  - Cervical length < 25 mm
  - Family history of preeclampsia
  - Essential hypertension
  - Chronic renal disease
  - Autoimmune disease
  - Last pregnancy> 10 years ago
  - Previous low birth weight< 10%
  - Previous still birth
  - Previous neonatal death within 4 weeks of life

- Adiposity measures
  - Ultrasound scans
    - Subcutaneous abdominal fat (SAT)
    - Visceral abdominal fat (VAT)
    - Total abdominal fat (TAT) as a sum of SAT and VAT
    - Subcutaneous pre-peritoneal fat
    - Visceral pre-peritoneal fat
    - Total pre-peritoneal fat
  - Anthropometry
    - BMI
    - Waist circumference
    - Hip circumference
    - Neck circumference

        - Mid upper arm circumference
        - Skinfold thicknesses (individual and sum)
        - Waist to hip ratio
        - Waist to height ratio
        - Body Adiposity Index (BAI)
        - 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
        - Body fat percentage
        - Subscapular/Triceps skinfold ratio
        - the combination of BMI and waist to hip ratio (NICE guidance)

- Adverse outcomes
    - Maternal outcomes
        - GDM
        - Gestational hypertension
        - Preeclampsia
        - Induction of labour
        - Caesarean delivery (total, elective and emergency)
        - Instrumental delivery
        - Retained placenta
        - Blood loss during delivery
        - Maternal infection
        - Maternal length of stay in hospital
    - Infant outcomes
        - Birth weight
        - Pre-term birth
        - Late-term birth
        - Large for gestational age
        - Small for gestational age
        - Apgar score
        - Feeding method (first feed and at discharge)
        - Infant admission to specialist care (SCBU, NICU, transitional)
        - Infant length of hospital stay

- Reason for loss to follow up/ withdrawal

The health economics team confirmed that maternal and infant length of hospital stay will not be considered as outcomes in the risk prediction analysis. Additionally, the clinical team advised against including maternal infection as a predictor due to insufficient detail on infection types. As a result, these variables will not be included in the analysis outlined in this SAP.

2.5. Analytical Methods

2.5.1. Assessment of Individual Predictor Performance

For each outcome measure, the SHAPES analysis will 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. Analysis will be repeated using Inverse Probability Weighting (IPW) to allow for missing outcome data.

An unadjusted logistic regression will be used to consider a single adiposity as an "independent" predictor of adverse pregnancy outcomes. The exponentiated coefficient $(e)^{\beta}$ indicates the OR. The Area Under the Receiver Operating Characteristic (AUC-ROC) curve will be used as a summary metric to evaluate how well each adiposity measure alone distinguishes individuals who develop adverse pregnancy outcomes from those who do not. All AUC-ROC curves will be summarised in a table for each adiposity measure and categorised as follows: fail (0.5 ≤ AUC < 0.6), poor (0.6 ≤ AUC < 0.7), fair (0.7 ≤ AUC < 0.8), considerable (0.8 ≤ AUC < 0.9) and excellent (0.9 ≤ AUC) [8]. We will compare all analyses to BMI (i.e., current practice) using a diagnostic accuracy test, such as the DeLong method [9], to assess the differences in the areas under the ROC curve between two models (new single adiposity vs. BMI). However, no final decisions will be made at this stage (see Section 2.5.3 for details on the decision-making process).

2.5.2. Development of Prognostic Models

After conducting univariate analyses for each adiposity measure, we will proceed with developing and evaluating multi-variable clinical prediction models to identify the most parsimonious model for predicting the risk of multiple outcomes. For each outcome measure, statistical methods will be employed to follow on from Steyerberg's Clinical Prediction Models to identify stable predictors of risk/probability [10, 11]. Prediction models incorporating risk factors for adverse pregnancy outcomes will be developed and presented in the following steps: 1) Variable Selection for the prediction model; 2) Internal validation of the prediction model; and 3) Presenting the predicted probability of adverse pregnancy outcomes.

2.5.2.1. Variable Selection

The SHAPES datasets contain extensive sets of both predictor and outcome variables. In an exploratory research setting, some of these variables may be redundant. Therefore, variable selection is essential for both outcomes and predictors.

2.5.2.1.1. Outcome Variable Selection

Outcome variable selection was discussed with clinicians and PPIE members during the Steering Group Meeting to support prioritisation. As a result, maternal infection was excluded as an outcome due to insufficient detail on infection types. Additionally, maternal and infant length of hospital stay are considered health economic variables and will be addressed in the SHAPES HEAP rather than in the risk prediction modelling.

While the remaining outcome variables are clinically relevant and meaningful, we will prioritise them based on the number of events for each outcome and available external (or prior) information before building the prediction models. Prioritisation will also consider their availability in previous cohorts we plan to use for external validation. From this ranking, we will select the most clearly defined outcomes with high prevalence, as well as their availability in previous cohorts to guide the outcome selection process. As a result, model prediction may not be conducted for all endpoints. The rationale for selecting outcomes will be documented in the final study report.

The healthcare setting and intended use of the model will be considered in the outcome selection process to ensure that clinically significant outcomes are chosen. We will also consider how to handle different types of outcomes, as they vary from binary to continuous measures. The approach to handling different outcome types, including potential dichotomisation, will be determined and specified in a later version of this SAP.

2.5.2.1.2. PREDICTORS VARIABLE SELECTION

In this study, we will work with many covariates/predictors, but only strong and practical predictors will be included in the model. Effective prediction models use variables that are accessible, cost-effective, and measurable with precision. For each outcome measure, this section aims to identify candidate predictors that are either well-established and routinely used in clinical practice with proven or suspected causal relationships, or newly identified in our study as having a significant statistical association. Not all predictors may be deemed useful in our multivariable clinical prediction models. Thus, an upper limit of seven predictor variables has been set based on sample size, practicality, and past research. Dichotomising or categorising continuous predictors reduces information and diminishes statistical power; however, we may still consider it in certain cases. The end of study report will outline the process for selecting predictors for inclusion in the model-building phase. The sample size is sufficient to support the inclusion of various transformations of continuous predictors, including binary conversions, nonlinear terms, and interactions. Multivariate fractional polynomial (MFP) modelling or restricted cubic splines can be used to preserve the continuous nature of covariates, especially when a nonlinear relationship is suspected [12].

In this study, model development will be based on a prospectively collected cohort so that subjects are well defined, all variables of interest are collected, and missing data are minimised. However, if any values—whether outcomes or candidate covariates—are missing, they will be assumed to be missing at random (MAR) and handled using multiple imputation by chained equations (MICE). Ten values will be imputed for each missing value, generating 10 imputed datasets.

To develop parsimonious prediction models, bootstrap resampling will be combined with automated variable selection methods, such as backword selection or with a penalised regression approach, such as Least Absolute Shrinkage and Selection

Operator (LASSO) or Elastic Net penalty. These models may exclude some predictors by setting their coefficients to zero.

For each outcome measure, we will randomly draw 100 samples with replacement from each of the 10 imputed datasets, resulting in a total of 1,000 datasets, effectively capturing the sampling variation in the population. Stepwise regression or LASSO regression will be applied to each bootstrap sample to identify a subset of up to 7 predictors. Priority should be given to predictors with proven or suspected causal relationships with the outcome, ensuring clinically relevant variables are considered in the model. When modelling across bootstrap samples, the prognostic variables that truly are important should be retained in most models fitted. The bootstrap inclusion frequencies (BIF) across all 1,000 datasets to assess the stability of the candidate predictors. We identified stable predictors with > 60% BIF across all imputations. Therefore, only variables retained in more than 60% of samples (i.e. 600 out of 1,000 samples) up to a limit of 7 predictors will be selected to construct the final model. It should be added that when independent variables are correlated, if the bootstrap inclusion frequency of correlated variables together exceed 90%, then the one with higher BIF should be offered to the model. Otherwise, both should be omitted [13].

The aim is that the model derived when variables are included in this way is closer to the optimal model in the population. If each bootstrap iteration is time-consuming, we may consider reducing the complexity by limiting the number of outcomes, decreasing the number of imputations, or using a smaller bootstrap sample. There may be a trade-off between the number of imputations and the number of bootstrap samples that can be reasonably run.

2.5.2.2. INTERNAL VALIDATION

For each outcome measure, the apparent performance of the developed models in the previous steps will be summarised using calibration, discrimination and internal validation analyses [14]. Calibration and discrimination of the developed model(s) will be summarised in the datasets (averaged over imputation datasets). Calibration will also be assessed graphically [15]. 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 AUC-ROC curve for logistic models). In a prognostic model, the C-index measures the likelihood that, when comparing two individuals—one who will experience the event of interest and one who will not—the model will correctly assign a higher probability of an event to the individual who develops the event.

The models will be internally validated using the bootstrap resampling method to assess optimism due to overfitting (i.e., too few outcome events relative to the number of candidate predictors). When evaluating a model's predictive ability on the same data used for its development, performance estimates tend to be overly

optimistic [16]. To account for this, optimism-adjusted measures of discrimination (C-index) and calibration (calibration slope) will be derived for each outcome [10, 17].

Two hundred bootstrap samples will be used. Overfitting, optimism, and miscalibration may also be addressed and accounted for during the model development through shrinkage methods based on bootstrapping techniques or penalisation procedures [17].

2.5.2.3. PRESENTING THE PREDICTED PROBABILITY OF ADVERSE PREGNANCY OUTCOMES

The key details on which predictors were examined, the handling and reporting of missing data, and model-building strategy will be described in the end of study report, adhering to the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidelines [16].

2.5.3. DECISION CURVE ANALYSIS

The final step will use decision curve analysis to identify the model with the highest net benefit. To understand the clinical utility of the final optimised models, decision curve analysis will be performed to compare the net clinical benefit of each predictive model against current practice, as well as up to three individual adiposity measures with superior predictive accuracy [18-20]. Decision curve analysis is a method for evaluating and comparing prediction models (in addition to the traditional validation measures of calibration and discrimination) in terms of their clinical utility i.e. whether one model offers greater net benefit than another when used to inform clinical decision making based on a threshold of predicted risk:

I) The net benefit of the model is plotted against different risk thresholds to produce a decision curve.

II) To obtain the curve, the prediction model is evaluated at different probability thresholds where the threshold is taken as a point above which a patient would be treated, and below which a patient would not be treated.

Decision curves may be plotted for different models on the same graph for comparison, and to help decide which model offers the most benefit. The model with the highest curve (over a range of thresholds) is considered to have the greatest net benefit [18].

2.5.4. EXTERNAL VALIDATION

To externally validate the findings of the SHAPES Cohort risk prediction analysis in heterogeneous external populations, an IPD-MA will be conducted. Please refer to the SHAPES IPD-MAP for detailed guidelines on the data analysis to be undertaken for the IPD-MA.

2.5.5. CONSIDERATION OF SUB-GROUPS

Our intention is to build predictive models that select the optimal set of predictors with the use of transformations where necessary to allow for nonlinear relationships.

This will ensure that sub-groups of prior interest such as ethnic group and categories of BMI (BMI <35 kg/m² and BMI ≥35 kg/m²) will have opportunity to be selected within the model building process. If they are retained in the final model, coefficients can be explored to understand relationships.

2.5.6. SENSITIVITY ANALYSES

If more than 20% of participants have missing in any outcome data, then a sensitivity analysis may be undertaken using only completed cases to explore the uncertainty caused by the missing data.

2.6. LOST TO FOLLOW-UP OUTCOMES

Participants may withdraw consent to provide data or may be lost to follow-up. The reasons for outcome assessments not being completed will be tabulated where available (due to withdrawal, late miscarriage, termination of pregnancy, or relocation to another area).

2.6.1. PREMATURE WITHDRAWAL

Numbers of withdrawals will be summarised as frequency and percentage.

2.6.2. ADVERSE EVENTS

Any unintended or unfavourable medical occurrence in a participant during the study period will be summarised at the NHS trust.

2.6.3. MISSING DATA

Missing values are present in the outcomes and in predictors. They will be identified in each variable for both outcome and predictor variables across the entire study dataset. The availability of predictors will be summarised, and reasons for missingness will be tabulated where reported.

We will further examine patterns of missingness, following the steps: 1) how many missing occur for each potential predictor? We might use packages such as {*naniar*} or {*ggmice*} in R to further visualise missing value patterns. 2) missing value mechanisms. For analysis of the mechanism of missingness, we may examine combinations of missing predictors, associations between predictors and missingness, and associations between outcome and missingness. This determines how well we may be able to impute a missing value, and how useful the remaining information on subjects without missing values is. If associations are found, the assumption of missing completely at random (MCAR) is violated. Although we cannot formally test whether data are

missing not at random (MNAR) versus missing at random (MAR), for the purposes of our analysis, we will assume the missingness is MAR [10].

When analysing the ITT population, model-based multiple imputation (MI) will be used for both primary and secondary outcomes, with 10 imputations. A five-step approach will be used for imputation: 1) explore the missing data patterns; 2) choose a method of imputation; 3) perform imputation; 4) assess diagnostics of the imputation; and 5) analyse the imputed data sets [21].

Sensitivity analysis may be conducted using only completed cases to assess the impact of missing data handling on the results.

3. TABLES AND FIGURES

Tables and figures will be produced to satisfy the requirements of this SAP. It is anticipated that the results of some analyses will lead to further exploratory work. Therefore, the precise content and layout of the statistical outputs are not specified here.

4. LISTINGS

All study data, including statistical analysis datasets, will be made available in a format to be agreed.

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6. APPENDIX

This appendix includes tables that describe how the outcome and predictors measures will be defined. Each table outlines the specific variables and calculation methods used to derive the outcomes and predictors, ensuring consistency and transparency in the analysis.

Table A. Outcomes Overview and Definitions

Adverse outcomes	**Definition**	**Derivation Process**	**Type (Binary, Categorical, Continuous, etc.)**	**Values/Units**
Maternal outcomes				
GDM	Diagnosis based on fasting plasma glucose ≥5.6 mmol/L OR 2-hour plasma glucose ≥7.8 mmol/L OR pre-recorded diagnosis	Oral Glucose Tolerance Test (OGTT) and pre-existing diagnosis. Final Diagnosis = Yes if either: - Existing Yes/No Column = Yes, OR - Fasting Plasma Glucose (FPG) ≥ 5.6 mmol/L, OR	Binary	Yes/No

		- 2-hour Plasma Glucose (2hPG) ≥ 7.8 mmol/L		
Gestational Hypertension	Hypertension onset after 20 weeks, defined as SBP ≥140 mmHg and/or DBP ≥90 mmHg on two occasions at least 4 hours apart OR pre-existing diagnosis	Blood pressure measurement & pre-recorded diagnosis. Final Diagnosis = Yes if either: - Pre-existing Yes/No Column = Yes, OR - Systolic Blood Pressure (SBP) ≥ 140 mmHg AND/OR - Diastolic Blood Pressure (DBP) ≥ 90 mmHg (on two occasions at least 4 hours apart after 20 weeks)	Binary	Yes/No
Preeclampsia (PE)	New onset of hypertension (≥140 mmHg SBP or ≥90 mmHg DBP) 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.	Blood pressure & urine protein measurement, clinical records Final Diagnosis = Yes if either: - Pre-existing Yes/No column = Yes, OR - New-onset Hypertension after 20 weeks (SBP ≥140 mmHg and/or DBP ≥90 mmHg on two occasions at least 4 hours apart) AND - Proteinuria (≥300 mg/24 hours or protein: creatinine ratio ≥30 mg/mmol or dipstick reading ≥2+), OR - Maternal organ dysfunction (e.g.,	Binary	Yes/No

		renal insufficiency, liver involvement, neurological complications) OR uteroplacental dysfunction (e.g., fetal growth restriction, abnormal umbilical artery doppler, or stillbirth.)		
Induction of labour	Non-surgical treatment to induce labour.	Administration of induction agents	Binary	Yes/No
Caesarean Delivery (Total, Elective, Emergency)	Surgical delivery of baby, categorised as elective or emergency.	Derived from Mode of Delivery and Type of Caesarean columns. Caesarean Delivery can be considered as a categorical variable with three categories (Vaginal, Elective C-section, Emergency C-section) or as a binary variable (Vaginal vs. Caesarean, where elective and emergency C-sections are grouped together).	Categorical/ Binary	Vaginal / Caesarean (Elective / Emergency)
Instrumental delivery	Assisted birth using forceps or ventouse suction cup	Hospital records	Binary	Yes/No
Retained placenta/Manual removal of placenta (MROP)	Placenta not delivered within 30 minutes postpartum	Hospital records	Binary	Yes/No
Blood loss during delivery	3rd stage of labour and immediate postpartum period blood loss	Hospital records	Continuous	mL
Maternal infection*	Any postnatal infection	Hospital records	Binary	Yes/No

	documented in medical records			
Maternal length of hospital stays*	Duration of hospital stay from admission to discharge	Hospital records	Continuous	Day
Infant outcomes				
Birth weight	Infant's weight at birth.	Measured at delivery	Continuous	Grams (g)
Pre-term birth	Birth before 37 weeks gestation	Derived from Gestational Age at Delivery If Gestational Age at Delivery < 37 weeks, then Yes, otherwise No	Binary	Yes/No No refers to term birth
Late-term birth	Birth extending beyond 41 weeks gestation	Derived from Gestational Age at Delivery If Gestational Age at Delivery > 41 weeks, then Yes, otherwise No	Binary	Yes/No No refers to term birth
Large for gestational age (LGA)	Birth weight >90th centile for gestational age and sex (INTERGROWTH chart)	Birth weight measured at delivery Birth weight percentile derived from INTERGROWTH chart Birth weight percentile >90th centile classified as LGA	Binary	LGA/Appropriate gestational age (AGA)
Small for gestational age (SGA)	Birth weight <10th centile for gestational age and sex (INTERGROWTH chart)	Birth weight measured at delivery Birth weight percentile derived from INTERGROWTH chart Birth weight percentile <10th centile classified as SGA	Binary	SGA/AGA
Apgar score <7	Newborn condition at 1-	Apgar assessment	Binary	Low/Normal

	and 5-minutes post-birth	The Apgar scores at 1- and 5-minutes post-birth, ranging from 0 to 10, will be categorised based on a cut-off point of 7. Scores were classified as follows: Low Apgar Score: < 7 Normal Apgar Score: >= 7 This classification will be applied separately to both the 1-minute and 5-minute Apgar scores.		
Feeding method (first feed)	Type of first feed given after birth	Hospital records	Categorical	Artificial/Breast mother/Breast donor/Mixed/No feed
Feeding method at discharge	Infant's feeding method at hospital discharge	Hospital records	Categorical	Breastfeeding/ Artificial/Both
Infant admission to specialist care	Infant admission to specialist care (admission to SCBU or NICU or high-dependency care, transitional care)	Hospital records	Binary	Yes/No
Infant length of hospital stay*	Duration of infant hospital stay if admitted to specialist care	Hospital records	Continuous	Day

* The health economics team confirmed that maternal and infant length of hospital stay do not need to be considered as outcomes for the risk prediction analysis. Moreover, the clinical team advised against using maternal infection as a predictor due to insufficient detail on infection types.

Table B. Predictors Overview and Definitions

Variable	Definition	Derivation Process	Type (Binary, Categorical, Continuous, etc.)	Values/Units
Demographics				
Age	The age of the individual at the time of data collection.	Medical records or self-report.	Continuous	Year
Parity	The number of previous live births a woman has had.	Medical records or self-report.	Count	Number of children (e.g., 0, 1, 2, etc.)
Ethnic group	The ethnic background of the individual.	Self-reported, based on a standardised survey or medical record.	Categorical	- White - British; - White - Irish; - White - Any other; White background; Mixed - White and Black Caribbean; - Mixed - White and Black African; - Mixed - White and Asian; - Mixed - Any other mixed background; - Asian or Asian British - Indian; - Asian or Asian British - Pakistani; - Asian or Asian British - Bangladeshi; - Asian or Asian British - Any other Asian background; - Black or Black British - Caribbean; - Black or Black British - African; - Black or Black British - Any other Black background;

				- Other Ethnic Groups - Chinese; - Other Ethnic Groups - Any other ethnic group
Indices of Multiple Deprivation (IMD)	A measure of deprivation based on income, employment, health, education, and other factors.	Calculated based on geographical location (postcode)	Continuous or Ordinal (depending on scale)	Score (range 0-100, or Quintiles)
Medical History				
Smoking status	A combined variable summarising smoking behavior in the past 12 months and at booking.	Derived from three self-reported questions: Smoking in past 12 months, Smoking status at booking, and Current cigarettes per day.	Categorical (Multi-category or Nested Categorical)	Non-smoker/ Yes (stopped before conception)/ Yes (and how many cigarettes per day)/ No at booking
Alcohol intake	Amount of alcohol consumed before pregnancy and currently (now), measured in glasses or pints per month.	Medical records or self-report.	Continuous	**Before Pregnancy**: Alcohol intake (in units) **Now**: Alcohol intake (in units) One unit of alcohol is equivalent to approximately 10 ml (or 8 grams) of pure alcohol.
Substance use before pregnancy	Type of substance used before pregnancy.	Medical records or self-report.	Categorical	Never / Acid / Aerosols / Amphetamines / Cannabis / Cocaine / Crack / Crystal meth / Diazepam / Ecstasy / Glue / Heroin / Ketamine / Khat / Lighter fuel / Methadone / Speed / Subutex / Temazepam / Other / Declined to answer
Blood Pressure	Systolic and Diastolic blood	Measured at booking by	Continuous	mmHg (millimeters of mercury)

at Booking	pressure at booking. Systolic is the higher value, and Diastolic is the lower value.	healthcare provider.		
Previous caesarean delivery	Whether the participant has had a previous caesarean delivery.	Self-reported or from medical records.	Binary	Yes / No
Previous Macrosomia	History of previous large baby (birth weight > 4,000g).	Medical records or self-report.	Binary	Yes / No
Previous GDM	History of GDM in a previous pregnancy.	Medical records or self-report.	Binary	Yes / No
Previous Bariatric Surgery	History of bariatric surgery before current pregnancy.	Medical records or self-report.	Binary	Yes / No
Previous Pregnancy Hypertension	History of hypertension during previous pregnancy.	Medical records or self-report.	Binary	Yes / No
Diabetes History	History of diabetes, including previous Gestational Diabetes (GDM) or type 1/type 2 diabetes.	Medical records or self-report.	Categorical	None / Previous GDM / Type 1 / Type 2
Family History of Diabetes	Family history of diabetes in first-degree relatives.	Self-report.	Categorical	None / Type 1 / Type 2
Previous Spontan	History of spontaneous	Medical records or self-report.	Binary	Yes / No

eous Preterm Birth or Mid Trimester Loss	preterm birth or pregnancy loss between 16+0 and 34+0 weeks gestation.			
Cervical Trauma	History of trauma to the cervix.	Medical records or self-report.	Categorical	Previous cone biopsy / Large loop excision of the transformation zone (LLETZ) / Radical diathermy / Other / None
Cervical Length < 25 mm	Measurement of cervical length less than 25mm.	Clinical measurement (ultrasound).	Binary	Yes / No
Family History of Preeclampsia	Family history of preeclampsia in first-degree relatives.	Self-report.	Binary	Yes / No
Essential Hypertension	History of essential hypertension before pregnancy.	Medical records or self-report.	Binary	Yes / No
Chronic Renal Disease	History of chronic kidney disease.	Medical records or self-report.	Binary	Yes / No
Autoimmune Disease	History of autoimmune disease (e.g., lupus, rheumatoid arthritis)	Medical records or self-report.	Binary	Yes / No
Last Pregnancy > 10 Years Ago	If the last pregnancy occurred more than 10 years ago.	Medical records or self-report.	Binary	Yes / No
Previous Low Birth Weight < 10%	History of previous low birth weight (< 10th percentile).	Medical records or self-report.	Binary	Yes / No
Previous Stillbirth	History of neonatal death within 4	Medical records or self-report.	Binary	Yes / No

	weeks of birth.			
Previous Neonatal Death Within 4 Weeks of Life	History of neonatal death within 4 weeks of birth.	Medical records or self-report.	Binary	Yes / No
Adiposity Measure				
Ultrasound Scans				
Subcutaneous Abdominal Tissue (SAT)	Measurement of subcutaneous fat located below the skin, using ultrasound.	Ultrasound scan using a GE E8 machine with a 2.3-8.4 MHz curvilinear probe. Three consecutive measurements are averaged.	Continuous	Number (mm)
Visceral Abdominal Tissue (VAT)	Measurement of fat surrounding internal organs, using ultrasound.	Ultrasound scan using a GE E8 machine with a 2.3-8.4 MHz curvilinear probe. Three consecutive measurements are averaged.	Continuous	Number (mm)
Total Abdominal Tissue (TAT)	Sum of subcutaneous and visceral abdominal fat.	SAT + VAT	Continuous	Number (mm)
Subcutaneous Pre-Peritoneal Fat	Measurement of the subcutaneous fat located between the cutaneous layer and the linea alba in the sagittal plane.	Ultrasound scan in the sagittal plane of the xiphisternum, from the lower border of the cutaneous layer to the upper border of the linea alba. Three consecutive measurements are averaged.	Continuous	Number (mm)

Visceral Pre-Peritoneal Fat	Measurement of visceral fat located between the linea alba and the liver capsule in the sagittal plane.	Ultrasound scan in the sagittal plane of the xiphisternum, from the lower border of the linea alba to the upper border of the liver capsule. Three consecutive measurements are averaged.	Continuous	Number (mm)
Total Pre-Peritoneal Fat	Sum of subcutaneous and visceral pre-peritoneal fat	Subcutaneous Pre-Peritoneal Fat + Visceral Pre-Peritoneal Fat	Continuous	Number (mm)
Anthropometry				
BMI	A measure of body fat based on weight and height.	Height was measured to the nearest 0.1 cm with shoes removed and the participant's head positioned in the Frankfort plane. Weight was measured in light clothing to the nearest 100 g. Two or three measurements were taken for both height and weight, with the median used for analysis. BMI will then be calculated using the formula: weight(kg)/height^2 (m)	Continuous	kg/m²

Waist Circumference	Circumference measured at the narrowest point of the abdomen	Measured at the narrowest point between the lower costal border and iliac crest, perpendicular to the trunk, at end of normal expiration. Two or three measurements taken, with the median used for analysis.	Continuous	Centimeters (cm)
Hip Circumference*	Circumference measured at the greatest posterior protuberance of the buttocks	Measured at the greatest posterior protuberance of the buttocks, perpendicular to the trunk, with gluteal muscles relaxed, feet together, over light clothing. Two or three measurements taken, with the median used for analysis.	Continuous	Centimeters (cm)
Neck Circumference	Circumference measured immediately superior to the thyroid cartilage	Measured immediately superior to the thyroid cartilage, perpendicular to the long axis of the neck, with the head in the Frankfort plane. Two or three measurements taken, with the median used for analysis.	Continuous	Centimeteres (cm)
Mid upper	Circumference measured at	Measured at the midpoint of the	Continuous	Centimeteres (cm)

arm Circumference	the midpoint of the upper arm between the acromiale and radiale.	upper arm between the acromiale and radiale, perpendicular to the long axis of the arm, to the nearest 0.1 centimetre. Two or three measurements taken, with the median used for analysis.		
Skinfold Thicknesses (individual and sum)	Skinfold thicknesses at subscapular, triceps, biceps, iliac crest, and supraspinale measured using Harpenden skinfold callipers.	Measured at subscapular, triceps, biceps, iliac crest, and supraspinale sites using Harpenden skinfold callipers. For each site, if two or three measurements are taken, the mean value will be used as the final thickness for that site. The sum of skinfolds will be calculated by adding the averaged values from all five sites.	Continuous	Millimetres (mm)
Waist to Hip Ratio	Ratio of waist circumference to hip circumference.	Waist circumference (cm)/ Hip circumference (cm)	Continuous	Ratio
Waist to Height Ratio	Ratio of waist circumference to height.	Waist circumference (cm)/ Height (cm)	Continuous	Ratio

Body Adiposity Index (BAI)	A measure of body fat based on hip circumference and height.	Hip circumference (cm)/ Height $(m)^{1.5}$ -18 (x1000; derive numbers in the order of magnitude of Waist circumference (cm))	Continuous	Unitless
A Body Shape Index (ABSI)	An index combining waist circumference, weight, and height to estimate risk of obesity-related diseases.	1000* Waist circumference (cm)* $Weight(kg)^{-2/3}$ * $Height(m)^{5/6}$	Continuous	Unitless
Hip Index	An index combining hip circumference, weight, and height to estimate body fat distribution.	Hip circumference (cm)* $Weight(kg)^{-0.482}$* $Height(m)^{0.310}$	Continuous	Unitless
Weight-Adjusted Waist Index	Index combining waist circumference and weight to estimate abdominal fat distribution.	(Waist circumference (cm) *100)/$(Weight(kg)^{0.5})$	Continuous	Unitless
Body Roundness Index	Index estimating body fat distribution and roundness based on waist circumference and height.	364.2 - (365.5*sqrt (1-(0.5* Waist circumference (cm) $/\pi)^2$/(0.5*Height(cm))^2)	Continuous	Unitless

Abdominal Volume Index	An index estimating abdominal volume based on waist and hip circumferences.	(2*(Waist circumference(cm) *100)^2 + 0.7*(Waist circumference(cm) *100- Hip circumference(cm) *100)^2)/1,000	Continuous	Unitless
Conicity Index	An index reflecting abdominal fat distribution based on waist circumference, weight, and height.	Waist circumference (cm)/ (0.109*(Weight (kg)/ Height(m))$^{0.5}$)	Continuous	Unitless
Estimated Total Body Fat	Estimated total body fat percentage based on waist circumference and weight.	100*(-Z+A-B)/C A = (4.15* Waist circumference (cm)*39.3701) B = (0.082* Weight (kg) *2.20462) C = (Weight (kg)*2.20462) Z =76.76 (females)	Continuous	Percentage (%)
Relative Fat Mass	A measure of body fat mass based on height and waist	76 - (20* Height (m)/ Waist circumference(m))	Continuous	Unitless
CUN-BAE	An estimator of body adiposity based on age, gender, and BMI.	−34.299 + (0.503* age) + (3.353*BMI) − (0.031*BMI2) − (0.02*BMI*age) + (0.00021* BMI2* age)	Continuous	Unitless
Body fat percentage	Proportion of total body weight that is fat.	Using Jackson & Pollock's 3-Site Formula:	Continuous	Percentage (%)

		0.29669*Sum of Skinfolds (mm)– 0.00043*(Sum of Skinfolds(mm))^2+ 0.02963*Age + 1.4072 BMI-Based Estimation Formula: 1.20*BMI + 0.23*Age−16.2		
Subscapular/triceps skinfold ratio	A proxy for fat distribution, particularly to differentiate between central (upper body) and peripheral (limb) fat.	subscapular skinfold ÷ triceps skinfold	Continuous	Ratio
The combination of BMI and waist to hip ratio (NICE guidance)**	This classification applies to individuals with BMI < 35 kg/m², regardless of sex or ethnicity, including those with high muscle mass: Healthy central adiposity: Waist-to-height ratio 0.40–0.49 — No increased health risks Increased central		Categorical	Healthy central adiposity/ Increased central adiposity/ High central adiposity/Very high central adiposity

	adiposity: Waist-to-height ratio 0.50–0.59 — Increased health risks High central adiposity: Waist-to-height ratio ≥ 0.60 — Further increased health risks For individuals with BMI ≥ 35 kg/m², central adiposity is assumed to be high, and this classification does not apply as-is. These individuals should be categorised as having very high overall adiposity, regardless of waist-to-height ratio.			

* Hip circumference will be used in combination with other measurements as a predictor and will not be analysed independently.
** Identifying and assessing overweight, obesity and central adiposity | Overweight and obesity management | Guidance | NICE