**Predicting the risk of childhood overweight and obesity at 4-5 years using population-level pregnancy and early-life healthcare data**

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**Abstract:**

**Background:** Nearly a third of children in the UK are overweight, with the prevalence in the most deprived areas more than twice that in the least deprived. The aim was to develop a risk identification model for childhood overweight/obesity applied during pregnancy and early life using routinely collected population-level healthcare data.

**Methods:** A population-based anonymised linked cohort of maternal antenatal records (January 2003 to September 2013) and birth/early-life data for their children with linked body mass index (BMI) measurements at 4-5 years (n=29060 children) in Hampshire, UK. Childhood age- and sex- adjusted BMI at 4-5 years, measured between September 2007 and November 2018, using a clinical cut-off of ≥91st centile for overweight/obesity. Logistic regression models together with multivariable fractional polynomials were used to select model predictors and to identify transformations of continuous predictors that best predict the outcome.

**Results:** Fifteen percent of children had a BMI≥91st centile. Models were developed in stages, incorporating data collected at first antenatal booking appointment, later pregnancy/birth and early life predictors (1 and 2 years). The area under the curve (AUC) was lowest (0.64) for the model only incorporating maternal predictors from early pregnancy and highest for the model incorporating all factors up to weight at 2 years for predicting outcome at 4-5 years (0.83). The models were well calibrated. The prediction models identify 21% (at booking) to 24% (at ~2 years) of children as being at high risk of overweight or obese by the age of 4-5 years (as defined by a ≥20% risk score). Early pregnancy predictors included maternal BMI, smoking status, maternal age and ethnicity. Early life predictors included birthweight, baby’s sex and weight at 1 or 2 years of age.

**Conclusions:** Although predictive ability was lower for the early pregnancy models, maternal predictors remained consistent across the models, thus high-risk groups could be identified at an early stage with more precise estimation as the child grows. A tool based on these models can be used to quantify clustering of risk for childhood obesity as early as the first trimester of pregnancy, and can strengthen the long-term preventive element of antenatal and early-years care.

**Keywords:** pregnancy, early life, overweight, obesity, prediction

**Introduction**

In 2016, 50 million girls and 74 million boys worldwide were obese1. Childhood obesity has adverse effects on cardiovascular structure and function, with increased lifetime risk of cardiovascular disease2. Overweight or obese children are over four times more likely to also have overweight or obesity at age 153. With high rates of overweight and obesity and evidence of tracking of weight status from childhood to adolescence to adulthood4, a higher proportion of the population is being exposed to obesity for longer. Obesity contributed to 617,000 hospital admissions in England in 2016/17, an 18% increase from the year before (2015/16)5. Data from the National Child Measurement Programme (NCMP) in England showed that in 2017/18, 22% of children aged 4 to 5 years and 34% aged 10 to 11 years were classified as overweight or obese6. Children living in the most deprived areas in England were twice as likely to be obese than children in the least deprived areas, and this gap has shown an increase over the last decade6.

Intervening early to prevent childhood obesity is key to tackling the obesity epidemic7. Prevention is a central theme of the UK Government’s vision for the nation’s health8-11. Key to effective prevention, complementing population-level policy change and intervention, is identifying groups at risk for targeted support. The first ‘1000’ days, the time from conception to age 2 years, is recognised to be a critical period of development. Maternal factors and early life factors consistently shown to be associated with risk of childhood overweight and obesity during this period include maternal pre-pregnancy overweight and obesity12,13, maternal smoking during pregnancy13,14, maternal excessive gestational weight gain14, high birth weight13,14, and rapid infant weight gain in the first two years13,14. Gestational diabetes, has also been identified as a risk factor14. Maternal educational attainment15-17 and employment status18-20 are also risk factors, but fewer studies have examined these associations. Evidence on breastfeeding and maternal postnatal depression as risk factors for childhood obesity is less consistent14. Research using birth cohort data from Singapore21 and the UK22 have shown that having a greater number of pregnancy and early life risk factors increases the risk of childhood overweight and obesity. However, quantifying the effect of this combined risk in clinical practice to target interventions using routinely available data is less explored.

Risk prediction based on single predictive factors tends to have poor prognostic accuracy. The use of multiple predictive factors combined in a prediction model improves the prediction23. Better predictive information is beneficial to identify children at risk early thus providing the ability to target interventions and support at an earlier stage. A systematic review of existing prediction models of overweight and obesity in childhood found eight existing models developed using data from Greece, Finland, Germany, USA, the Netherlands, Seychelles and two from the UK24. Only two of these eight models could be applied to routinely-collected healthcare data in the UK. The other six models included predictors related to the father (such as paternal BMI or employment) or household (such as smoking in the household and income) which are not measured routinely as part of antenatal or postnatal healthcare records. Both models that could be applied to a routine dataset included the same predictors – maternal BMI, birthweight (z-score), early life weight gain (z-score) and infant gender. However there are other maternal and child variables that can be included to potentially enhance predictive power and do not involve extra data collection by healthcare professionals in their everyday practice, and this is what we set out to test.

We aimed to develop and internally validate prediction models of childhood overweight and obesity using antenatal, birth and early life data, all of which are routinely collected as part of healthcare records, utilising an objective measure of weight status at school age. This offers the unique perspective of assessing whether routinely collected data can be used to predict overweight and obesity at an early stage with reasonable accuracy, and ultimately whether such a childhood obesity risk estimation tool can be effectively applied during pregnancy and early life to help healthcare professionals target extra support towards high risk families.

**Methods**

SLOPE (Studying Lifecourse Obesity PrEdictors) is a population-based anonymised linked cohort of maternal antenatal and birth records and child health records for all births registered at University Hospital Southampton (UHS), in the South of England between 2003 and 2018. UHS provides maternity care to residents in the city of Southampton and the surrounding areas of Hampshire. Child healthcare for the same area is provided by two community National Health Service (NHS) trusts; Solent and Southern Health. Thus, the antenatal and birth records (n=83481) were then linked to child health data from these two community NHS trusts (n=74770, 90% linked). Only singleton pregnancies with feasible gestational age, maternal weight and maternal height measurements were included in this analysis. All the variables described below are routinely-collected for pregnant women and children receiving healthcare in the study region.

*Outcome measurement*

As part of the NCMP, the height and weight of children in all state-maintained schools in England are measured by school nurses at Year R (4-5 years) and Year 6 (10-11 years)25. In the UK, children start school in the September after their fourth birthday and they can be measured at any point during the school year. For the purposes of this study, this was defined as the first measurement of weight and height on the same day between the ages of 4 and 6 years. Thus, all children with a valid weight and height measurement at reception year constituted the sample for outcome (n=30958). BMI was then calculated as weight/(height)2 and converted to age- and sex- adjusted BMI z-scores according to the UK 1990 growth reference charts26. A z-score of +1.33 equates to the 91st percentile and this was used to specify the outcome of childhood overweight and obesity used in the prediction models. This cut-off was chosen as it is the most relevant to healthcare professionals in the UK, given it is the one used by national guidance on the clinical management of childhood overweight27,28, and has been used in another UK-based prediction model29.

*Candidate predictors*

The prediction model was developed in stages, incorporating data collected at the booking appointment, birth and early life (1 and 2 years of age). Thus, model predictors were identified at each of these stages. For later time-points (birth and early life), the candidate predictors are in addition to the candidate predictors from the earlier stage.

*First antenatal (booking) appointment*: The first antenatal booking appointment is recommended to ideally take place by the 10th week of gestation, according to the National Institute for Health and Care Excellence (NICE) Guidelines30. Maternal age (in years) was calculated from date of birth in the clinical electronic records. Maternal BMI was calculated using weight in kilograms measured at the booking appointment by the midwife and self-reported height. Smoking was self-reported as current smoker, ex-smoker or non-smoker. Highest maternal educational qualification was categorised as secondary (GCSE) and under, college (A levels) and university degree or above. Self-reported ethnicity was recorded under 16 categories and condensed to White, Mixed, Asian, Black/African/Caribbean and Other. Employment status was categorised as employed, unemployed and in education. Intake of folic acid supplements was categorised as taking before becoming pregnant, started taking once pregnant and not taking supplement. Maternal first language English, history of stillbirth/miscarriage, previous caesarean section, maternal disability status, maternal substance use and partnership status was categorised as yes or no. Infertility treatment was categorised as no, yes (hormonal only, in-vitro fertilisation, gamete intrafallopian transfer and other surgical) and investigations only. Maternal history, obstetric history and family history were asked as separate questions such as “do you have an existing medical conditions” and recorded if any existing conditions were reported to each of the three questions. Parity was recorded as the number of previous live births reported and condensed to 0, 1, 2 and ≥3 for this analysis. Maternal diet was recorded as no special diet, pescatarian, vegetarian, vegan and other.

*Birth*: Birthweight (grams) was measured by healthcare professionals at birth. Gestational age was based on a dating ultrasound scan which takes place between 10 weeks and 13 weeks 6 days gestation30. Mode of birth was categorised as vaginal and caesarean. In this population, an oral glucose tolerance test was used for screening for gestational diabetes (GDM) in women with one or more risk factors (BMI > 30kg/m2; GDM in previous pregnancy; previous baby weighing ≥4.5kg; diabetes in parents or siblings and of Asian, African-Caribbean or Middle Eastern ethnicity)31. GDM diagnosis was then reported in the database. Pre-eclampsia was reported as yes or no.

*Early life*: Breastfeeding status was reported at hospital discharge and during early life. The recording during early life was done differently by the two community NHS Trusts. One used NHS Read codes and thus was recorded at 10 days, 2 weeks, 6 weeks, 4 months and 9 months. At each point, this was recorded as breastfed, bottle-fed or breast and bottle fed. Breastfeeding could be recorded at any or all of the time-points specified by the Read codes. The other Trust recorded breastfeeding at 56 days (8 weeks) as yes or no so there was no information on whether this was exclusive or partial breastfeeding. The 10 days and 2 weeks categories were combined into one as there were very few instances of the 2 weeks category recorded and the two categories are only four days apart. Using all the information available, a breastfeeding variable was derived with categories of no breastfeeding, minimum 10 days, minimum 6 weeks, minimum 8 weeks, minimum 4 months and minimum 9 months. Minimum duration was chosen as there was no information how long breastfeeding was continued for beyond the point of the last record.

Early life weight was calculated at two ages – 1 year and 2 years. To maximise the number of records and accounting for the routine development checks offered within the NHS where children are measured (9 to 12 months and 2 to 2.5 years), weight measured between 9 and 13 months was used as the 1 year weight. Similarly, weight measured between 23 and 30 months was used as the 2 year weight. In the 2 year models, we have not included the 1 year weight measured to maximise sample size.

In sensitivity analysis, we assessed whether the inclusion of area-level characteristics improve the discrimination of the birth prediction model. Geographical area at birth was characterised for children living in the Southampton area32. The unit of analysis was Lower layer Super Output Area (LSOA) boundaries in order to preserve anonymity. These areas have an average population of around 1,500 and cover an average area of 4km2. Area-characteristics for these LSOAs were collated and included the 2015 Index of Multiple Deprivation (IMD), household median price quintile, measures of air pollution (PM2.5, PM10, NOx), Income Support claimant rate, social renting households, supermarket density, unhealthy food index, greenspace, spaces for social interaction and walkability. Further information on how the area-level data were sourced, collated and derived is available on the project website: <https://www.southampton.ac.uk/slope/data/area-data.page>.

*Statistical analysis*

All analysis was performed using Stata 1533. Clustering by mother was adjusted for by including a clustering indicator in the model as some women had more than one pregnancy in the dataset. Both complete case and multiple imputed analysis was carried out. Multiple imputation by chained equations (MICE) was carried out using truncated regression for continuous variables and predictive mean matching for categorical variables. The sample was limited to those with the outcome of interest and only missing predictor values were imputed. The percentage of missing data was low for the antenatal and birth data (5%) but there was a high percentage of missing data during early life for all variables at this stage (70%) and so we carried out 70 imputations of the sample generating 70 imputed datasets (with 10 iterations per imputed dataset). This was based on the recommendation that the number of imputations equal the percentage of missing data in the dataset34. The estimated regression parameters (coefficients and variances) were combined over the imputed datasets using Rubin’s rules34.

Stepwise backward elimination was used to select variables to be included in the model35. This automatic selection procedure starts with the full model (including all candidate predictor variables) and sequentially removes variables based on a series of hypothesis tests. Automatic selection procedures are data driven and makes decisions regarding inclusion/exclusion of variables based on hypothesis tests with a pre-specified significance level for inclusion/exclusion. In backward elimination, variables are removed sequentially if the p-value for a variable exceeds the specified significance level which was set at 0.157 for this analysis which was chosen conservatively to reduce the risk of overfitting. This is equivalent to the Akaike information criterion (AIC)36.

As the outcome was binary, the models were developed using logistic regression. All continuous variables were retained as continuous to avoid loss of information. Fractional polynomials were used to investigate non-linear relationships between continuous candidate predictors and the outcome. The best transformation for each continuous predictor was identified through backward elimination with the selection of a fractional polynomial function by starting with the most-complex permitted fractional polynomial and attempt to simplify the model by reducing the degree. This was then used when fitting the models.

Events per variable (EPV) is used to ensure that the sample size is large enough to avoid issues related to precision and over-fitting especially when using automatic selection procedures. A rule of thumb from simulation studies is that there should be a minimum of 10 events per variable37,38. Considering this in model development, there were sufficient cases of the outcomes to develop a prediction model using booking and birth factors. However, there were insufficient cases of outcome during early life in the complete case analysis so it was decided to include fewer candidate predictors at the model development stage in the early life models. Predictors included were guided by the literature (maternal age, maternal BMI, ethnicity, smoking status, educational attainment, birthweight, child sex) and those that remained in the booking and birth models.

Bootstrapping (1000 repetitions) was chosen as the method for internal validation as this method provides stable estimates with low bias39. It also provides an estimate of the expected optimism which can be used to weight down the model parameter estimates. Internal validation was only carried out in complete case models. This was because the complexities involved in model development (combination of variable selection, fractional polynomials and multiple imputation) in the multiple imputation models meant that the steps involved could not replayed. Thus these models could not be internally validated using bootstrapping. Instead, apparent model performance was assessed in the multiply imputed models and compared to the complete case models.

To test if the prediction models at birth could be improved with the inclusion of area-level characteristics at birth, we first included IMD as an additional candidate predictor. We then excluded education as a candidate predictor as population-level educational attainment is included in the IMD. All individual and area-level predictors as outlined above were then considered for inclusion in the final birth model.

*Model performance and shrinkage*

Model performance was assessed using discrimination and calibration*.* Discrimination is a measure of how well the model differentiates between individuals37. The area under receiver operating characteristic curve (AUC) was used to summarise the overall discriminatory ability of the models. The AUC was classified as: 0.6-0.7 poor, 0.7-0.8 fair, 0.8-0.9 good and 0.9-1.0 excellent.

Calibration measures how well the predicted outcome of the model agrees with the observed outcome on average. The predicted probability (x-axis) is plotted against the observed outcome proportion (y-axis) for each risk group. The slope of a line fitted through the points on the graph is the calibration slope and has been calculated for the models. Calibration slope would be one in a perfectly-calibrated model. A slope of less than one or greater than one indicates over- and under-prediction respectively40. The recommendation of overlaying calibration curves from each imputed dataset in the calibration plots was followed41.

Prediction models tend to be optimistic in the development data as a result of overfitting and use of a newly developed model in independent data tends to lead to worse predictions. Heuristic shrinkage factors were calculated for each model to estimate the extent of overfitting present in the developed models42. The heuristic shrinkage factor is calculated as:

(model χ2 – df)/ model χ2

where model χ2 is the model likelihood ratio and df is the degrees of freedom in the fitted model. A shrinkage factor of 1 implies no shrinkage.

The regression coefficients from the models were multiplied by the shrinkage factor to adjust the models for optimism. A logistic model was then fitted for the outcome to estimate the shrinkage of the intercept by including the linear predictor calculated using the shrunken coefficients as the only independent variable and constraining its coefficient to one.

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated at multiple risk score cut-off points as no standard criteria for identifying a risk threshold exist for the prediction of childhood obesity. As the models have been designed in a sequential manner and risk can be calculated at each of these stages, the accumulation of risk for individuals over time if the model is applied at each of these stages was calculated.

*Calculating risk score*

The log-odds (Y) can be calculated using the regression equation as follows:

Y = constant + [estimate1 x predictor1] + [estimate2 x predictor2] + ………………………. + estimaten x predictorn]

The log-odds (Y) is then converted into probability (P) as follows:

P = 1/[1 + exp(-Y)]

where P is the probability of developing the outcome and Y is the log-odds estimated using the model.

**Results**

Of the 51,861 children who were old enough to be in school (4-5 years) based on the maternal dataset, outcome data were included in the linked dataset for 30,958 children (60%). This reduced to 29,060 children after exclusions for unfeasible gestational age, maternal weight and maternal height measurements and multiple births (twins/triplets) (Figure 1). Of these, 4,311 children (14.8%) were overweight/obese (≥91st centile for age and sex). Baseline characteristics are summarised in Table 1. Maternal age at booking was 28.4 years (SD 5.9). Mean maternal BMI at booking was 25.5 kg/m2 (SD 5.5). Over 50% of women reported being ex- (33.6%) or current- (17.4%) smokers. A quarter of the women had a university degree or a higher qualification, and over two–thirds were employed at the first antenatal (booking) appointment. Eight percent of mothers reported being a lone parent at the booking appointment. Nearly half the mothers reported no breastfeeding.

The prediction models for the risk of childhood overweight and obesity are presented in Table 2 and Additional file 1: Table S1. Eight predictors were retained in the final model at booking: maternal age, BMI, smoking status, ethnicity, intake of folic acid supplements, first language, partnership status and parity. For the outcome at birth, the same predictors were retained in the final model with the addition of maternal educational attainment, birthweight and gestational age at birth. At early life, all maternal predictors with the exception of mother’s first language and parity were retained. Child predictors included birthweight, sex and weight at ~1 or ~2 years respectively. Gestational age at birth remained a predictor at ~1 years but not at ~2 years. Transformations were identified for maternal age, maternal BMI and birthweight.

Predictors retained in the model in the complete case and multiple imputation were the same for the booking and birth models (Table 3). However, there were some differences in the predictors retained in the early life models. Maternal age at booking and gestational age at birth were retained in the early life model at ~1 year in the multiple imputed but not in the complete case model. Maternal ethnicity and intake of folic acid supplements were retained in all the multiple imputed models but not in the complete-case early life model at ~2 years. Birthweight was retained in the complete-case birth model but was additionally included in both multiple-imputed early life models.

Discrimination (AUC) improved across the stages identified for model development from poor (0.66) at booking appointment to good (0.83) at early life (~2 years). AUC were the same in the multiply imputed and complete case models after internal validation (Table 3). Sensitivity analysis including area-level predictors did not improve the model discrimination (Additional file 1: Table S2).

Calibrations plots overlaying the results of the analysis of the imputed datasets for the model stages are presented in Figures 2a-d. The calibration across all models were consistently strong as evidenced by the calibration slope and the gradient. There was more variation across the imputed models in the early life models however this is the stage with the highest percentage of missing data and thus more variation across the datasets is to be expected. The estimated shrinkage factors was 0.99 for all models suggesting that only a small percentage of the model fit was noise. The shrunken coefficients and intercepts are presented in Table 2.

The percentage of children identified as at risk of childhood overweight/obesity, sensitivity, specificity, PPV and NPV for different risk score cut-offs are presented in Additional file 1: Table S3. As there is no agreed cut-off in the literature on what constitutes ‘high risk’ of future childhood overweight or obesity, a 20% risk threshold was used as deemed the most appropriate by the parameters reported in Additional file 1: Table S3, local stakeholder consultation and previous prediction models utilised as risk scores in routine UK healthcare43. For example, using a 20% risk cut-off in the early life model at ~2 years identifies 24.1% of children as at risk, with a sensitivity of 65.5%, specificity of 83.1%, PPV of 40.3% and NPV of 93.3%. The sensitivity, specificity, PPV and NPV at each risk threshold cut-off improve across the assessment time points from pregnancy booked to 2 years of age. PPV increase and NPV decrease as the risk threshold increases. For example, for the booking model at Year R, PPV of 18.2% and NPV of 92.7% at risk threshold of 10%, PPV of 25.9% and NPV of 88.2% at risk threshold of 20% and PPV of 35.3% and NPV of 86.3% at risk threshold of 30%.

Figure 3 shows the categorisation of children as high risk (≥20%) or not if the model is applied at each time point. Based on this, 57.9% of the sample is consistently not identified at risk from booking to 2 years of age, and 7.5% is consistently identified at risk. The remaining 34.6% are identified at risk at one or two time points but not consistently.

**Discussion**

Our analysis shows that it is possible to predict childhood overweight and obesity using routine linked healthcare data collected during pregnancy and early life with reasonable accuracy. We have developed and internally validated prediction models at multiple time-points starting from early pregnancy to 2 years following birth. These could be used to identify high risk groups at each of these stages for provision of additional support/early intervention. Although the model at 2 years had better discrimination (AUC 0.83) than the models at booking (AUC 0.66), the maternal predictors remain fairly consistent across models and thus high-risk groups could be identified as early as the first antenatal appointment with more precise risk estimation as the child grows.

NICE guidelines in the UK recommend the use of age- and sex-adjusted BMI as a practical estimate of adiposity in children and young people to identify overweight and obesity27. However, the UK has different centile cut-offs for population monitoring (85th for overweight/obese and 95th for obese) and clinical diagnosis (91st for overweight and 98th for obesity)27,28. Clinical cut-offs for children are used to classify children in the parental feedback letter sent as part of the NCMP. This may be because NICE guidelines have recommendations on follow-up for children who exceed this cut-off, however this means that parents of children with BMI between the 85th (the population cut-off for overweight) to 90th percentile are being informed that their child is normal weight. The scientific rationale for the UK cut-offs is not obvious and appears to be a historical precedent selected pragmatically at the time. The 85th and 95th centiles in the UK were selected as the exact values to estimate population prevalence whereas the 91st and 98th correspond to major centile lines on the UK growth charts28. Although we use the clinical cut-off point for overweight/obesity in our analysis here, we have also performed the prediction models using the 85th centile cut-off and found that the included parameters are broadly the same.

Established childhood obesity risk factors that have been included in the prediction equations include maternal BMI, ethnicity, smoking status, parity, birthweight and infant weight during early life. English as maternal first language, partnership status and intake of folic acid supplements were consistent predictors in our models, although the evidence supporting their classification as risk factors is less strong. Offspring of women who reported English as their first language were at lower risk of childhood overweight/obesity compared to offspring of women who reported English as not their first language. This could be indicative of inequalities in healthcare access and utilisation. Lone mothers are at higher risk of poverty 44 and ill health 45 which could lead to increased levels of stress or anxiety. Folic acid supplementation could be a proxy for a variety of factors such as unplanned pregnancy, low health literacy, maternal nutrient intake status and income. Folic acid supplements are purchased over the counter and thus could also be related to income and affordability. A systematic review found that intake of folic acid supplements from preconception reduced the risk of SGA births 46 which is a risk factor for overweight and obesity if the child then exhibits catch-up growth in early life.

Breastfeeding was not retained as a predictor but the evidence on the association between breastfeeding and childhood overweight and obesity is conflicting14 and only three out of eight prediction model studies considered breastfeeding as a predictor and it was included in two models24. Another factor not considered in our models is gestational weight gain, which is not routinely collected in the UK. However, the additional effect of gestational weight gain on childhood obesity is small on top of the effect of pre-pregnancy weight47-49.

The development of prediction models in a large population-based sample is a key strength of this analysis which enhances the generalisability. This is a relatively large population-based cohort of women from all socioeconomic and ethnic backgrounds resident in Southampton and surrounding areas of Hampshire and thus representative of the local population. Although Southampton is more deprived than average with the situation having worsened between 2010 and 201550, about half of the women included in this analysis reside in the rest of Hampshire (the region where Southampton is situated), which is less deprived. We used robust statistical methods to develop the models (retained continuous variables as continuous, investigated variable transformations using multivariable fractional polynomials and corrected for optimism by calculating model shrinkage) and to assess the performance of the models where possible.

There was a low percentage of missing data in the antenatal care and birth. Both early life time-points (1 and 2 years) considered in this analysis align with two of the five NHS child health and development reviews (9-12 months and 2-2.5 years) at which weight is measured. However, a high percentage of missing weight data was observed during early life (70%). Only 13.7% of children in the 2 year model also had a recorded weight at around 1 year, which prevented the inclusion of this variable at that stage. The reasons could potentially be that the measurements were entered in free text boxes or appointments did not take place within the designated period. Multiple imputation of missing data was carried out which generally enables more robust analyses but requires some caution in interpretation due to the number of imputations required. Additionally, outcome data was not available for a high proportion of children who were old enough to be in school. Factors contributing to this potentially include changes in recording practices; a child had moved and was no longer under the care of the community trust; were not attending state school or the child NHS number (required for linkage) was not recorded with the measurement. However, the prevalence of overweight and obesity in the modelled sample was similar to the national prevalence (~22% using the population monitoring cut-off of 85th percentile).

This study has identified key stages for risk prediction based on routine care in the UK. No other prediction models have considered prediction as early as first trimester of pregnancy. No single risk factor was included in all eight existing prediction models identified in a systematic review of childhood obesity prediction models24 but maternal pre-pregnancy BMI, child sex and birthweight were the most commonly included predictors. These three predictors were retained in our models at all stages (maternal BMI) or at the appropriate stages (birthweight and child sex).

Our prediction equations have been developed using routine linked data and so all the predictors are maternal or child factors unlike prediction models developed using birth cohort data which have incorporated paternal or family data such as paternal BMI51 or family income52. The use of routine data in the development of these prediction equations means that these can be readily implemented, unlike prediction models developed using research birth cohort data incorporating data not routinely collected. For example, paternal BMI51 could be challenging to collect in a systematic way as not all fathers attend booking appointments and missing data would be non-random. Additionally, the application of the risk prediction tool could lead to better data recording, for instance of breastfeeding status, exclusivity and duration.

Both modifiable and non-modifiable predictors have been identified for inclusion in the models. Although these are predictors, the relationship with the outcome is not necessarily causal and thus interventions do not have to act on factors identified by the model. Key modifiable maternal predictors (maternal BMI, smoking status and intake of folic acid supplements) remained consistent predictors across the stages. Identifying these high risk families and intervening early could modify long-term risk for both mother and child as well as subsequent children particularly if identified at first pregnancy. The interpregnancy period provides a key opportunity for intervention in high risk families for subsequent pregnancies.

The next step, following external validation of the models, is to test the feasibility, acceptability and usability of a Childhood Obesity Risk Estimation Tool by health visitors. On public involvement, mothers have expressed interest in early identification of risk with support and advice to help modify risk. Thus, as part of the feasibility study, we are testing the use of this tool as an aid to health visitors to guide delivery of an intervention on the healthy weight pathway, rather than a screening test. Our practitioner consultation work suggests that health professionals would like an ‘objective’ way to stratify risk rather than individualised clinical judgement, as this feels subjective and can make the conversation with the family more sensitive. The risk estimation tool is envisaged to enable the provision of obesity prevention intervention at an early stage before the child is overweight or obese, to provide a prompt for the health professional to introduce this topic and to help target extra support in resource-limited settings. Although, the application of the tool may increase anxiety among parents, which will be explored as part of the feasibility study, the intervention is unlikely to produce significant unintended harm as it would not be a clinical or medicinal intervention.

We need to identify a risk threshold above which children would be considered at risk for the practical implementation of the risk estimation tool. As a definitive method for doing this could not be identified from the literature, we were guided by the sensitivity, specificity, PPV and NPV as well as the number of individuals identified as high risk based on this threshold. For example, for outcome at Year R, the specificity and sensitivity is comparable at a risk threshold of 15% but this identifies around 40% of the sample at risk whereas the prevalence of the outcome is 14.8%. A risk threshold of 20% would identify around 20% of the sample at risk with higher specificity but lower sensitivity and slight increase in PPV. Sensitivity and specificity are improved in the later stages (birth and early life) compared to booking.

The PPV for our 2 year model at 20% risk threshold is 40% and the NPV is 93%. This means that a significant proportion of children identified at risk will not become overweight or obese. However, the high NPV provides confidence that very few children identified as low risk will become overweight or obese and therefore miss out on a targeted intervention. A previous childhood obesity prediction model using birth cohort data51, which was then used to develop a prediction and intervention tool53, had a lower PPV than ours (37%). Provided we examine the population impact and cost effectiveness of using a risk estimation tool based on routinely collected data as a decision strategy, targeting obesity prevention interventions, which would in an ideal work be universally available if resources were not limited, is unlikely to produce harms. The potential harms of a behavioural, environmental or social support complex intervention to tackle obesity are likely to be low compared to a clinical intervention.

Children move between low and high risk between the stages (between pregnancy and 2 years of age) but a high proportion remain consistently at high risk (7.5%). To implement this prediction in practice and intervene early, an intervention will need to take this fluctuation in risk into consideration. Withdrawing intervention or support from individuals who have previously been deemed high risk but are now low risk can have negative consequences on their risk at the next stage. However, it may not be feasible to maintain an intensive intervention during all these. Thus, interventions may need to be administered in stages or have flexible layers in terms of intensity.

**Conclusions**

Most maternal predictors of childhood overweight and obesity at primary school entry remained consistent across models starting from early pregnancy, indicating that risk could be quantified even before birth, with more precise estimation in early-years than straight after birth, when model performance was moderate. These prediction models demonstrate that utilising routinely collected healthcare data can form the basis of a risk identification system to strengthen the long-term preventive element of antenatal and early years care by quantifying clustering of future obesity risk in families.

**List of abbreviations:**

|  |  |
| --- | --- |
| BMI | Body mass index |
| AUC | Area under the curve |
| PPV | Positive predictive value |
| NCMP | National Child Measurement Programme |
| SLOPE | Studying Lifecourse Obesity PrEdictors |
| UHS | University Hospital Southampton |
| NHS | National Health Service |
| NICE | National Institute for Health and Care Excellence |
| GDM | Gestational diabetes |
| LSOA | Lower Super Output Area |
| IMD | Index of multiple deprivation |
| MICE | Multiple imputation by chained equations |
| AIC | Akaike Information Criteria |
| EPV | Events per variable |
| NPV | Negative predictive value |
| SD | Standard deviation |
| CORE | Childhood Obesity Risk Estimation Tool |

**Declarations**

**Ethics approval**

All data were anonymised by the data holders before being accessed by the research team. Approval was granted by the University of Southampton Faculty of Medicine Ethics Committee (ID 24433) and the Health Research Authority (HRA) approval (IRAS 242031).

**Consent to participate**

Not applicable.

**Availability of data and materials**

The data owners are University Hospital Southampton NHS Trust, Solent NHS Trust and Southern Health NHS Foundation Trust. Anonymised data are only available upon request from the PI (NAA) conditional on approval of the appropriate institutional ethics, research governance processes and data holders.

**Competing interests**

The authors have no competing interests to declare.

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**Author Contributions**

Study concept (NAA), study design (NZ, PJR, NSM, DS, DC, NAA), acquisition and interpretation of the data (NZ, NAA), data cleaning and management (NZ), statistical analysis (NZ, SW), drafting of the manuscript (NZ) and revising for content (NZ, SW, PJR, NSM, DS, DC, NAA). All authors read and approved the final manuscript. NAA is the project’s PI.

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**Figure legends:**

Figure 1: Flow diagram showing the eligible sample

Figure 2a-d (top left to bottom right): Calibration plot of the prediction model at booking, birth, early life (~1 year) and early life (~2 years)

Figure 3: The categorisation of children as high risk (red) or low risk (blue) if the prediction model is applied at each stage using the risk threshold of 20%

**Table legends:**

Table 1: Summary of baseline characters (candidate predictors) for the SLOPE sample using the multiply imputed data

Table 2: Intercept and regression coefficients of the prediction models for overweight and obesity (≥91st centile) in children aged 4-5 years before and after shrinkage including discrimination and calibration

Table 3: Predictors included (+) in the final complete case and multiply imputed models

Additional file 1: Table S1: Estimates of the final models for the prediction of outcome of overweight and obesity (≥91st centile) in children aged 4-5 years Additional file 1: Table S2: Estimates of the final models for the prediction of outcome of overweight and obesity (≥91st centile) in children aged 4-5 years under in Southampton, UK with and without area-level predictors

Additional file 1: Table S3: Predictive parameters for the outcome of overweight and obesity (≥91st centile) in children aged 4-5 years

Table 1: Summary of baseline characters (candidate predictors) and outcome for the SLOPE sample using the multiply imputed data

|  |  |  |
| --- | --- | --- |
| Stage recorded  | Variable | Mean ± SD |
|  | N | 29060 |
| Booking appointment | Maternal age at booking, years | 28.4 ± 5.9 |
| Booking appointment | Gestation at booking, days | 80 ± 19 |
| Booking appointment | Maternal BMI at booking, kg/m2 | 25.5 ± 5.5 |
| Birth | Birthweight, kg | 3.4 ± 0.6 |
| Birth | Gestation at birth, days | 279 ± 13 |
| Early life (~1 year) | Weight at 1 year, kg | 9.4 ± 1.2 |
| Early life (~1 year) | Weight at 2 years, kg | 13.0 ± 1.6 |
|  |  | %, 95% CI |
| Booking appointment | Maternal smoking status at booking |  |
|  | Never smoked | 49.0 (48.4 to 49.5) |
|  | Ex-smoker | 33.6 (33.1 to 34.2) |
|  | Current smoker | 17.4 (17.0 to 17.9) |
| Booking appointment | Maternal highest educational attainment |  |
|  | University degree or above | 25.5 (25.0 to 26.0) |
|  | College (A levels) | 40.9 (40.4 to 41.5) |
|  | Secondary school or below  | 33.6 (33.1 to 34.1) |
| Booking appointment | Maternal employment status at booking |  |
|  | Employed | 68.9 (68.4 to 69.5) |
|  | Unemployed | 28.8 (28.3 to 29.4) |
|  | Student or in training | 2.2 (2.1 to 2.4) |
| Booking appointment | Maternal ethnicity |  |
|  | White | 90.4 (90.0 to 90.7) |
|  | Mixed | 1.1 (1.0 to 1.2) |
|  | Asian | 6.1 (5.8 to 6.3) |
|  | Black/African/Caribbean | 1.5 (1.3 to 1.6) |
|  | Other | 1.0 (0.9 to 1.1) |
| Booking appointment | Intake of folic acid supplements |  |
|  | Taking prior to pregnancy  | 31.0 (30.4 to 31.5) |
|  | Started taking once pregnant | 58.3 (57.7 to 58.8) |
|  | Not taking supplement at booking | 10.8 (10.4 to 11.1) |
| Booking appointment | Maternal first language English | 97.1 (96.9 to 97.3) |
| Booking appointment | Partnership status at booking | 91.7 (91.4 to 92.0) |
| Booking appointment | Infertility treatment |  |
|  | No | 92.5 (92.2 to 92.8) |
|  | Yes | 4.2 (4.0 to 4.4) |
|  | Investigations but no treatment | 3.3 (3.1 to 3.5) |
| Booking appointment | History of mental health | 20.5 (20.1 to 21.0) |
| Booking appointment | Previous stillbirth | 0.8 (0.7 to 0.9) |
| Booking appointment | Parity at booking |  |
|  | 0 | 45.0 (44.5 to 45.6) |
|  | 1 | 35.2 (34.6 to 35.7) |
|  | 2 | 13.0 (12.6 to 13.4) |
|  | ≥3 | 6.8 (6.5 to 7.1) |
| Booking appointment | Previous caesarean section |  |
|  | 0 | 87.9 (87.5 to 88.2) |
|  | 1 | 10.1 (9.7 to 10.4) |
|  | 2 | 2.0 (1.9 to 2.2) |
| Booking appointment | Maternal diet |  |
|  | No special diet | 93.3 (93.0 to 93.6) |
|  | Pescatarian | 2.3 (2.2 to 2.5) |
|  | Vegetarian  | 2.2 (2.1 to 2.4) |
|  | Vegan  | 0.1 (0.1 to 0.1) |
|  | Other | 2.1 (1.9 to 2.2) |
| Booking appointment | Maternal disability status | 1.0 (0.9 to 1.1) |
| Booking appointment | Maternal substance use | 0.1 (0.1 to 0.2) |
| Booking appointment | Obstetric history of GDM | 0.9 (0.7 to 1.0) |
| Booking appointment | Obstetric history of preeclampsia | 0.2 (0.1 to 0.2) |
| Booking appointment | Family history of diabetes | 14.2 (13.8 to 14.6) |
| Booking appointment | Family history of hypertensive disorder | 31.6 (31.0 to 32.1) |
| Booking appointment | Family history of mental health conditions | 16.1 (15.7 to 16.6) |
| Birth  | Delivery method |  |
|  | Vaginal  | 77.8 (77.3 to 78.2) |
|  | Caesarean section | 22.2 (21.8 to 22.7) |
| Birth | Gestational diabetes in current pregnancy | 2.0 (1.9 to 2.2) |
| Birth  | Preeclampsia in current pregnancy | 0.5 (0.4 to 0.6) |
| Birth  | Child sex |  |
|  | Male | 51.2 (50.6 to 51.8) |
|  | Female | 48.8 (48.2 to 49.4) |
| Early life | Duration of breastfeeding |  |
|  | No breastfeeding | 48.2 (47.4 to 49.0) |
|  | Minimum 10 days | 19.6 (19.0 to 20.2) |
|  | Minimum 6 weeks  | 21.8 (21.1 to 22.5) |
|  | Minimum 8 weeks | 9.5 (9.1 to 10.0) |
|  | Minimum 4 months  | 0.3 (0.2 to 0.4) |
|  | 9 months | 0.6 (0.4 to 0.7) |
| 4-5 years | Childhood overweight or obesity (≥91st centile) | 14.8 (14.4 to 15.2) |

Table 2: Intercept and regression coefficients of the prediction models for overweight and obesity (≥91st centile) in children aged 4-5 years before and after shrinkage\*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Predictors | Booking | Birth | Early life (~1 year) | Early life (~2 years) |
|  | Coefficient | Shrunken coefficient | Coefficient | Shrunken coefficient | Coefficient | Shrunken coefficient | Coefficient | Shrunken coefficient |
| Intercept | 0.877 | 0.845 | 2.215 | 2.169 | -5.186 | -5.160 | -10.510 | -10.466 |
| Maternal age at booking, years | 1.394 | 1.377 | 1.114 | 1.101 | -0.006 | -0.006 |  |  |
| Maternal BMI at booking, kg/m2 | -7.061 | -6.971 | -6.371 | -6.295 | -6.733 | -6.686 | -6.687 | -6.656 |
| Maternal smoking status at booking |  |  |  |  |  |  |  |  |
| Never smoked | Ref |  | Ref |  | Ref |  | Ref |  |
| Ex-smoker | 0.099 | 0.098 | 0.080 | 0.079 | 0.047 | 0.047 | 0.044 | 0.044 |
| Current smoker | 0.436 | 0.431 | 0.583 | 0.576 | 0.532 | 0.528 | 0.536 | 0.534 |
| Maternal educational attainment |  |  |  |  |  |  |  |  |
| University or above |  |  | Ref |  | Ref |  | Ref |  |
| College |  |  | 0.088 | 0.087 | 0.130 | 0.129 | 0.116 | 0.115 |
| Secondary or lower |  |  | 0.103 | 0.102 | 0.190 | 0.188 | 0.174 | 0.173 |
| Maternal ethnicity |  |  |  |  |  |  |  |  |
| White | Ref |  | Ref |  | Ref  |  | Ref |  |
| Mixed | 0.020 | 0.020 | 0.105 | 0.103 | 0.098 | 0.098 | 0.019 | 0.019 |
| Asian | 0.274 | 0.271 | 0.444 | 0.439 | 0.589 | 0.585 | 0.402 | 0.400 |
| Black/African/Caribbean | 0.655 | 0.647 | 0.778 | 0.769 | 0.771 | 0.766 | 0.511 | 0.509 |
| Other | 0.084 | 0.083 | 0.124 | 0.122 | 0.235 | 0.234 | -0.073 | -0.073 |
| Maternal intake of folic acid supplements |  |  |  |  |  |  |  |  |
| Taking prior to pregnancy | Ref |  | Ref |  | Ref |  | Ref |  |
| Started taking once pregnant | 0.094 | 0.093 | 0.120 | 0.118 | 0.156 | 0.155 | 0.155 | 0.154 |
| Not taking supplement | 0.053 | 0.053 | 0.084 | 0.083 | 0.160 | 0.158 | 0.159 | 0.159 |
| Maternal first language English |  |  |  |  |  |  |  |  |
| No | Ref |  | Ref |  |  |  |  |  |
| Yes | -0.319 | -0.315 | -0.285 | -0.282 |  |  |  |  |
| Partnership status at booking |  |  |  |  |  |  |  |  |
| Partnered | Ref |  | Ref |  | Ref |  | Ref  |  |
| Single | 0.182 | 0.179 | 0.193 | 0.190 | 0.196 | 0.195 | 0.176 | 0.175 |
| Parity at booking |  |  |  |  |  |  |  |  |
| 0 | Ref |  | Ref |  |  |  |  |  |
| 1 | 0.017 | 0.016 | -0.108 | -0.106 |  |  |  |  |
| 2 | 0.093 | 0.092 | -0.057 | -0.056 |  |  |  |  |
| 3 | 0.173 | 0.171 | 0.019 | 0.018 |  |  |  |  |
| Birthweight, kg |  |  | 0.107 | 0.106 | 0.129 | 0.128 | -0.114 | -0.113 |
| Gestational age at birth, days |  |  | -0.011 | -0.011 | -0.008 | -0.008 |  |  |
| Infant gender |  |  |  |  |  |  |  |  |
| Male |  |  |  |  | Ref  |  | Ref |  |
| Female |  |  |  |  | 0.426 | 0.423 | 0.366 | 0.364 |
| Infant weight, kg |  |  |  |  | 0.753 | 0.748 | 0.825 | 0.821 |
| **Transformations:** |  |  |  |  |
| Maternal age at booking | (Maternal age/10)^-2 | (Maternal age/10)^-2 |  |  |
| Maternal BMI at booking | (Maternal BMI/10)^-1 | (Maternal BMI/10)^-1 | (Maternal BMI/10)^-1 | (Maternal BMI/10)^-1 |
| Birthweight |  | Birthweight^2 |  |  |
| **Discrimination and calibration:** |  |  |  |  |
| AUC | 0.660.65 to 0.67 | 0.690.68 to 0.70 | 0.780.77 to 0.79 | 0.830.82 to 0.84 |
| Calibration slope (standard error) | 0.98 (0.03) | 0.98 (0.03) | 0.99 (0.01) | 0.99 (0.01) |

\*Only predictors significant at p<0.157 were included in the prediction models. Categorical variables with at least one significant category has been included.

Table 3: Predictors included (+) in the final complete case and multiply imputed models

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Predictors | Booking | Birth | Early life (~1 year) | Early life (~2 years) |
|  | Complete case model | Multiple imputation model | Complete case model | Multiple imputation model | Complete case model | Multiple imputation model | Complete case model | Multiple imputation model |
| Maternal age at booking | + | + | + | + |  | + |  |  |
| Maternal BMI at booking | + | + | + | + | + | + | + | + |
| Maternal smoking status at booking | + | + | + | + | + | + | + | + |
| Maternal educational attainment |  |  | + | + | + | + | + | + |
| Maternal ethnicity | + | + | + | + | + | + |  | + |
| Maternal intake of folic acid supplements | + | + | + | + | + | + |  | + |
| Maternal first language English | + | + | + | + |  |  |  |  |
| Partnership status at booking | + | + | + | + |  | + | + | + |
| Parity at booking | + | + | + | + |  |  |  |  |
| Birthweight |  |  | + | + |  | + |  | + |
| Gestational age at birth |  |  | + | + |  | + |  |  |
| Child sex |  |  |  |  | + | + | + | + |
| Child weight |  |  |  |  | + | + | + | + |
|  |  |  |  |  |  |  |  |  |
| **Discrimination and calibration:** |  |  |  |  |  |  |  |  |
| AUC | 0.660.65 to 0.67 | 0.660.65 to 0.67 | 0.690.68 to 0.70 | 0.690.68 to 0.70 | 0.780.77 to 0.80 | 0.780.77 to 0.79 | 0.830.82 to 0.84 | 0.830.82 to 0.84 |
| Calibration slope (standard error) | 1.00 (0.03) | 0.98 (0.03) | 1.00 (0.03) | 0.98 (0.03) | 1.00 (0.04) | 0.99 (0.01) | 1.00 (0.04) | 0.99 (0.01) |