

treated with phlebotomy. We aimed to test *HFE* p.C282Y homozygote associations with prevalent and incident morbidity in the large UK Biobank sample of European descent. We also examined how iron supplement use may affect associations between p.C282Y homozygosity and morbidity.

**Methods** We studied 451,243 participants of European descent (aged 40 to 70 years) from the UK Biobank. Data were available on prevalent and incident adverse health outcomes from baseline questionnaires and from up to 9.4 years hospital inpatient follow-up (mean 7 years). Participants also reported baseline dietary supplement use. We tested associations between p.C282Y homozygosity, prevalent and incident outcomes, and iron supplement use, using logistic regression and Cox proportional hazard regression, adjusted for age, sex, genotyping array type and genetic principal components.

**Results** 2,890 participants were p.C282Y homozygotes (0.6%, or 1/156), of whom 7.3% (210/2890) had haemochromatosis diagnosed at baseline, increasing to 15.1% (437/2890) by the end of follow-up. p.C282Y homozygotes had substantial excess prevalent and incident morbidity including haemochromatosis, liver disease, arthritis and diabetes compared to those with no mutations (combined measure of excess incident morbidity; men, HR: 3.37, 95% CI: 2.87–3.97; women, HR: 2.99, 95% CI: 2.51–3.55). A sub-analysis of 200,975 older participants (aged 60–70 years) showed that both male and female p.C282Y homozygotes also had an increased likelihood of Fried frailty and chronic pain.

In p.C282Y homozygotes undiagnosed with haemochromatosis, the intake of iron supplements or multivitamins increased the likelihood of frailty (OR: 2.15, 95% CI: 1.22–3.77) and incident osteoarthritis (HR: 1.86, 95% CI: 1.02–3.41)

**Conclusion** In a large community volunteer sample, *HFE* p.C282Y homozygosity was associated with substantial excess morbidity, frailty and chronic pain in both men and women. In p.C282Y homozygotes undiagnosed with haemochromatosis, taking iron supplements or multivitamins was an additional risk factor for developing morbidity, including frailty and osteoarthritis. Since the p.C282Y associated iron overload can be prevented and treated, these findings suggest there is a need for expanded case finding and screening for hereditary haemochromatosis. It also suggests that warnings and controls on iron containing supplements may be needed.

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#### PREDICTING THE RISK OF CHILDHOOD OVERWEIGHT AND OBESITY AT 4–5 YEARS USING PREGNANCY AND EARLY LIFE HEALTHCARE DATA

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**Background** In England, 9.5% of children aged 4–5 years and 20.1% aged 10–11 years are obese, with the prevalence in the most deprived areas being more than twice as that in the least deprived. There is evidence illustrating the developmental origins of obesity, but it focuses on individual risk factors and comes mostly from research birth cohorts which are not necessarily representative of the wider population. There is no

system-based early identification of childhood obesity risk at pregnancy stage and onwards. The aim was to develop and validate a risk identification system for childhood obesity using existing routinely collected maternal and early-life population-level healthcare data in Hampshire.

**Methods** Studying Lifecourse Obesity PrEdictors (SLOPE) study is an anonymised population-based linked cohort of maternal antenatal and delivery records for all births taking place at University Hospital Southampton 2003–2018, and child health records including information on postnatal growth, type of feeding and childhood body mass index (BMI) up to 14 years. Childhood age- and sex- adjusted BMI at 4–5 years was used to define the outcome of overweight and obesity in the models. 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. Predictive accuracy was evaluated by assessing model discrimination and calibration.

**Results** Childhood BMI was available for approximately 30000 children aged 4–5 years (9% obese). Models were developed in stages, incorporating data collected at first antenatal booking appointment, birth and early life predictors. The area under the curve (AUC) was lowest (0.64) for the model only incorporating maternal predictors from the booking appointment and highest for the model incorporating all factors up to weight at 2 years for predicting outcome at 4–5 years (0.82 for overweight and obesity and 0.89 for obesity excluding overweight). Maternal predictors included BMI, smoking status at first antenatal appointment, age and ethnicity. Early life predictors included birthweight, gender, breastfeeding and weight at 1 or 2 years of age. Although AUC was lower for the booking 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.

**Conclusion** This prediction modelling can be used to identify and 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.

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#### DEVELOPMENT OF A SHORT FOOD FREQUENCY QUESTIONNAIRE TO ASSESS DIET QUALITY IN POPULATION STUDIES

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**Background** Food frequency questionnaires (FFQs) are a popular tool in nutritional epidemiology, enabling estimates of habitual diet in large populations, but are time-consuming to complete. There is an increasing need for a short, accurate dietary tool that characterises healthy dietary patterns for use in observational and interventional research.

**Methods** The National Diet and Nutrition Survey (NDNS) is a general population national survey. Randomly-selected