Project Details	
Project Code	MRCPHS24Ex Freathy
Title	Understanding how ethnic differences may influence diabetes diagnosis and control in pregnancy
Research Theme	Population Health Sciences
Summary	When diabetes occurs in pregnancy, monitoring of maternal glucose is crucial to avoid complications. HbA1c is a convenient test, increasingly used to assess glucose control or detect new diabetes in at-risk women. However, the effect of ethnic variation on HbA1c accuracy in pregnancy is unclear. This PhD will address knowledge gaps using comprehensive datasets, for targeted antenatal care. The student will receive full training and support to publish their work.
Description	Diabetes in pregnancy may result if a woman has pre-existing diabetes, or may develop for the first time in pregnancy (gestational diabetes mellitus, GDM). Obtaining an accurate picture of glycemia is vital since high glucose levels can lead to adverse pregnancy outcomes. Glycated haemoglobin (HbA1c) is a convenient non-fasting blood test, indicating glucose levels during the preceding 3 months. HbA1c is not currently recommended for the diagnosis of GDM. However, there is increasing interest in whether HbA1c might be useful for GDM prediction in early pregnancy, or diagnosis in late pregnancy, because it correlates with risk of complications and is far quicker and easier than an oral glucose tolerance test (gold standard for GDM diagnosis) as it does not require several hours of fasting. In some populations, at-risk women are screened with HbA1c for pre-existing diabetes in early pregnancy. In the UK, HbA1c is routinely used to evaluate glycaemic control in women who are already known to have diabetes. However, HbA1c can be influenced by variation in red blood cell characteristics, so its usefulness for estimating glucose control varies between women. Conflicting evidence suggests that HbA1c may underestimate glucose levels in pregnancy, likely due to reduced haemoglobin levels. In contrast, iron deficiency anaemia (which is common in pregnancy) can lead HbA1c to overestimate glucose levels. As rates and causes of anaemia vary among groups of different ethnicities, this can lead HbA1c accuracy also to vary among those groups. Overall research question: What are the ethnic similarities and differences in relationships between HbA1c and measured glucose levels in pregnancy? For the analyses “ethnic” groups will be defined using either self-identified ethnicity or genetic similarity. Ultimately, this PhD may help to identify women for whom different glucose measures are more or less informative, and thereby contribute to better, targeted antenatal care. The student will be supported to take ownership of the project from the start, with opportunities to steer the work, guided by the following objectives: 1a. Identify datasets in which pregnant women have HbA1c and fasting (and/or post-load) glucose levels measured at the same time. Already, data from >25,000 women in the multi-national HAPO and EFSOCH studies are available. 1b. Investigate the relationship between HbA1c and measured glucose from oral glucose tolerance testing (OGTT) in pregnancy in women of different self-identified ethnicity. Analysis is already feasible in existing datasets, and 1a will contribute more data. 2a. Find out how often HbA1c is tested in pregnancy in clinical practice,

	in women with & without known pre-pregnancy diabetes. Electronic health records may be accessed via Clinical Practice Research Datalink or Genes&Health. 2b. Investigate whether relationships between early pregnancy HbA1c and diagnosis of pre-existing diabetes vary by ethnicity. 3a. Understand the role of genetic factors in the relationship between HbA1c and glucose levels in pregnancy in samples of different genetic similarity. There are known genetic variants which influence HbA1c via their effect on red bood cell characteristics or via their effect on glucose levels, but these have not been studied in pregnancy. 3b. Investigate whether genetics can help us to understand why the relationship between maternal glucose levels and birth weight varies across groups of different genetic similarity. All genetic analyses are highly feasible in existing samples. Rich datasets are available for analyses, including >30,000 mother-child pairs of multiple ethnicities from various cohorts, and potential for analysis of hundreds of thousands of women with electronic health records. The supervisory team have leading roles in large genetics consortia: Diabetes in Pregnancy, MAGIC (glycemic traits) and EGG (early growth) Consortia, which will directly enhance the PhD.
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