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Approaches to Optimising Care for Women with Gestational Diabetes Mellitus in the UK

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Declaration

I declare that this thesis is a presentation of my own original research. I confirm that the work submitted is my own, except where work which has formed part of jointly authored publications has been included. My contribution and those of the other authors to this work have been explicitly indicated in the introductory paragraph of chapters involving jointly authored publications. I confirm that appropriate credit has been given within this thesis where reference has been made to the work of others. I have not submitted this work in candidature for any other degree or professional qualification.

Niamh-Maire Mclennan

January 2025

Preface

This preface outlines my journey through my PhD from 2020 to 2024, a period shaped by significant challenges and milestones.

After completing five years of clinical Obstetrics and Gynaecology training, I began pursuing my academic interests in 2019, securing a competitive grant from Tommy's Charity. This grant supported a laboratory-based study investigating phenotypic variation in the gestational diabetes mellitus population, under the supervision of the late Professor Fiona Denison and Professor Rebecca Reynolds.

I enrolled in the University of Edinburgh's PhD program in February 2020. However, just a month later, the SARS-CoV-2 pandemic triggered a national lockdown, halting all non-essential research activities. I was recalled to clinical practice until August 2020. During this time, I was informed that my PhD funding had been revoked due to structural changes and the closure of the Tommy's Centre in Edinburgh. Fortunately, I secured alternative funding through the University of Edinburgh's Albert McKern Endowment, which allowed me to continue my academic training, albeit with adjustments. Funding was allocated for two years, prompting me to convert my PhD program to an MD.

Given the pandemic restrictions and the uncertainty of returning to laboratory-based work, I shifted my focus to a research direction that could be feasibly delivered within the available timeframe. Laboratory studies, which required substantial technical training, were no longer viable. With guidance from my supervisor, I identified an opportunity to utilise the pandemic as a natural experiment whilst maintain a focus on gestational diabetes. I designed a mixed-methods study to examine the indirect effects of the COVID-19 pandemic on GDM care pathways in Scotland. This work encompassed both a data study and a qualitative research study, with Professor Julia Lawton joining as my principal supervisor for the qualitative component.

In early 2021, I faced the profound loss of my principal supervisor, Professor Denison, who passed away after a long battle with mental health challenges. Fiona had been a source of immense encouragement and inspiration, supporting me from my early days

as a specialty registrar at Edinburgh's Simpson Centre. She played an instrumental role in fostering my academic ambitions and remained a guiding force throughout her illness. Fiona's contributions to maternal and fetal health were transformative, and it is my hope that this work serves as a small testament to her legacy.

With Fiona's encouragement, I continued seeking funding opportunities to expand my research. In March 2021, I secured a 12-month grant from the Research Excellence Award through the British Heart Foundation Centre (Edinburgh). This grant enabled me to extend recruitment for my study on the impact of COVID-19 on GDM care delivery, incorporating perspectives from women and healthcare professionals in both Scotland and England. The additional funding also enabled me to convert my studies back to a PhD. The findings from this expanded research are presented in this thesis.

In the final year of my PhD, I experienced another significant life event: the birth of my son, Ruairidh. This led to a one-year interruption in my studies. During this period, two pieces of work presented in this thesis were published in high-impact journals.

Reflecting on this journey, I am grateful for the opportunities, challenges, and the unwavering support of my supervisors. The work presented here represents not only an academic endeavour but a deeply personal one, shaped by resilience and the pursuit of meaningful contributions to GDM care and maternal health. I hope that sharing my navigation through the COVID-19 pandemic, interruptions in my studies, funding challenges, and changes in supervision will provide context for the work presented in this thesis.

Acknowledgements

First and foremost, I would like to express my gratitude to my primary supervisor, Professor Rebecca Reynolds (RR). Her unwavering support, tireless encouragement, and expertise have guided me through this unpredictable journey. It has been an absolute privilege to work with and learn from her.

I am also profoundly grateful to my qualitative research supervisor, Professor Julia Lawton, for warmly welcoming me into the world of qualitative research. Her practical guidance and insightful advice, from the conception of this project to the final thesis submission, have been invaluable.

I extend my heartfelt thanks to the funders of this research: Tommy's Charity, the Albert McKern Endowment Trust, and the British Heart Foundation. I am especially thankful to my supervisors, Professor Rebecca Reynolds and Professor Fiona Denison (FD), as well as Edinburgh University's College of Medicine, for their support in securing alternative funding from the Albert McKern Endowment and the British Heart Foundation. Without this support, neither this thesis nor the work it contains would have been possible.

I am deeply indebted to the guidance and mentorship I have received from the numerous research groups I have collaborated with over the past four years. My gratitude goes first to the Diabetes and Pregnancy Working Group, who welcomed me into their community and patiently guided me as I completed the first chapter of this thesis. I also thank the PMDI team, who endured countless Zoom calls to help me get to grips with identifying precision markers. Finally, I am grateful to the Diabetes in Pregnancy JLA Partnership, whose unique introduction to GDM evidence synthesis and PPI approaches helped me identify gaps in GDM knowledge, ultimately shaping the research presented in this thesis.

I extend my sincere thanks to all the healthcare professionals who willingly shared their time and experiences caring for women with GDM during the SARS-CoV-2 pandemic. The qualitative study would not have been possible without the enthusiasm and cooperation of so many NHS colleagues.

A huge thank you to all the past and present members of the Edinburgh Pregnancy Research Team, formerly Tommy's Group. I have been lucky to share this journey with a fantastic group of researchers, fellow students, and midwives.

To my family, I am forever grateful for your endless love and support over these last four years. A special thanks to Sinclair and Ruairidh, who always made me smile when things went wrong.

Finally, I dedicate this thesis to my supervisor and mentor, Professor Fiona Denison. Fiona was instrumental in encouraging me to pursue my academic ambitions and continued to support me in this research, even during her battle with ill health. Her guidance and contributions have left a lasting impact on this work.

Abstract

Gestational diabetes mellitus (GDM) is the most common pregnancy complication, affecting one in six pregnancies globally. It is associated with both short- and long-term health risks for mothers and offspring, including adverse perinatal outcomes and an elevated risk of developing future obesity, type 2 diabetes, and cardiovascular disease. While effective screening, diagnosis, and blood glucose management can mitigate these risks, there remains no consensus on the optimal strategies for addressing GDM.

This thesis, based on research conducted between 2020 and 2023, investigates approaches to optimise care for women with GDM. The primary focus is a multi-methods study exploring the impact of enforced changes in clinical management during the SARS-CoV-2 pandemic. Additionally, it presents a systematic review assessing the potential of precision markers for improving GDM outcomes.

The introduction offers a review of the literature on GDM screening, diagnosis, and management, with a particular focus on the modifications to clinical care precipitated by the pandemic. The subsequent three chapters present the key findings of this research.

Chapter 1 presents a retrospective multicentre cohort study examining the impact of pandemic-related changes in GDM diagnostic criteria and care provision on pregnancy outcomes. This study compares data from 4,915 women diagnosed with GDM prior to the pandemic (April 2018 – March 2020) with data from 3,467 women diagnosed during the pandemic (April 2020 – March 2021) across nine NHS trusts and health boards. The new diagnostic criteria more often identified women with GDM who were multiparous, had a higher BMI, and came from more deprived backgrounds, while fewer had a history of GDM (all $p<0.05$). During the pandemic, key pregnancy outcomes remained stable despite changes in screening and diagnostic thresholds. Remote care was found to be as effective as traditional in-person care, even for higher-risk women identified during this period.

Chapter 2 explores the experiences of healthcare professionals delivering multidisciplinary GDM care during the pandemic through a qualitative interview study. Participants (n=23 from three sites, representing members of the multidisciplinary team including diabetes specialist nurses, midwives, dietitians, diabetologists, and obstetricians) highlighted pre-pandemic inefficiencies in care delivery. Remote care adaptations—including virtual glycaemic management and task-shifting to allied health professionals—were generally viewed positively, facilitated by mobile technologies. However, remote care posed challenges for women with language barriers, and healthcare professionals reported increased isolation and concerns about the sustainability of virtual care due to burnout and limited IT infrastructure. A hybrid model combining in-person and remote care emerged as the preferred solution.

Chapter 3 investigates precision medicine approaches in GDM care through two systematic reviews. Although studies on precision lifestyle interventions were scarce, several clinical markers, such as a history of GDM, BMI, and blood glucose levels at diagnosis, were identified as potential predictors of the need for pharmacological intervention.

In summary, this thesis highlights several strategies for optimising GDM care in the UK. Key findings from the pandemic include the rising incidence of GDM, the potential for adjunct screening tools to better detect overt diabetes and reach marginalised women, and the effectiveness of remote antenatal care. Beyond existing approaches, precision methods may refine treatment pathways by enabling earlier identification of women requiring escalated care.

Lay Summary

Gestational diabetes mellitus (GDM) is a common condition affecting one in six pregnancies worldwide. It can lead to serious health issues for both mothers and their babies, not only during pregnancy but also later in life, such as a higher risk of developing diabetes, obesity, and heart disease. While early diagnosis and proper management of blood sugar levels can reduce these risks, experts still debate the best ways to handle GDM.

This research, conducted from 2020 to 2023, looks at ways to improve care for women with GDM, focusing on changes made to healthcare practices during the COVID-19 pandemic. The research included studying how these changes impacted pregnancy outcomes, examining healthcare professionals' experiences during this time, and exploring new ways to tailor treatments to individual needs.

One major part of the study compared the care of nearly 5,000 women diagnosed with GDM before the pandemic with over 3,000 women diagnosed during it. Despite changes to how GDM was diagnosed and managed, pregnancy outcomes remained stable, and remote care (such as virtual check-ups) was found to be just as effective as in-person care.

Interviews with healthcare providers revealed that they welcomed many of the new methods introduced during the pandemic, such as using technology for blood sugar monitoring. However, they also noted challenges, including difficulties for women with language barriers and concerns about the long-term sustainability of remote care due to issues like staff burnout.

Finally, the research explored new approaches, such as using specific health markers (like blood sugar levels and a history of GDM) to predict which women may need additional medical treatment.

In summary, this research shows that changes made during the pandemic, including the use of remote care, can improve GDM management. It also highlights the potential for

more personalised treatment approaches to improve outcomes for women with GDM in the future.

List of Figures

List of Tables

Publications and presentations related to this thesis

Publications

McLennan NM, Hazlehurst J, Thangaratinam S, Reynolds RM. ENDOCRINOLOGY IN PREGNANCY: Targeting metabolic health promotion to optimise maternal and offspring health. Eur J Endocrinol. 2022;186(6):R113-R26. https://doi.org/10.1530/eje-21-1046

McLennan NM, Lindsay R, Saravanan P, Sukumar N, White SL, von Dadelszen P, et al. Impact of COVID-19 on gestational diabetes pregnancy outcomes in the UK: A multicentre retrospective cohort study. BJOG. 2024;131(6):858-68. https://doi.org/10.1111/1471-0528.17716

Benham JL, Gingras V, **McLennan NM**, Most J, Yamamoto JM, Aiken CE, et al. Precision gestational diabetes treatment: a systematic review and meta-analyses. Commun Med (Lond). 2023;3(1):135. https://doi.org/10.1038/s43856-023-00371-0

Ayman G, Strachan JA, **McLennan N**, Malouf R, Lowe-Zinola J, Magdi F, et al. The top 10 research priorities in diabetes and pregnancy according to women, support networks and healthcare professionals. Diabet Med. 2021;38(8):e14588. https://doi.org/10.1111/dme.14588

Presentations

Dr Niamh Mclennan, Professor Rebecca M Reynolds, On Behalf of the Diabetes in Pregnancy Working Group, UK. The impact of changes in GDM care pathways during COVID-19 on disease incidence and pregnancy outcomes. Oral presentation, British Maternal & Fetal Medicine Society Conference, Brimingham November 2022

Niamh Mclennan, Professor Rebecca M Reynolds, On Behalf of the Diabetes in Pregnancy Working Group, UK. The impact of changes in GDM care pathways during COVID-19 on disease incidence and pregnancy outcomes. Poster presentation. Diabetic Pregnancy Study Group Annual meeting, Madrid September 2022

List of Abbreviations

Abbreviation	Full definition
ACHOIS	Australian Carbohydrate Intolerance Study in Pregnant Women
ACOG	American College of Obstetricians and Gynaecologists
ACCORD	Academic and Clinical Central Office for Research and Development
ADA	American Diabetes Association
AGA	Appropriate for gestational age
BMI	Body mass Index
CMW	Community midwives
COREQ	Consolidated criteria for reporting qualitative research
DIP	Diabetes in pregnancy
EASD	European Association for the Study of Diabetes
FPG	Fasting plasma glucose
GDM	Gestational diabetes mellitus
HAPO	Hyperglycaemia and Adverse Pregnancy Outcome study
HbA1c	Haemoglobin A1C (glycosylated haemoglobin)
HCP	Health care professionals
IADPSG	International Association of Diabetes in Pregnancy Study Group
ICU	Intensive care unit
IOL	Induction of Labour
JLA	James Lind Alliance
LGA	Large for gestational age
ML	Machine Learning
MBRRACE-UK	Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK
MDT	Multidisciplinary Team
NHS	National Health Service
NICU	Neonatal intensive care unit

NICE	National Institute for Health and Care Excellence
NPT	Normalisation process theory
NNT	Number needed to treat
OGTT	Oral Glucose tolerance test
PMID	Precision Medicine Diabetes Initiative
PPE	Personal protective equipment
PSP	Priority setting partnership
QALY	Quality-adjusted life years
RCOG	Royal College of Obstetrics and Gynaecology
RCT	Randomised controlled trial
RCM	Royal College of Midwives
RDS	Respiratory distress syndrome
RPG	Random plasma glucose
RR	Relative risk
SGA	Small for gestational age
SIGN	Scottish Intercollegiate Clinical Guidelines
TOBOGM	The Treatment of Booking Gestational Diabetes Mellitus Study
T1DM	Type 1 Diabetes mellitus
T2DM	Type 2 Diabetes mellitus
UK	United Kingdom
WHO	World Health Organisation

Contents

1 Introduction

1.1 Gestational Diabetes Mellitus

1.1.1 Epidemiology

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy, that is not clearly overt diabetes (1). It is the most common metabolic disturbance during pregnancy and is estimated to affect one in six pregnancies globally (2). The prevalence of GDM is growing due to increasing rates of obesity in women of childbearing age and rising maternal age, placing strain on maternity healthcare services (3). In the United Kingdom (UK), women with GDM represent the largest high-risk group accessing antenatal care, with prevalence rates of up to 25% depending on the demographics and glucose thresholds used for diagnosis (4).

1.1.1.1 Risk factors

Figure 1 illustrates modifiable and non-modifiable risk factors for GDM. The strongest predictor is a previous pregnancy affected by GDM, with recurrence risks ranging from 29% to 80% (5, 6). Ethnicities at higher risk for Type 2 diabetes (T2DM); Asian, Pacific, and Black African/Afro-Caribbean women, also face increased GDM risk and in the UK, South Asian women are over twice as likely to develop GDM compared to white women (7).

Key risk factors for GDM

- **Previous GDM**
- **Family minority ethnic origin with a high prevalence of T2DM**
- **Family history of diabetes (first-degree relative)**
- **BMI >30kg/m^2**
- **Previous macrosomia (birth weight >4500kg)**

Figure 1 Recognised risk factors for Gestational diabetes (SIGN 2024) (8)

Family history of diabetes represents a major risk factor, with GDM risk increasing twofold with a parental history of T2DM and fivefold with a sibling history (8).

Maternal obesity (BMI >30 kg/m^2) and advancing age are also significant predictors. GDM risk increases threefold (95% CI 2.1-3.4) for women with class I obesity (BMI 30-35 kg/m^2) and fourfold (95% CI 3.1-5.2) for class II obesity (BMI 35-40 kg/m^2) (9). Women aged 35-39 years have an adjusted odds ratio (OR) of 3.54 (95% CI 2.88-4.34) rising to 4.86 (95% CI 3.78-6.24) for women aged 40 and above (10).

Further associations have been drawn between GDM and polycystic ovary syndrome, multiparity, multiple pregnancy, use of medications including glucocorticoids and antipsychotic drugs (11). However, the strength of these associations is lower than those of the major risk factors.

1.1.2 Pathophysiology

GDM arises from a complex interplay between the increasing insulin demands of pregnancy and the ability of maternal pancreatic beta cells to produce sufficient insulin, leading to varying degrees of hyperglycaemia (12).

As pregnancy progresses, placental hormones—including human placental lactogen, progesterone, cortisol, and growth hormone—regulate maternal metabolism to prioritise the fetus' energy needs. These hormones gradually increase insulin resistance, reducing glucose uptake in maternal skeletal and adipose tissues while stimulating hepatic gluconeogenesis. As a result, blood glucose levels rise, along with free fatty acids, to support both maternal and fetal growth (13). Maternal adiposity, particularly in early pregnancy, further disrupts lipid metabolism and exacerbates insulin resistance (13, 14).

In a healthy pregnancy, the pancreas compensates for this rising insulin resistance by increasing production. However, in women who develop GDM, pancreatic beta cells fail to secrete enough insulin to meet the increased demand, leading to persistent hyperglycaemia, the hallmark of GDM (13).

Early studies showed that women with GDM exhibit reduced insulin sensitivity compared to controls, with this impairment often present even before conception and persisting throughout pregnancy (12, 14, 15). This suggests that women with GDM may have pre-existing insulin resistance and underlying beta cell dysfunction, which is revealed by the metabolic stresses of pregnancy (16).

1.1.3 Maternal and offspring outcomes

1.1.3.1 Maternal short-term outcomes

Compared to the general maternity population, women with GDM have a higher risk of developing gestational hypertension and pre-eclampsia (3, 17). These conditions are understood to be linked to impaired glucose metabolism through mechanisms which disrupt early placental development by affecting trophoblast invasion and placental function (18).

Women with GDM are at higher risk of intrapartum complications, including increased rates of labour induction (IOL), preterm birth (before 37 weeks), Caesarean birth, shoulder dystocia, uterine rupture, and birth trauma (17, 19). These complications are closely associated with the accelerated fetal growth driven by maternal hyperglycaemia (19).

1.1.3.2 Offspring short-term outcomes

Infants born to mothers with GDM are at a higher risk of large for gestational age (LGA) (19, 20). This finding is explained by the modified Pedersen hypothesis, whereby maternal hyperglycaemia leads to fetal hyperglycaemia as glucose passes freely across the placenta. In response, the fetus produces excess insulin (fetal hyperinsulinemia), driving anabolic processes that result in increased fat storage and rapid growth (21). Consequently, infants are more likely to be LGA (birth weight above the 90th percentile) or macrosomic (birth weight over 4000g). Maternal hyperlipidaemia is now believed to play a significant role in promoting excessive fetal growth (21, 22). In a cohort of 867 obese pregnant women, specific lipid species detected at 28 weeks of gestation—such as elevated plasma concentrations of diglycerides and triglycerides, indicating evidence of de novo lipogenesis—were associated with a diagnosis of GDM. In fully adjusted

models, these lipid abnormalities were also linked to increased abdominal circumference in the offspring (23). These findings require validation in further cohorts.

Birth weight is a significant risk factor for complications including shoulder dystocia, brachial plexus injury, neonatal respiratory distress syndrome (RDS), neonatal hypoglycaemia, hyperbilirubinemia and iatrogenic preterm birth (20). A large cohort study of 36,241 pregnancies in the U.S reported that shoulder dystocia occurred more frequently in infants of mothers with GDM compared to those without, at rates of 1.6% vs. 0.9% for infants <4000g and 10.5% vs. 6.0% for infants ≥4000g, demonstrating that GDM presents an independent risk for perinatal complications, regardless of birth weight. Similar patterns were observed for neonatal hypoglycaemia, brachial plexus injury, and RDS, confirming that GDM increases the risk of perinatal complications independently of the infant's birth weight (24).

In addition to excessive fetal growth, infants of mothers with GDM are at risk of metabolic disturbances, including hypoglycaemia, hyperbilirubinemia, and respiratory distress. These are driven by fetal hyperinsulinemia, and the severity of neonatal complications is closely linked to the level of maternal hyperglycaemia. (19, 20)

1.1.3.3 Maternal and offspring long-term outcomes

Although glucose metabolism typically returns to normal after delivery, women who develop GDM have a significantly increased risk of future cardiometabolic disease (17). A systematic review, including 20 studies, and 675 455 women with GDM, conferred a relative risk (RR) of 7.42 (95% CI: 4.79, 11.51) of developing T2DM, representing a seven-fold increased risk over women without GDM (25). A second review including 5 390 591 women demonstrated a two-fold higher risk (95% CI: 1.57, 2.50) of future cardiovascular events in women with GDM and identified this doubling of risk was independent of onset of T2DM (26), placing GDM as a major predictor of the leading cause of death worldwide.

Children born to mothers with GDM are also at a higher risk of developing T2DM and cardiovascular diseases (17). A follow-up of the offspring born to women with GDM, at 10–14 years of age, demonstrated childhood impaired glucose tolerance and childhood adiposity, independent of maternal BMI (27, 28). Data linkage studies also link maternal

GDM to an increased risk of neurodevelopmental disorders in the offspring, including autism and attention deficit hyperactivity disorder (ADHD) (29).

1.1.4 Screening and diagnosis

1.1.4.1 Historical context

The first evidence based, diagnostic criteria for GDM were proposed in 1964 by O'Sullivan (30). Glucose screening tests were used to determine glucose handling based on a 3-hour 100g oral glucose tolerance test (OGTT), performed in the second and third trimester of pregnancy, in a cohort of 752 American women. O'Sullivan identified that screening, diagnosing and treating hyperglycaemia in women not known to have diabetes, improved outcomes. These thresholds were validated by identification of subsequent diabetes at >5 years postpartum in an additional cohort of women. Diagnostic criteria were selected and based on identifying 2% prevalence, equivalent to the prevalence of diabetes in the background population. In 1965 the World Health Organisation (WHO) established diagnostic criteria recommending use of the 2 hour glucose load on an OGTT with diagnostic criteria set on glucose thresholds for diabetes in the nonpregnant population (31). Over a 30-year period multiple iterations were proposed to this diagnostic approach. Changes largely reflected improvements in processing and analysing blood glucose, including transitioning from venous whole blood glucose to plasma blood glucose. Further amendments to screening and diagnostic criteria were made considering emerging data. However, the guiding principle of screening and diagnosing GDM based on glucose tolerance testing aimed at detecting rates equivalent to those of diabetes in the non-pregnant population and validated for the development of future maternal T2DM remained, until the early 2000s (32, 33).

After the millennium, evidence from observational studies demonstrated a correlation between increasing levels of maternal hyperglycaemia, including those below recommended values for a diagnosis of GDM and risk of poor obstetric and neonatal outcomes, including LGA, shoulder dystocia, neonatal unit admission, Caesarean birth and hypertensive spectrum disorders (34). The international diabetes in pregnancy

community called for a revision of the diagnostic criteria whereby diagnostic criteria should aim to identify women at risk of adverse maternal and neonatal outcomes.

The landmark Hyperglycaemia in pregnancy outcome study (HAPO) published in 2008, was an international cohort study recruiting a diverse group of 25,505 women, from 15 centres around the world, examining the relationships between mild hyperglycaemia and pregnancy outcomes. In the absence of treatment, the study demonstrated a strong, continuous relationship between maternal hyperglycaemia and primary outcomes of primary Caesarean birth, LGA, neonatal hypoglycaemia and increase cord c-peptide (a surrogate for fetal insulinaemia) (35). This included glucose levels below that diagnostic of diabetes, which were not previously known to be harmful. Based on the findings in the HAPO study the International Association of Diabetes in Pregnancy Study Groups (IADPSG) recommended the diagnosis of GDM is made when any of the following three 75g 2-hour OGTT, at 24-28 weeks gestation, thresholds are met or exceeded: Fasting 5.1mmol/L (92 mg/dl), one hour 10.0mmol/L (180 mg/dl), two hours 8.5mmol/L (153 mg/dl).

1.1.4.2 The oral glucose tolerance test

The OGTT is the gold standard test for diagnosing GDM. Most organizations, including IADPSG (36), WHO (37), American Diabetes Association (ADA) (1), Canada and National Institute for Health and Care Excellence (NICE) (38) recommend a 75-g OGTT at 24–28 weeks of gestation for the screening of GDM. Variations in the glucose load include using a 100g glucose load. Women undergoing an OGTT must fast for at least 8 h before the test and take at least three blood samples within 2 h, during which time patients must not undertake physical exertion.

Despite it being the gold standard test used internationally for the diagnosis of GDM, concerns have long been raised on the reproducibility of OGTT results. It is estimated, in up to 35% of cases the diagnosis of GDM is not reproducible, with subjects showing improvements in glycaemic status on repeat testing (39, 40). The sources of poor reproducibility have been linked to preanalytical, analytical and post analytical factors. Preanalytical variation can be driven by patient factors including physiological (exercise,

gastric emptying, stress and sleep) and patient preparation (pre-test fasting state, pre-test diet and the self-directed glucose load). The most prominent source of error in assessing plasma glucose lies in glycolysis post sampling. Recommendations to minimise this error involve immediate placement in an ice slurry and centrifugation within 30 minutes (41). Alternative strategies include the use of citrate buffered specimen tubes. Glucose processing variability greatly impacts the prevalence of GDM and therefore pre analysis sampling represents a major limitation in determining GDM prevalence (42) and drawing conclusions across GDM studies (43).

1.1.4.3 Risk factor verses universal screening

Currently there are two overarching approaches used when screening for GDM, selected risk-factor based screening and universal screening. Universal screening offers testing for all pregnant women, regardless of individual risk factors, while selective screening targets women with specific risk factors, (such as obesity, advanced maternal age, or a family history of diabetes).

In a UK population, universal screening has been shown to have a 4-fold increase in the incidence of GDM, increasing the identification of mild to moderate hyperglycaemia (44). This may potentially lead to earlier interventions and improved maternal-fetal outcomes (7, 44). However, it requires more healthcare resources and may increase the burden of unnecessary testing. Selective screening focuses on high-risk populations, is more cost-efficient but it risks underdiagnosing GDM in women without identifiable risk factors (44). The Pregnancy Outcome for Women with Pre-gestational Diabetes Along the Irish Atlantic Seaboard study found that the prevalence of women with GDM who had no risk factors was low, ranging from 2.7% to 5.4% (45). However, these women with GDM with no recognisable risk factors had more pregnancy complications than those with normal glucose tolerance. In other studies selective risk factor screening estimates to miss up one-third of women with GDM (46). Thus, clinical risk factors alone are not predictive of GDM risk for all women.

Without a strong evidence base to support the decision, health care providers are left to decide between universal and selective screening based on factors such as healthcare system capacity, population risk profiles, and cost-effectiveness. Worldwide, universal

screening is the preferred screening approach, recommended by governing bodies and expert panels in the USA, Canada, Australia (47-49).

1.1.4.4 One step verse two step screening tests

In addition to the choice between selective risk factor verse universal screening there is a choice between the type of screening tests used. Two approaches are generally considered. The one-step approach (recommended by the IADPSG), whereby a fasting patient undergoes a 2-hour, 75-g oral glucose tolerance test. The result is "abnormal" if any one glucose result (the fasting, 1-hour, or 2-hour result) is above a specified threshold. In the second approach, the two-step approach (recommended by the American college of Obstetricians and gynaecologists (ACOG), non-fasted patients ingest a 50-g oral glucose load, followed by a 1-hour glucose measurement. If the 1-hour glucose level is ≥200 mg/dL (11.1mmol/L), a diagnosis of GDM is made and no further testing is needed. If the 1-hour glucose is between 130 mg/dL (7.2mmol/L) and 200 mg/dL (11.1mmol/L) the patient undergoes a fasting 3-hour glucose tolerance test, and GDM is diagnosed if two or more hourly glucose measurements are above specified thresholds.

In two recent randomized trials, researchers evaluated the performance of the one step verses the two-step testing approach. Both studies demonstrated a large increase in the number of women diagnosed with GDM using the one step approach compared with the two-step approach, 14.4-16.5% versus 4.5-8.5% respectively. Additionally, both studies reported no differences in primary maternal and neonatal outcomes between the treated populations of women (50, 51). Adding these recent findings into a metanalysis of RCTs confirmed the risk of LGA was similar between the two approaches (pooled rates 8.8% one-step vs. 9.2% two-step) with a pooled RR of 0.95 (95% CI 0.88–1.04) (52).

1.1.4.5 Diagnostic thresholds

Global inconsistencies in the diagnostic criteria for GDM have made it difficult to meaningfully compare study results, complicating the process of drawing conclusions from systematic reviews and meta-analyses. A 2019 systematic review highlighted this issue while evaluating the diagnostic performance of various glycaemic measures. Among the 23 studies included, 14 different diagnostic criteria for the OGTT were identified.(53)

Based on the findings from the HAPO study, the IADPSG recommend setting diagnostic thresholds for GDM at glucose values associated with an estimated odds of 1.75 for birth weight, cord C-peptide, and percent infant body fat >90th percentiles, compared with the odds of these outcomes at mean glucose values for the entire study cohort. These recommendations were widely accepted by many clinical governing bodies. Multiple international observational studies, including those conducted in the UK, have shown that women diagnosed with GDM under the IADPSG criteria—who would previously have been classified as having normal glucose tolerance—are at increased risk for obstetric and neonatal complications. These complications include gestational hypertension, preeclampsia, Caesarean birth, macrosomia, shoulder dystocia, and neonatal intensive care admission (54-56). A systematic review and meta-analysis further confirmed these findings, including studies that utilized both one-step and two-step diagnostic testing approaches, as well as universal and selective screening processes (57).

Over the decade since the HAPO study findings and the publication of the IADPSG recommendations, significant debate has persisted. While evidence suggests that detecting maternal hyperglycaemia at lower thresholds detects women at risk of obstetric and neonatal outcomes, this has come at the cost of a substantial increase in GDM prevalence. A 2021 systematic review of 31 cohort and cross-sectional studies involving 136,705 women found that implementing the IADPSG criteria led to a 75% increase in GDM diagnoses (RR 1.75, 95% CI 1.53–2.01) (58).

Until recently, there was minimal evidence supporting the benefits of treating women diagnosed with GDM under the IADPSG criteria. Potential benefits have largely been extrapolated from the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) and the randomized trial of treatment for mild gestational diabetes (59, 60) where maternal glucose levels overlapped with the IADPSG thresholds. In 2022, results from a randomized controlled trial using a 75-g 2-hour OGTT with two sets of glycaemic thresholds (lower and higher) were published. The study found that raising the diagnostic threshold did not affect the primary outcome of LGA, suggesting that detecting and treating women with fasting glucose levels between 5.1 and 5.5 mmol/L or 2-hour glucose levels between 8.5 and 9.0 mmol/L offers no significant benefit in preventing LGA (61).

Additionally, the trial highlighted potential downsides of intervening in this population, such as increased rates of induction of labour (IOL) and associated chorioamnionitis in the lower-threshold group, without improvement in primary outcomes. Notably, the study did not include an economic analysis. Evidence supporting the cost-effectiveness of the IADPSG criteria remains scarce. One large U.S. cohort study suggested that cost-effectiveness was driven by reduced risks of infrequent adverse outcomes, such as neonatal intensive care admissions (NICU) (62).

The debate continues, focusing on the increased prevalence of GDM and the limited evidence supporting the cost-effectiveness of adopting the IADPSG criteria.

1.1.4.6 Early screening of overt diabetes

The rising rates of obesity and advanced maternal age have contributed to an increase in the prevalence of undiagnosed pre-existing diabetes among women of childbearing age (63). This group is particularly significant because they face higher rates of congenital malformations compared to women diagnosed with GDM (64). Despite their distinct risk profile, data suggest that treatment can normalise outcomes for these women, bringing them in line with those observed in women with GDM (64)

To recognise this distinct group, the terms 'overt diabetes' or 'diabetes in pregnancy' (DIP) have been introduced and are used interchangeably. For the remainder of this thesis, the term 'overt diabetes' will be used.

The IADPSG recommendations, endorsed by the WHO, advocate for screening pregnant women at high risk of diabetes to identify overt diabetes. Women are classified as having overt diabetes if their plasma glucose values meet or exceed the thresholds for diabetes outside of pregnancy: fasting plasma glucose (FPG) ≥ 7 mmol/l, 2-hour glucose value ≥ 11.1 mmol/l, and/or HbA1c ≥ 48mmol/l.

1.1.4.7 Early screening for GDM

A relationship between increasing maternal glycaemia and excess fetal growth and adiposity prior to a GDM diagnosis at 24 weeks gestation has been demonstrated in large cohort studies. These studies show excess fetal growth as early as 20 weeks gestation (65, 66). This observational data forms a basis for defining GDM before 24 weeks.

In 2010, the IADPSG recommended screening high risk women in early pregnancy and classifying GDM when FPG levels of 5.1-6-9 mmol/l were detected. However, these criteria have not been validated for early pregnancy use. Some observational studies supported this decision, reporting that first trimester fasting glucose levels in the non-diabetic range were associated with higher risks of adverse pregnancy outcomes, including more Caesarean births, LGA and macrosomia (67).

However, a large study from China, corroborated by data from Italy, found that the IADPSG thresholds used in early pregnancy did not accurately predict a GDM diagnosis in later pregnancy (68, 69). The IADPSG early diagnostic criteria were later revoked. This has left uncertainty regarding how clinicians should manage women with intermediate FPG (5.1–6.9 mmol/l) and 2hr OGTT levels (8.6-11mmol/l) identified on early screening tests.

The adoption of early diagnostic testing for overt diabetes has generated extensive biochemical data in early pregnancy, enabling researchers to evaluate screening and treatment during this period. Recent reviews, including a systematic review in 2022 and a narrative review in 2021 have synthesised the evidence (70, 71). Data from eight randomised controlled trials comparing early screening and treatment to routine care found no significant difference in the risk of LGA (8.1 vs 9.0%; RR, 0.94; 95% CI, 0.73-1.22) (71). Meanwhile, the narrative review of 46 studies - including observational cohorts and RCT's - highlighted conflicting findings regarding adverse pregnancy outcomes (70). Another systematic examined the longer term outcomes of identifying early GDM, reporting that women with early GDM had a twofold increased risk of developing T2DM 6 weeks to 20 years postpartum compared to those with late GDM (RR) 2.13 (95% CI 1.52–3.56) (72)

Synthesising and interpreting studies on early diagnosis and treatment of GDM is challenging due to the wide variety of screening tests and diagnostic criteria used in available research. Recently, much-anticipated findings from an international multicentre RCT evaluating diagnostic criteria and treatment for less severe hyperglycaemia than overt diabetes in early pregnancy among women with risk factors were published. The Treatment of Booking Gestational Diabetes Mellitus Study (TOBOGM) found that immediate treatment of GDM resulted in modest reduction in the

incidence of a composite of major adverse neonatal outcomes (odds ratio 0.82; 95% CI 0.68–0.98; number needed to treat (NNT) = 18). However, no significant differences were observed for pregnancy-related hypertension or neonatal lean body mass (73). A subsequent economic evaluation of the TOBOGM study indicated that earlier treatment was more effective and less costly for women in the higher glycaemic range of FBG 5.3-6.0 mmol/l, and or 2 hour 9-11 mmol/l, and for those diagnosed prior to 14 weeks gestation (74).

While a modest and cost-effective benefit has been demonstrated, the findings remain inconclusive regarding the support for early GDM screening in high-risk women (75).

1.1.5 Alternative screening and diagnostic tools

Although the OGTT remains the universally recommended diagnostic test for GDM, it presents several challenges, including issues with reproducibility, acceptability, and a lack of consensus regarding who, when, and how to diagnose GDM. These challenges are compounded by ongoing debates about screening timing, target populations, and the optimal diagnostic criteria. Consequently, significant efforts have been directed toward developing alternative tools that offer a simpler diagnostic approach, with the goal of better identifying women at risk of GDM.

1.1.5.1 HbA1c

HbA1c measures the percentage of glycated haemoglobin, providing an indication of average blood glucose levels over the past 90 days. It is recommended for diagnosing diabetes mellitus (DM) in the general population, supported by strong evidence linking reductions in HbA1c levels with decreased microvascular complications, cardiovascular risk, and mortality (76). As a single blood test, HbA1c is generally more acceptable than OGTT, as it does not require fasting, glucose ingestion, or multiple venepunctures. Additionally, it avoids the preanalytical handling variations commonly associated with the OGTT.

The accuracy of HbA1c depends on stable red blood cell turnover and the absence of haematological conditions such as iron deficiency, inherited haemoglobin variants, or

other disorders affecting haemoglobin (77). In early pregnancy, increased red blood cell turnover and lower fasting blood glucose levels necessitate trimester-specific reference ranges for HbA1c to ensure accurate interpretation. Additionally, evidence supports the need for ethnic and population-specific reference values, as variations in HbA1c levels have been observed across different demographic groups (78, 79).

Results from the HAPO study demonstrated a significant correlation between increasing HbA1c levels and all measures of plasma glucose. Higher HbA1c levels were strongly associated with an increased frequency of adverse primary outcomes. Specifically, the frequency of birth weights >90th percentile rose from 7.3% in the lowest HbA1c category (<26 mmol/mol) to 17.6% in the highest category (> 40 mmol/mol). However, after adjusting for confounding factors, HbA1c was not significantly associated with neonatal anthropometric outcomes. Consequently, the 2010 IADPSG consensus did not recommend HbA1c as a diagnostic test for GDM (80)

A 2019 systematic meta-analysis reviewed the diagnostic accuracy of HbA1c during pregnancy. Among 6,848 pregnant women across nine studies who underwent both the OGTT and HbA1c tests in the second or third trimesters, the analysis reported an overall good level of accuracy, with a combined area under the curve (AUC) of 0.825 (95% CI: 0.751–0.899). Sensitivity and specificity were evaluated at specific cut-off values (81):

- At 36 mmol/mol (5.4%): Sensitivity was 50.3% (95% CI: 24.8%–75.7%) and specificity was 83.7% (95% CI: 67.5%–92.7%).
- At 39 mmol/mol (5.7%): Sensitivity was 24.7% (95% CI: 10.3%–48.5%) and specificity was 95.5% (95% CI: 85.7%–98.7%).
- At 40 mmol/mol (5.8%): Sensitivity was 10.8% (95% CI: 5.7%–19.4%) and specificity was 98.7% (95% CI: 96.2%–99.5%).
- At 42 mmol/mol (6.0%): Sensitivity was 12.9% (95% CI: 5.5%–27.5%) and specificity was 98.7% (95% CI: 97.6%–99.3%) (81).

Overall, the study highlighted the low sensitivity but relatively high specificity of HbA1c, making it a poor diagnostic tool compared to fasting glucose (81). Similar findings were reported in studies using alternative approaches to the 75g OGTT as the reference

test(82). Evaluating HbA1c as a diagnostic tool in early pregnancy also revealed inadequate sensitivity (53, 83).

A limited number of studies have investigated the predictive value of HbA1c for maternal and fetal complications (81, 84-88). A large cohort study in New Zealand found that an HbA1c ≥41 mmol/mol at the first antenatal visit identified all cases of GDM and was associated with a twofold increased risk of congenital anomalies, preeclampsia, and shoulder dystocia, as well as a threefold increased risk of perinatal death (84) Similar findings were reported in an Australian Cohort (86). Additionally, a systematic review assessing HbA1c levels at 24–28 weeks for predicting fetal macrosomia and LGA outcomes found that women with HbA1c levels ≥37 mmol/mol (5.5%) had a higher risk of LGA compared to those with levels <31 mmol/mol (5%). The pooled RR was 1.70 (95% CI: 1.23–2.35) (87) However, studies in other cohorts indicate that while an elevated HbA1c in early pregnancy is highly specific, it lacks sensitivity for detecting hyperglycaemia and certain perinatal complications (86, 89). Currently, there is no clear evidence supporting the treatment of women with HbA1c levels between 39–46 mmol/mol (5.7%–6.4%) in early pregnancy.

The combined evidence suggests that early pregnancy HbA1c may serve as a "rule-in" test when used alongside standard diagnostic tests. One recent study indicated that it could potentially reduce the number of OGTTs performed by up to 40% (90). HbA1c is presently recommended only for identifying overt diabetes, using a cut-off point of 6.5% (48 mmol/mol), which is equivalent to the diagnostic threshold for diabetes in the non-pregnant population.

1.1.6 Clinical management of GDM

The recommended approach to managing a woman diagnosed with GDM involves a multidisciplinary strategy (38, 91, 92). This includes educating the patient on self-monitoring of blood glucose levels, implementing dietary modifications and nutrition monitoring, encouraging lifestyle changes, and managing maternal weight. Approximately 70–85% of women with GDM can be effectively managed through physical

activity, dietary changes, and lifestyle modifications and 15–30% of patients will require pharmacological therapy, which may include oral hypoglycaemic agents or insulin (11).

The positive impact of medical intervention on fetal and maternal morbidity was first demonstrated in the landmark 2005 ACHOIS (59). Interventions such as dietary advice, blood glucose monitoring, and insulin therapy, when needed, led to a 67% reduction in the primary composite outcome of infant death, shoulder dystocia, bone fracture, and nerve palsy compared to usual care. A second study conducted four years later confirmed these findings, showing that a similar intervention package for women with "mild" GDM reduced the incidence of macrosomia, caesarean birth, shoulder dystocia, and pre-eclampsia compared to standard care (60).

1.1.6.1 Lifestyle and dietary intervention

The cornerstone of GDM treatment is lifestyle intervention, including dietary modification, physical activity, and weight management. A wide variety of lifestyle interventions have been evaluated, often in combination, making it challenging to determine their individual impacts. Cochrane conducted two systematic reviews in 2017 to address this (93, 94). The first review included randomized controlled trials comparing lifestyle interventions with usual care or alternative interventions for GDM treatment. Results showed that lifestyle interventions were associated with a decreased risk of LGA infants and reduced neonatal adiposity. Women in these studies were also less likely to experience postnatal depression and were more likely to achieve postpartum weight goals. (93)

The second review compared different types of dietary advice but found no significant differences in outcomes for mother and child, including hypertensive disorders, Caesarean birth, T2DM, LGA infants, and markers of fetal adiposity (94).

In current clinical practice, GDM is typically diagnosed after 24–28 weeks of gestation. This timing raises questions about the effectiveness of lifestyle interventions on GDM outcomes, as opportunities for prevention and intervention may be limited by the late diagnosis. Consequently, the role of lifestyle interventions in preventing GDM remains a topic of ongoing debate and research.

1.1.6.2 Pharmacological intervention

When blood glucose targets cannot be achieved through lifestyle interventions alone, glucose-lowering pharmacological therapy becomes necessary. Two landmark randomized trials (59, 60) demonstrated significant reductions in birth weight and the incidence of LGA infants in women with GDM who received treatment. These findings spurred extensive research into the benefits of various glucose-lowering agents and subcutaneous insulins (95). A meta-analysis of 35 trials on pharmacological interventions for GDM reported that metformin is an effective alternative to insulin for managing hyperglycaemia, although up to 50% of women may still require supplemental insulin (96). In the UK, metformin is recommended as the first-line pharmacological therapy unless blood glucose levels at diagnosis are markedly elevated (38, 97).

The proportion of women requiring pharmacological therapy varies widely, with estimates ranging from 15% to 68%, depending on the population demographic. For example, a cohort study in a predominantly South Asian GDM population in the UK found that as many as 68% of women required pharmacological treatment (98).

1.1.6.3 Clinical practice across the UK

In the UK, the NICE (2015) and the Scottish Intercollegiate Guidelines Network (SIGN, 2017) recommend screening pregnant women for GDM using clinical risk factors in early pregnancy. Women with any of the following risk factors—raised BMI (>30 kg/m^2), ethnic background associated with a higher risk of diabetes (South Asian, Middle Eastern, Black African, Black Caribbean, or Black British), family history of diabetes, or previous large baby (≥4.5 kg)—are advised to undergo biochemical screening with a fasting, 2-hour, 75g OGTT at 24–28 weeks of gestation (38, 97).

In 2021 the UK national screening committee review of GDM screening, did not endorse population level screening, recommending NICE guidelines for women at high risk. The decision to adopt risk-factor-based screening, rather than universal screening as advocated internationally following the HAPO trial, was informed by UK-specific health economic data. These analyses demonstrated that routine identification and treatment of GDM were not cost-effective based on perinatal outcomes. Using the national standard cost-effectiveness threshold of £20,000 per quality-adjusted life year (QALY), a National Institute for Health Research-funded Health Technology Assessment found

that universal screening for hyperglycaemia in pregnancy, even among high-risk groups, did not meet this criterion (99). NICE's 2015 criteria were developed using health economic models that prioritized reducing the historical average NHS costs of selected adverse outcomes. These outcomes were common enough to yield sufficient statistical power in randomized controlled studies (99).

While NICE and SIGN agree on employing risk-factor-based screening and on use of a one-step 75g OGTT at 24-28 weeks, their diagnostic criteria differ. SIGN endorses the IADPSG criteria, whereas NICE uses a modified version of the 2010 WHO criteria**. Table 1** outlines the diagnostic criteria recommended by each guideline.

Guideline committee	Glucose load (g)	Fasting mmol/l (mg/dl)	1-hour mmol/l (mg/dl)	2-hour mmol/l (mg/dl)
SIGN[b]	75	≥5.1 (92)	≥10.0 (180)	≥8.5 (153)
NICE[b]	75	≥5.6 (101)	–	≥7.8 (140)

Table 1 Diagnostic thresholds for GDM based on OGTT at 24-28 weeks' gestation.

[a] *Plasma glucose levels fasting, 1 hour and 2 hours following oral glucose load*

[b] *GDM diagnosed if one or more glucose value met or exceeded*

Since the publication of the 2015 NICE guidelines, significant limitations of risk-factor-based screening have been identified. Studies have highlighted both suboptimal compliance with OGTT testing and high rates of GDM detection in women without recognized risk factors (100, 101). A UK cohort study found that 39% (255/650) of eligible women who should have undergone an OGTT were not appropriately screened. The primary reason was a failure to identify risk factors, with ethnicity being the most overlooked factor, rather than issues with patient noncompliance (101).

For women with a history of GDM in a prior pregnancy, glucose testing earlier in pregnancy is recommended. This includes either self-monitoring of blood glucose or a 75g 2-hour OGTT at booking, with a repeat OGTT at 24–28 weeks if the initial test is normal. Additionally, SIGN recommends early screening for "overt diabetes" or "diabetes mellitus in pregnancy" among high-risk women. This involves testing using HbA1c or

fasting glucose, with diagnostic thresholds aligned with WHO criteria: fasting glucose ≥7 mmol/l, 2-hour glucose ≥11.1 mmol/l, random glucose ≥11.1 mmol/l, or HbA1c ≥48 mmol/mol.

Both NICE and SIGN emphasize the importance of multidisciplinary care for women diagnosed with GDM. Care should be led by a named obstetrician and a physician with expertise in diabetes, supported by a diabetes specialist nurse, midwife, and dietitian. Women should receive education on lifestyle modification and capillary blood glucose monitoring, including fasting and postprandial testing (1- or 2-hours post-meal). Regular contact with a joint diabetes and antenatal clinic is advised for blood glucose review every 1–2 weeks

1.2 GDM research landscape

1.2.1 Precision medicine approach

Over the past two decades, research has demonstrated that screening and treatment for GDM can improve maternal and fetal outcomes. Following the HAPO trial, efforts have continued to optimize the benefits of screening while minimizing potential harms. Despite these advancements, the latest evidence on screening and diagnostic methods has not provided definitive guidance on identifying women and offspring at the greatest risk of adverse outcomes (50, 61, 73). As a result, attention is shifting toward alternative approaches to better define and diagnose GDM.

Precision medicine aims to enhance diagnostics, prognostics, prediction, and treatment in GDM by integrating diverse biological domains—such as metabolomics, genomics, lipidomics, and proteomics—with technology, clinical risk factors, biomarkers, and computational modelling (102). In 2018, the ADA, in partnership with the European Association for the Study of Diabetes (EASD), launched the Precision Medicine Diabetes Initiative (PMID), which included GDM within its scope (102). Current precision medicine efforts focus on subtype classification, risk prediction modelling, and the utility of biomarkers.

1.2.1.1 Biomarkers and early pregnancy risk prediction models

The WHO defines a biomarker as "any substance, structure, or process that can be measured in the body or its products and that may influence or predict the incidence of a disease or its outcomes."(103) Traditionally, the identification of GDM risk has relied on maternal characteristics to predict GDM in early pregnancy. Researchers have repeatedly explored measures of glycaemia during both the first and late second trimesters in efforts to better predict pregnancy outcomes and identify those at risk for adverse events (53, 57).

Recent research on biomarkers has focused on early predictive molecules in the first and early second trimesters, as well as diagnostic biomarkers in the second and third trimesters that indicate GDM and its maternal and fetal outcomes. Advances in metabolic and proteomic techniques have enabled the exploration of maternal blood and urine biomarkers, such as amino acids, peptides, proteins, lipids, enzymes, saccharides, and microRNAs. While small studies have shown promise, no biomarkers have yet demonstrated sufficient diagnostic performance for clinical use (104).

The potential utility of biomarkers lies in combining them with clinical risk factors in early pregnancy prediction models. Early pregnancy risk stratification could help mitigate diabetes-associated comorbidities through timely interventions, such as physical activity and dietary changes (105). Current clinical practice guidelines, such as those from NICE/SIGN, use established GDM risk factors to determine who should undergo biochemical screening, based on one or more pre-specified risk factors. Decades of observational data have clarified the risk posed by individual factors; however, composite risk scores that combine maternal characteristics have shown only moderate discrimination (the ability to distinguish low- from high-risk individuals) and poor calibration (the agreement between predicted and observed risk), limiting their effectiveness in predicting GDM (106). Similarly, proposed prediction models for pregnancy complications have demonstrated poor predictive performance (107). While current approaches have fallen short, they highlight the potential of prediction models to provide individualized absolute risk assessments for GDM and its complications.

Machine learning (ML), a subset of artificial intelligence, offers the potential to recognise patterns and correlations in large datasets. By incorporating GDM risk factors, routine

clinical measures, and novel biomarkers, machine learning algorithms could generate individualized risk scores to predict GDM, treatment responses, and clinical outcomes (108, 109).

1.2.1.2 Subgroup classification

Phenotypic heterogeneity among women with GDM was first recognised in early studies exploring its pathophysiology (12, 14). More recently, research has advanced this understanding, highlighting variations in the roles of insulin resistance and insulin deficiency. Women with predominantly insulin-resistant GDM exhibit distinct baseline characteristics compared to those with normal glucose levels, including higher BMI, elevated lipids, and increased fasting glucose (110, 111). When these subtypes are linked to pregnancy outcomes, an insulin-resistant phenotype is associated with a heightened risk of adverse outcomes, such as LGA infants, Caesarean births, and neonatal hypoglycaemia, compared to women with normal glucose tolerance. Conversely, women with insulin-deficient GDM patterns do not exhibit an increased risk of fetal overgrowth or adverse outcomes when compared to those without GDM (110, 111).

These findings—showing that the insulin-resistant subtype carries a more adverse metabolic profile and higher risk of complications—have been consistently replicated across independent cohorts. Recent studies have also sought to classify GDM subtypes using readily available clinical parameters, such as OGTT patterns (106, 112, 113). Other potential classifications, including genetic subtypes, remain underexplored (114). However, these phenotypic and genetic subgroups could pave the way for personalized risk assessments and tailored therapies for women with GDM.

1.2.2 Diabetes in pregnancy James Lind Alliance PSP

The literature on GDM screening, diagnosis, and management reveals significant inconsistencies and unresolved debates within clinical practice. National guidelines and systematic reviews underscore variability in research quality, study designs, and reliability, all of which contribute to the absence of clear, evidence-based treatment protocols. This issue is further exacerbated by the disconnect between healthcare

research—often driven by academic or industry interests—and the actual priorities of women living with GDM and their caregivers.

With limited funding and resources available for research, there is growing emphasis on ensuring that research efforts address the most pressing needs of those affected by disease and ill health. This is the central mission of the James Lind Alliance (JLA), a UK-based initiative dedicated to aligning research priorities with patient and caregiver concerns.

In 2018, the JLA launched a Priority Setting Partnership (PSP) for diabetes in pregnancy, bringing together patients, caregivers, and clinicians to identify and rank unresolved questions and uncertainties. Using a structured methodology, the PSP gathered these questions and, through a standardized prioritization process, identified the most urgent areas for research.

In 2020, I was fortunate to join the Diabetes in pregnancy James Lind Alliance Priority Setting Partnership (JLA PSP) during its initial survey stage. Women with experience of pregnancy or planning pregnancy with any type of diabetes, along with their support networks (partners, families, friends, and carers) and healthcare professionals, were invited to propose up to three questions they considered important for future research. These questions were analysed using content analysis, grouped into categories, and further refined by the steering group into indicative questions that captured the key issues raised.

My primary role in the PSP was evidence checking. I implemented a pragmatic, broad-level strategy to determine whether substantial uncertainty existed for each indicative question. The search was focused on the Cochrane Database of Systematic Reviews, systematic reviews published since 2017, and UK guidelines for diabetes in pregnancy.

The prioritization process involved three online stages, conducted during the COVID-19 pandemic to comply with social distancing measures. Detailed methods for this process are described in the published paper (Appendix 1). I acted as a silent observer during the second and third stages, where women, their support networks, and healthcare providers ranked their top 10 priorities. In the final stage, 25 participants engaged in

discussions and ranking exercises to determine the final list of the 10 most important research priorities.

Figure 2 presents the top 10 research priorities identified through the JLA PSP process. The top three priorities are listed below.

1. How can diabetes technology be used to improve outcomes for pregnancy, birth, and maternal and child health?
2. What is the most effective test for diagnosing diabetes in pregnant women?
3. What is the best way to manage blood sugar levels through diet and lifestyle during pregnancy?

Figure 2 Research priorities in diabetes and pregnancy (115). Figure made available from the JLA with permission.

1.3 SARS-CoV-2

In December 2019, a novel coronavirus (SARS-CoV-2) was identified in Wuhan, China, associated with a cluster of pneumonia cases (116). The clinical disease caused by this virus was named COVID-19. Transmission occurs primarily through respiratory droplets from breathing, sneezing, or coughing, as well as via contact with contaminated surfaces (116).

In the following weeks, the virus spread rapidly, crossing international borders and leading to outbreaks in multiple countries. By January 2020, cases were reported in Japan, South Korea, Thailand, United States and other nations. This rapid escalation led to widespread concern and public health interventions, including lockdowns, travel restrictions, and the implementation of social distancing measures.

Recognizing the global threat, the WHO declared COVID-19 a Public Health Emergency of International Concern on January 30, 2020. On March 11, 2020, the WHO officially classified COVID-19 as a pandemic—the first coronavirus pandemic in history. This unprecedented event led to significant public health interventions, widespread economic disruption, and profound changes in daily life and healthcare systems.

1.3.1 Impact on the NHS

The initial wave of COVID-19 overwhelmed the UK's National Health Service (NHS). Hospitals faced an unprecedented surge in cases, necessitating rapid reorganization of services. Elective surgeries and routine medical appointments were postponed, while intensive care units (ICUs) were expanded. Emergency field hospitals, such as the NHS Nightingale hospitals, were established to manage critically ill patients. Frontline healthcare workers contended with shortages of personal protective equipment (PPE) and high infection risks, compounding the pressure.

1.3.2 SARS-CoV-2 and pregnancy

A systematic review and meta-analysis, *PregCOV-19*, examined 192 studies involving 64,676 pregnant women and 569,987 non-pregnant women with COVID-19. The analysis revealed higher odds of ICU admission and invasive ventilation among pregnant women compared to non-pregnant women of reproductive age. Risk factors for severe COVID-19 in pregnancy included pre-existing comorbidities, non-white ethnicity, chronic hypertension, pre-existing diabetes, advanced maternal age, and high BMI (117).

1.3.3 GDM care during the pandemic

To address the dual challenges of GDM care and COVID-19 risks, emergency diagnostic strategies were implemented in several countries, including the UK, Australia, New Zealand, Canada, and parts of Europe. These strategies aimed to minimize COVID-19 exposure while ensuring the identification of women with severe hyperglycaemia who were at the highest risk of adverse obstetric and neonatal outcomes.

In the UK, pregnant women were advised to practice social distancing and self-isolation. On April 1, 2020, the Royal College of Obstetricians and Gynaecologists (RCOG) introduced new national guidance outlining modifications to maternity services (Figure 3) (118). These changes included adjustments to glucose screening and diagnostic thresholds, as well as reduced in-person consultations. Telemedicine was widely adopted to facilitate remote education and monitoring of glycaemic control. Low-risk women with diet-controlled GDM received all care remotely, in coordination with community midwifery services.

1.3.3.1 Alternative diagnostic testing and thresholds

Figure 3 outlines the RCOG recommended GDM care pathways for diagnosis of GDM during COVID-19 (118). Guidance recommended suspending the 2-hour OGTT and adopting a two-step testing approach. Women with risk factors for GDM (as per pre-pandemic guidelines) were tested at booking using HbA1c and/or random plasma glucose (RPG). Diagnostic thresholds were as follows:

- **RPG ≥11.1 mmol/L** or **HbA1c ≥48 mmol/mol**: Diagnosed as T2DM and treated as overt GDM.
- **HbA1c 41–47 mmol/mol**: Treated as GDM from diagnosis.

Further testing at 24- 28 weeks was recommended and a diagnosis of GDM made if any of the following criteria were satisfied

- **Fasting glucose ≥5.3 mmol/L**, **HbA1c ≥39 mmol/mol**, or **RPG ≥9 mmol/L**.

This pragmatic approach aimed to reduce physical contact, minimize healthcare burden, and focus on identifying women at greatest risk of complications (118). While prioritising high-specificity tests reduced false-positive rates, it also lowered sensitivity, potentially missing some GDM cases. A systematic review supported the 39 mmol/mol HbA1c threshold, noting a 10% false-positive rate at high specificity, amongst women with risk factors (53).

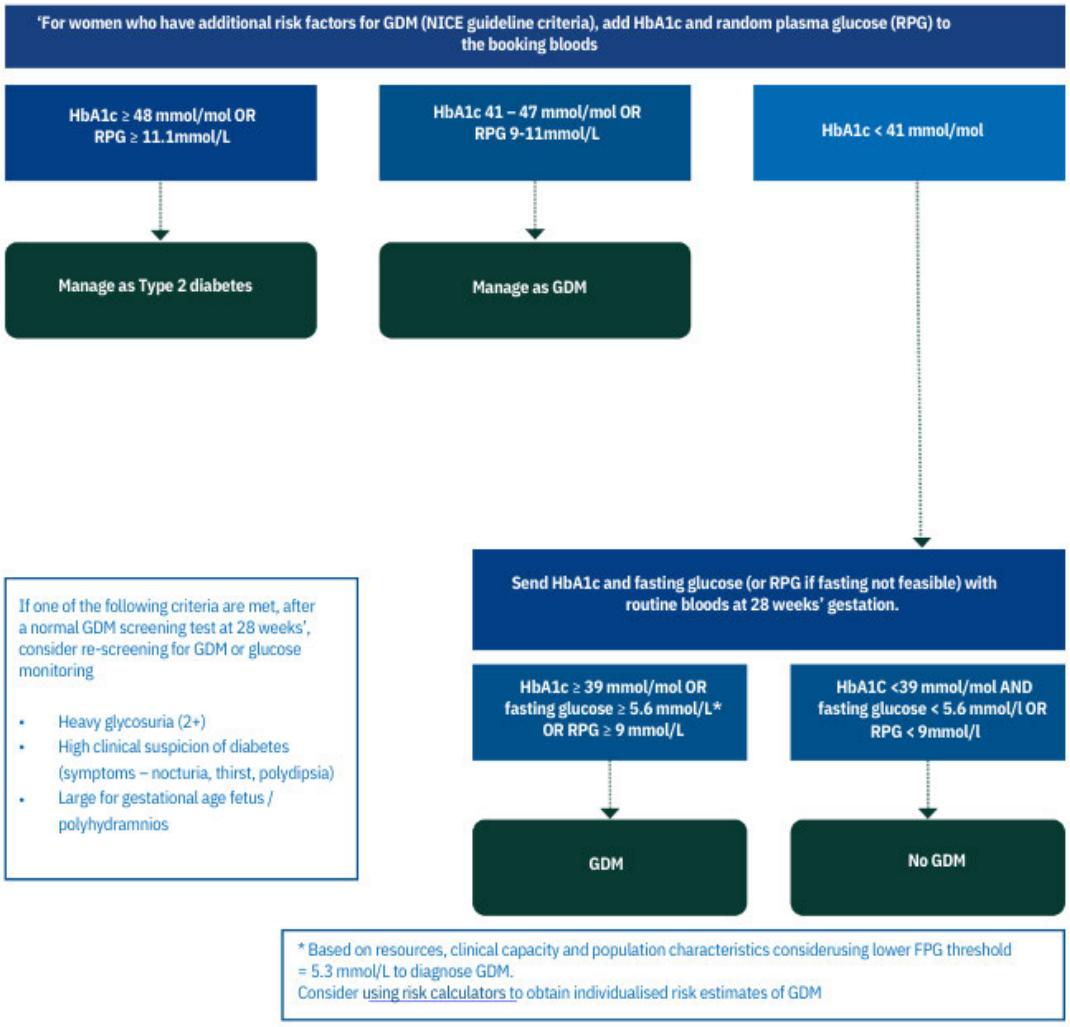

Figure 3 RCOG GDM care pathways during COVID-19

Figure adapted from guidance for maternal medicine services in the evolving coronavirus (COVID-19) pandemic (118)

1.3.3.2 Early evaluation of the RCOG emergency guidance for diagnosis and screening

Several studies evaluated the impact of the RCOG guidance on GDM detection:

1. Modelling from the HAPO study predicted an 81% reduction in GDM detection when applying revised criteria. However, this analysis only included universal screening at 24–28 weeks and did not consider risk-factor-based screening pathway (119).

2. A UK single-centre study found GDM detection decreased from 7.7% to 4.2% over six weeks, but clinical outcomes were not reported (120)

3. Another retrospective study estimated a 29% reduction in GDM cases using alternative diagnostic thresholds (121)

A further study evaluated the utility of HbA1c, RPG, and FPG for diagnosing GDM. At 24–28 weeks, HbA1c and RPG demonstrated good diagnostic performance, with areas under the receiver operating characteristic curve (AUROC) of 0.83 and 0.81, respectively, using NICE criteria. When applying IADPSG criteria, FPG had superior predictive performance (AUROC: 0.92). This study did not evaluation use of HbA1c at booking and data were based on a two-step screening approach (122)

1.3.3.3 Remote clinical care and Telemedicine interventions

Figure 4 outlines the RCOG guidance for antenatal care for women with GDM during COVID-19. Recommendations include use of remote consultations whenever possible. This included glucose meter training, dietary education, and follow-up with diabetes midwives or nurses. Women monitored their blood glucose at home, while routine antenatal checks (e.g., fundal height, blood pressure, urinalysis) continued with community midwives.

- **Diet-controlled GDM**: No hospital visits or growth scans were required.
- **Pharmacologically treated GDM**: Remote obstetric reviews were conducted at 28 and 32 weeks, coinciding with in-person ultrasound appointments if indicated. An in-person review at 36 weeks assessed maternal and fetal health, birth planning, and follow-up care.

An in-depth literature review on remote antenatal care is provided in results chapter 2.

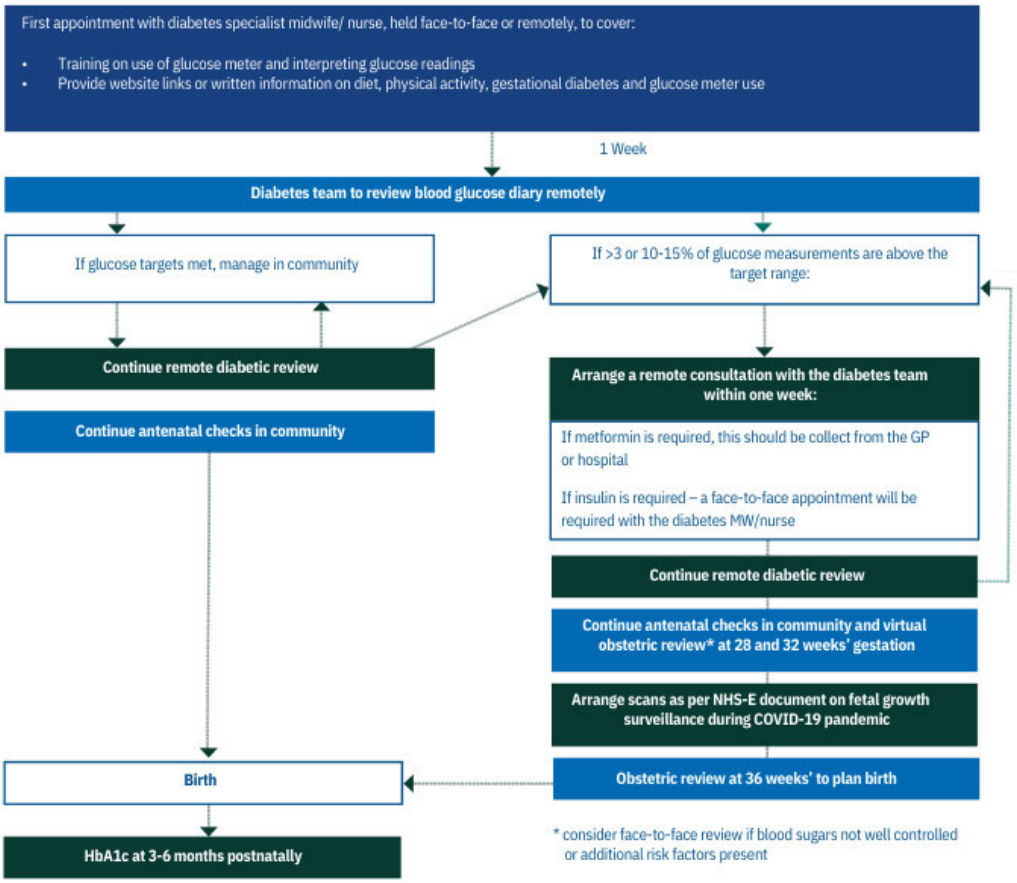

Figure 4 RCOG GDM antenatal care provision during COVID-19

Figure adapted from guidance for maternal medicine services in the evolving coronavirus (COVID-19) pandemic (118).

1.4 Complex interventions and their evaluation

Complex interventions in healthcare are strategies or programs with multiple interacting components aimed at optimising health outcomes (123). Evaluating such interventions is challenging because they are dynamic and context dependent. Traditional methods, such as RCTs often fail to account for variations in implementation and contextual factors.

Recognizing these challenges, frameworks from the UK Medical Research Council (MRC) and the National Institute for Health Research (NIHR) advocate for a phased approach to evaluation (123, 124). This approach includes development, feasibility testing, implementation, and impact assessment. These frameworks emphasize the need to assess not only an intervention's effectiveness but also its feasibility, acceptability, and fit within specific contexts.

Greenhalgh et al. further highlight that the success of interventions depends on local adaptability and their capacity to integrate into practice (125). By combining quantitative and qualitative methods, evaluations can capture the complexities of interventions, offering actionable insights for scaling and improving healthcare delivery.

Interventions introduced in response to SARS-CoV-2 illustrate the integration of clinical practices, rapid behavioural changes, and complex organizational processes. Evaluating these interventions requires adherence to the guidance above. Employing a multimethod approach to examine changes in GDM care during the pandemic can provide deeper insights into their effectiveness and adaptability. Such an approach will enable evidence-based recommendations for future clinical practices and care pathways.

1.5 Research questions, hypotheses and thesis outline

1.5.1 Research objectives

Current practices for screening and diagnosing GDM vary considerably, both internationally and within the UK's NHS. This variation largely stems from a lack of contemporary evidence and a reliance on expert consensus. The rising prevalence of GDM further complicates these challenges, increasing pressure on healthcare systems and service delivery.

The SARS-CoV-2 pandemic brought significant changes to GDM care delivery in the UK. Emergency adaptations prioritised identifying and treating women at the highest risk of

complications while minimising the need for in-person appointments. Evaluating these changes presents an opportunity to explore alternative approaches to GDM care. Additionally, leveraging individual patient characteristics may improve the ability to predict poor outcomes, offering valuable insights for optimizing GDM management.

This multimethod research has two main objectives:

1. **To evaluate the impact of pandemic-related changes on the incidence of GDM and associated maternal, obstetric, and neonatal outcomes, to inform the future of GDM care in the NHS.**
2. **To assess the evidence for applying a precision medicine approach to GDM management.**

1.5.2 Research questions

This research addresses the following questions:

- What is the impact of emergency care pathways on the incidence of GDM and maternal, obstetric, and neonatal outcomes?
- How do healthcare professionals perceive and experience the delivery of remote antenatal care for women with GDM during the COVID-19 pandemic?
- Can patient characteristics predict treatment responses in women diagnosed with GDM?

1.5.3 Thesis outline

This thesis addresses these research questions through three parallel streams of work conducted during my PhD studies from 2020 to 2023. There is a methodology chapter which briefly outlines the methodology adopted for each stream. The subsequent 3 chapters address each research question(s), presenting methods, results, and discussion. Results chapters 1 and 3 present peer-reviewed published work, presented as per publication format, with brief introductions and discussions.

Chapter 1 investigates the impact of changes in GDM screening, diagnosis, and management during the SARS-CoV-2 pandemic compared to pre-COVID practices.

Hypotheses:

1. The incidence of GDM declined following the implementation of RCOG emergency care pathways.
2. Adverse maternal and neonatal outcomes increased after these pathways were introduced.
3. Women from lower socioeconomic groups and non-white ethnic backgrounds experienced a disproportionate rise in adverse outcomes compared to women from higher socioeconomic groups and white ethnic backgrounds.

Chapter 2 presents a qualitative interview study exploring healthcare professionals' experiences of delivering remote antenatal care to women with GDM during the pandemic. Semi-structured interviews were conducted with multidisciplinary professionals across three NHS Trusts in England and Scotland to address 3 key research questions.

RQ 1 What did HCPs at individual sites do to reconfigure their services to provide remote multidisciplinary antenatal care and why?

RQ2 What did HCPs find successful and unsuccessful when delivering remote multidisciplinary antenatal care during the early phase of the pandemic and why?

RQ 3 What lessons can be learnt from delivering remote multidisciplinary GDM care during the pandemic and which aspects of pandemic GDM care delivery do HCPs think should be retained in the longer-term, and why?

Chapter 3 presents a systematic review of evidence for precision markers of GDM treatment success. The objectives were to identify patient-level characteristics that predict:

(i) Responses to personalised diet and lifestyle interventions delivered alongside standard care

(ii) The need for treatment escalation in women initially managed with diet and lifestyle alone, as well as those receiving pharmacological treatments.

Each review considers whether precision markers predict glucose target achievement, as well as maternal and neonatal outcomes.

A concluding **discussion** provides a summary of each chapter, highlighting the strengths and limitations of the body of work, and offers recommendations for future research.

2 Methodology

This chapter outlines the methodologies used in the three parallel studies presented in this thesis. Detailed methodologies for the qualitative and systematic review studies are provided in Chapters 2 and 3, respectively. Supplementary methodological details for the observational cohort study are included here to complement those reported in Chapter 1. Chapters 1 and 3 present results as peer-reviewed publications, while Chapter 2, structured as a traditional thesis chapter, includes all relevant methodology details for that study.

2.1 Chapter 1 Methodology

Chapter 1 presents findings from a pre- and post-implementation observational cohort study that examines the impact of the COVID-19 RCOG emergency care pathways on GDM incidence and pregnancy outcomes across the UK.

2.1.1 Diabetes in pregnancy working group

The study was conducted in collaboration with the Diabetes in Pregnancy Working Group, a multidisciplinary team formally associated with the RCOG. Members of the group represent diabetes and obstetrics expertise across the UK, with a focus on clinical research. The group agreed to contribute to this study in September 2020, following the publication of the RCOG emergency care pathways for GDM in April 2020.

Through collective consensus, the group identified NHS health boards and trusts as the most suitable data sources for GDM-related pregnancy episodes. Nationally available data repositories of routinely collected healthcare data were deemed unlikely to capture the required detail on GDM status and pregnancy outcomes for this study. Members of

the working group also provided guidance on data analysis and co-authored the subsequent publication.

2.1.2 Ethical approval

Ethical approval was granted by the Southeast Scotland Research Ethics Committee 01 in April 2021 (REC Reference: 21/SS/0031). The study was co-sponsored by NHS Lothian and the University of Edinburgh through the Academic and Clinical Central Office for Research and Development (ACCORD) (R&D No 2021/0063). A single non-substantial amendment was approved in August 2021.

2.1.3 Regulatory approvals

2.1.3.1 Public Benefit and Privacy Panel for Health and Social Care

Approval from the HSC-PBPP, which reviews public benefit and information governance for healthcare data in Scotland, was granted in September 2021.

2.1.3.2 NHS Research Scotland Permissions Coordinating Centre

The NRSPCC facilitated centralized R&D management permission for the three Scottish NHS sites. After NRSPCC approval, local R&D officers at each contributing health board were contacted for final data-sharing agreements. Local R&D approval was granted after satisfying all governance requirements.

2.1.3.3 Confidentiality Advisory Group

Approval from the confidentiality advisory group (CAG) England, under Regulation 5 of the Health Service (Control of Patient Information) Regulations 2002, was not required. The study involved identifiable information handled only by the direct care team, with pseudonymization prior to data transfer, mitigating breaches of confidentiality.

2.1.3.4 Local NHS trust R&D approval process

Unlike in Scotland, R&D approvals in England required individual applications for each health board/trust. Governance requirements varied significantly across trusts, leading to substantial variability in the approval process.

2.1.4 Study site recruitment

NHS study sites were identified through the Diabetes in Pregnancy Working Group. Clinical leads at potential sites were contacted to assess feasibility for local data collection and sharing. Initially, 14 NHS sites were recruited; 9 contributed data to the study.

Exclusions:

- In four cases, data were not supplied by the study end date or local R&D approvals were delayed.
- One site was excluded due to pre-COVID universal screening policies, which rendered their pre-COVID GDM population non-comparable.

Inclusions:

- One site, which had exclusively delivered remote care and maintained pre-COVID screening and diagnostic pathways during the pandemic, was included as a comparator group, as they had partially adopted the RCOG emergency care pathways.

2.1.5 Data collection

Data on the implementation of the RCOG COVID-19 care pathway were collected using an online survey (Jisc Online Survey Platform V2). Clinical leads for antenatal diabetes services were identified through the Diabetes in Pregnancy Network and invited by email to complete the survey. The survey captured information on clinical practices before and during the COVID-19 pandemic.

All data were pseudorandomised by individual study sites and distributed in accordance with local regulations and restrictions set by the local R&D teams at each site. Data were securely transferred via encrypted NHS email before being stored and processed on UoE servers. All data handling adhered to our data management plan and was approved through the HSC-PBPP process.

2.1.6 Data handling

2.1.6.1 Missing data

A decision was made not to impute missing data. This was based on a review of the collated dataset, which identified minimal missing data (<2%) for all key study outcomes.

Further details on the data collection and sharing processes are presented in Chapter 3.

2.2 Chapter 2 Methodology

Chapter 2 presents findings from a qualitative interview study exploring health care professionals' experiences of delivering multidisciplinary GDM care during the pandemic. The full methodology is detailed in chapter 2.

2.3 Chapter 3 Methodology

Chapter 3 includes findings from two systematic reviews investigating precision markers for GDM management. The full methodology is outlined within the chapter.

2.4 Statistical methods

All statistical methods used in this thesis are detailed in their respective chapters.

2.4.1 Software programs

Chapter 1: Data analysis was conducted using RStudio, an open-source software package for the R programming language. Additionally, the JISC Online Survey tool was employed in the data study.

Chapter 2: Qualitative data analysis was performed using NVivo, a dedicated software package for qualitative research.

Chapter 3: The systematic review(s) utilized two statistical tools. Covidence, a web-based platform, facilitated abstract screening, data extraction, and the population of risk-of-bias data. ReviewManager (RevMan), a specialized software developed for Cochrane reviews, was used for conducting meta-analyses.

3 Results Chapter 1

3.1 Introduction

The following materials were published in the *British Journal of Obstetrics and Gynaecology* under the same title by Niamh-Maire Mclennan, Robert Lindsay, Ponnusamy Saravanan, Nithya Sukumar, Sara White, Laura Magee, Peter von Dadelszen, and Rebecca Reynolds, on behalf of the Diabetes in Pregnancy working group.

My contributions to the study included co-designing the study, obtaining ethical and regulatory approvals, collating and analysing data, and preparing the first draft of the manuscript under the guidance of Rebecca Reynolds. All authors contributed to the conception, design, and analysis of the study, and provided critical insights during manuscript development.

3.1.1 Background and rationale

The impact of the RCOG emergency diagnostic strategy on GDM incidence and short-term maternal and neonatal outcomes remains unknown. While some single-centre studies have sought to estimate incidence and model retrospective datasets, these efforts are limited by small sample sizes, simplistic analyses, and data that do not adequately represent UK populations or screening practices (119-122) . To address these gaps, we designed a larger, multi-centre study to evaluate the impact of this diagnostic strategy on GDM incidence and short-term maternal and fetal outcomes across the UK

In the UK, women from Black, Asian, and minority ethnic (BAME) backgrounds, as well as those from lower socioeconomic groups, experience significantly higher morbidity and mortality during pregnancy and postpartum compared to other groups (126-128). National surveillance reports from MBRRACE-UK (Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK) highlight that Black and Asian

women are up to 3.7 times more likely to die during pregnancy or postpartum than White women (126). Additionally, disparities in morbidity and mortality between the most and least socioeconomically deprived women have widened in recent years.

Population-level data from the USA, encompassing over 1.5 million GDM pregnancies from 2014 to 2020, show that women from non-White ethnic backgrounds face significantly increased risks for almost all assessed clinical outcomes compared to White women, except for LGA infants (129). Although emergency care pathways were designed to identify women at the highest risk (118), I hypothesized that the emergency COVID-19 pathways for GDM diagnosis may disproportionately affect women from lower socioeconomic and non-White ethnic groups. This hypothesis is addressed as a secondary aim of my study, with findings reported in a detailed subgroup analysis.

The following section presents the findings in a publication format. The full paper can be accessed at: https://doi.org/10.1111/1471-0528.17716

3.2 Impact of Covid-19 on GDM pregnancy outcomes in the UK: A multicentre retrospective cohort study

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RESEARCH ARTICLE

Maternal medicine

Impact of COVID-19 on gestational diabetes pregnancy outcomes in the UK: A multicentre retrospective cohort study

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Abstract

Objective: To determine the impact of implementing emergency care pathway(s) for screening, diagnosing and managing women with gestational diabetes (GDM) during COVID-19.

Design: Retrospective multicentre cohort.

Setting: Nine National Health Service (NHS) Hospital Trusts/Health boards in England and Scotland.

Population: 4915 women with GDM pre-pandemic (1 April 2018 to 31 March 2020), and 3467 women with GDM during the pandemic (1 May 2020 to 31 March 2021).

Methods: We examined clinical outcomes for women with GDM prior to and during the pandemic following changes in screening methods, diagnostic testing, glucose thresholds and introduction of virtual care for monitoring of antenatal glycaemia.

Main Outcome Measures: Intervention at birth, perinatal mortality, large-for-gestational-age infants and neonatal unit admission.

Results: The new diagnostic criteria more often identified GDM women who were multiparous, had higher body mass index (BMI) and greater deprivation, and less frequently had previous GDM (all $p < 0.05$). During COVID, these women had no differences in the key outcome measures. Of the women, 3% were identified with pre-existing diabetes at antenatal booking. Where OGTT continued during COVID, but virtual care was introduced, outcomes were also similar pre- and during the pandemic.

Conclusions: Using HbA1c and fasting glucose identified a higher risk GDM population during the pandemic but this had minimal impact on pregnancy outcomes. The high prevalence of undiagnosed pre-existing diabetes suggests that women with GDM risk factors should be offered HbA1c screening in early pregnancy.

KEYWORDS
COVID-19, gestational diabetes

1 | INTRODUCTION

In the UK, women with gestational diabetes (GDM) are the largest high-risk group accessing antenatal care.[1] GDM is associated with an increased risk of a range of obstetric and neonatal complications compared with the general maternity population.[2] A high proportion of women with GDM are from minority ethnic backgrounds and live in deprived

areas – additional known risk factors for adverse pregnancy outcomes.[3]

Risk factor-based screening for GDM diagnosis using the 75-g oral glucose tolerance test (OGTT) at 24–28 weeks' gestation and antenatal care in a multidisciplinary clinic, is recommended as best practice in UK National Guidelines.[4] However, at the start of the COVID-19 pandemic, pregnant women were advised to practice social distancing and self-isolation to lower their risk of viral exposure. On 1 April 2020, the UK Royal College of Obstetricians and Gynaecologists (RCOG) issued guidance on 'service modifications' to protect the maternity population.[5] These emergency guidelines were rapidly implemented in National Health Service (NHS) Trusts and Health Boards across the UK.[6] The recommended changes in biochemical tests and glucose thresholds for screening, diagnosis and management of GDM (Figure 1) were selected to identify the approximately 5% of women at highest risk of obstetric and neonatal complications related to maternal hyperglycaemia. Reducing face-to-face consultations with the multidisciplinary team by introduction of telemedicine clinics for remote education and monitoring of antenatal glycaemia was also recommended.[5] Similar changes were implemented in Canada and Australia.[7,8]

With knowledge that pregnancy outcomes are poorer in women with untreated GDM,[9,10] these pandemic-related changes to standard antenatal care led to concerns about potential indirect harms of COVID-19 on pregnancy outcomes for women with GDM.[11–13] Studies using retrospective data to model outcomes associated with introduction of the emergency GDM care pathway reported the potential for a decrease in the prevalence of GDM and poorer pregnancy outcomes.[14–16]

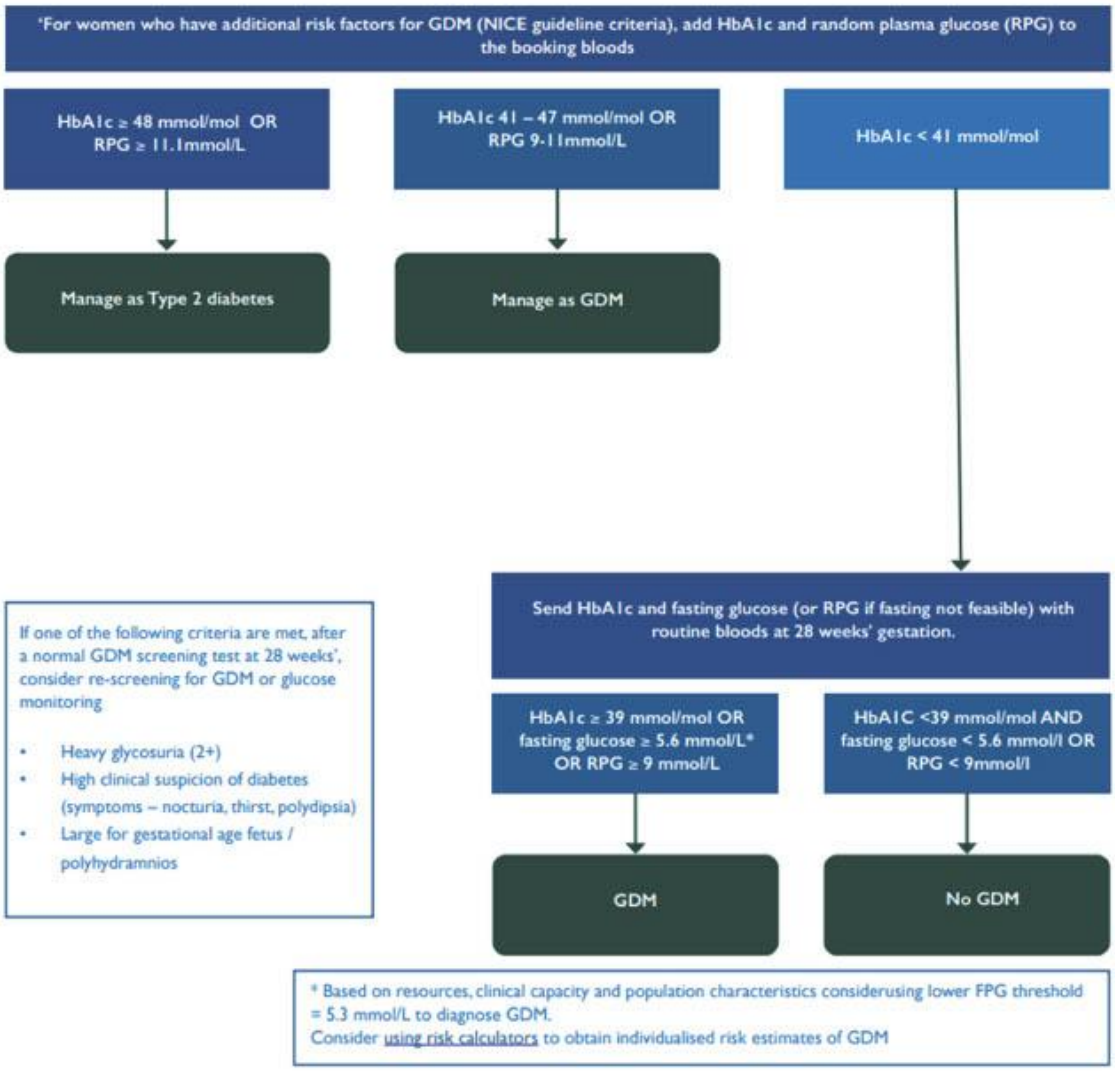

FIGURE 1 RCOG-recommended GDM care pathways for diagnosis of GDM during COVID-19. Adapted from Guidance for Maternal Medicine Services in the evolving coronavirus (COVID-19) pandemic.[6]

We aimed to determine whether adoption of the emergency GDM care pathway was associated with more adverse clinical outcomes in women with GDM in the UK, and to determine whether women from minority ethnic groups and lower socio-economic groups were particularly disadvantaged by these pathway changes. We report on individual patient data from nine NHS Hospital Trusts in England and Scotland where the emergency GDM care guidelines were fully or partially adopted.

2 | METHODS

2.1 | Study design

We conducted a multicentre retrospective cohort study of women with GDM before and during the COVID-19 pandemic.

2.2 | Setting

Individual-level patient data from pregnancies diagnosed with GDM were collected from local maternity and neonatal records at nine NHS Hospital Trusts/Health boards in England and Scotland from 1 April 2018 to 31 March 2021. Eight NHS Hospital Trusts/Health boards fully adopted the emergency guidelines recommended by RCOG for diagnosis and management, as well as introduction of virtual clinic reviews. One continued with their pre-pandemic pathway for screening and diagnosing women; prior to the pandemic, this Trust had an established virtual model of care for women with GDM which was rolled out for all women during the pandemic (partial adoption of the emergency guideline).

2.3 | Participants

We included singleton pregnancies with a diagnosis of GDM. The diagnosis of GDM and its management were in accordance with local care pathways at individual Trusts (Table S1). We excluded pregnancy episodes with major congenital anomalies, pregnancies ending before 20 weeks, maternal age <16 years and women with known, pre-existing diabetes.

2.4 | Group allocation/exposure

Women with a diagnosis of GDM before or after 1 April 2020 were allocated to the 'Pre-COVID' or 'COVID' cohorts, respectively.

2.5 | Data collection

Methods of data collection from the electronic health record varied at each site from data release by a clinical auditor to hand-data collection by medical students or members of the clinical team.

Demographic data included maternal age at booking, parity, smoking status (non-smoker or smoker), ethnicity (self-assigned and grouped for analysis into white, Asian, black, and other), body mass index (BMI), history of GDM, history of hypertension and index of multiple deprivation (IMD in England, SIMD in Scotland), grouped into low (deciles 8–10), middle (4–7) and high (1–3).[17,18]

Data on GDM included gestational age at diagnosis (days), diagnostic test confirming the diagnosis (oral glucose tolerance test [OGTT], booking glycated haemoglobin [HbA1c] or random plasma glucose [RPG], or 24- to 28-week fasting glucose or HbA1c), and pharmacological treatment (metformin or insulin).

We selected outcomes based on the recommended GDM core outcomes set.[19] Maternal outcomes included hypertensive disorders (defined as any one of gestational hypertension or pre-eclampsia), induction of labour, gestational age at birth (days), mode of birth, postpartum haemorrhage (>1500 mL blood loss, as this definition is used in the maternity services dashboard key performance indicator as part of a nationally agreed set of indicators in NHS England), shoulder dystocia (defined by birth attendant) and obstetric anal sphincter injury, as documented in the maternal health record. Neonatal outcomes included birth outcome (non-registerable birth [defined as births between 20^{+0} and 23^{+6} weeks' gestation], stillbirth [fetal death at ≥24 weeks' gestation] or live birth), neonatal death (at <6 weeks after birth); preterm birth (<37 weeks' gestation), birthweight (g), sex, large-for-gestational age (LGA), small-for-gestational age (SGA), appropriate-for-gestational age (AGA) infants at birth (defined as birthweight >90th or <10th, and 10th–90th centiles respectively, using Intergrowth 21 population-based centile charts[20]), Apgar score at 5 min, neonatal unit admission, neonatal hypoglycaemia and respiratory distress (all defined by local clinical protocols).

For comparison, aggregate data on the incidence of LGA, SGA and AGA births in term births between 1 April 2018 and 31 March 2021 were obtained from routinely collected national data sources. Data on infants born in England were derived from Hospital Episode Statistics (HES), collated and supplied by the National Maternity and Perinatal Audit (NMPA) group. Data on infants born in Scotland were derived from Scottish maternity records (SMR02), collated and supplied by Public Health Scotland (PHS) via the Scottish Health and Social Care open data platform. Full technical reports from PHS and NMPA are available.[21,22]

2.6 | Key outcomes

The key maternal outcome was the need for intervention at birth, including operative vaginal delivery, and caesarean section (emergency and elective).

Key neonatal outcomes were perinatal mortality (as the total of non-registered births, stillbirths and live births), LGA and neonatal unit admission.[19]

All other maternal and neonatal outcomes were considered secondary outcomes.

2.7 | Statistical analysis

Analyses were undertaken using R studio (version 2022.2.1.461). Normal distribution of continuous variables was tested using the Kolmogorov–Smirnov normality test. Differences between groups were tested using the Student *t*-test (for continuous normally distributed), Mann–Whitney *U*-test (for non-normally distributed variables), and χ^2 test (for categorical variables). Data are mean (standard deviation [SD]) or number (%) in text and tables. Missing data for covariates are represented with a categorical-variable term given the low frequency of missing values, rather than as imputed values. Multivariate logistic regression analysis was performed to calculate adjusted odds ratios (aOR), with 95% confidence intervals (CI), to evaluate the effect on maternal and neonatal outcomes of full or partial adoption of the emergency GDM care pathway, compared with pre-pandemic. Analyses were adjusted for confounders (including maternal age, BMI, ethnicity, parity, induction of labour, gestational age at birth, birthweight centile, mode of birth, neonatal unit admission), depending on the outcome. A random effects model was applied to account for clustered data among the population that adopted the RCOG emergency guideline.

Analyses were conducted separately for Trusts that fully or partially adopted the emergency GDM care guidelines.

GDM incidence before and during COVID-19 was estimated using time-matched cohorts between April and December in 2019 and 2020. This was calculated using month of GDM diagnosis and monthly pregnancy booking rates.

We undertook a secondary analysis comparing key study outcomes in women from non-white ethnicity backgrounds and those from the most deprived socio-economic groupings.

To control for changes in practice over time and seasonal variation in GDM,[23] we undertook a sensitivity analysis, comparing data from April 2019 to April 2020, with those from April 2020 to April 2021.

We did not correct for multiple hypothesis testing, as we had prespecified our analysis plan and there were no significant findings for our key outcomes.

Statistical significance was set at $p < 0.05$ for all tests.

2.8 | Patient and public involvement

The research question and outcome measures were informed by the recent James Lind Alliance Priority Setting Partnership that involved individuals with GDM and their healthcare providers. Optimising the diagnosis and management of GDM was identified as a priority for diabetes pregnancy research.[24]

3 | RESULTS

3.1 | Participants

We identified 8523 pregnancy episodes with a GDM diagnosis, from nine NHS Trusts/Health Boards, between 1 April 2018 and 31 March 2021. A total of 141 (1.7%) GDM pregnancy episodes were excluded because of missing data on GDM diagnosis date. Of the 8382 GDM pregnancy episodes included, 4915 were in the 'Pre-COVID' cohort and 3467 in the 'COVID' cohort (Figure 2).

Eight Trusts (5251 [62.6%] GDM pregnancy episodes) fully adopted the emergency GDM care guideline, and one Trust (3131 [37.4%] GDM pregnancy episodes) partially adopted the guideline by continuing OGTT for GDM diagnosis but rolling out virtual antenatal care.

3.2 | Incidence of GDM

GDM incidence before and during COVID-19 was estimated at six study sites. We identified significant between-site variation in GDM incidence, during both Pre-COVID (range 2.2–8.5%) and COVID epochs (2.1–11.5%) (Figure S1). Of the five regions that had adopted the emergency care pathway, GDM incidence increased during versus pre-pandemic at two sites (sites 3 and 6, Figure S1); was stable at two sites (sites 1 and 8, Figure S1) and decreased at one site (site 7, Figure S1). GDM incidence increased (8.5–11.2%) at the site which had only partially adopted the emergency care pathway with introduction of virtual monitoring but with continuation of OGTT.

3.3 | Characteristics of women diagnosed with GDM

Table 1 presents the demographics of included women. Several differences were noted Pre-COVID versus COVID, for women overall and according to whether the Trusts fully or partially adopted the emergency GDM care guidelines.

Overall, compared with women diagnosed Pre-COVID, those diagnosed during COVID were more often multiparous, had a higher BMI, more often experienced deprivation and were less likely to have had previous GDM. Data on parity, ethnicity, BMI and deprivation were less likely to be missing during the pandemic (Table 1).

In the eight Trusts ($n = 5382$) that adopted all aspects of the emergency GDM care guideline, pregnancies during versus Pre-COVID were more likely to be of Asian or black ethnicity, have higher BMI and experience higher levels of deprivation, and less likely to have a history of previous GDM (Table 1).

In the one Trust which continued OGTT, pregnancies during versus Pre-COVID experienced lower levels of deprivation and had significantly fewer women with prior GDM (Table 1).

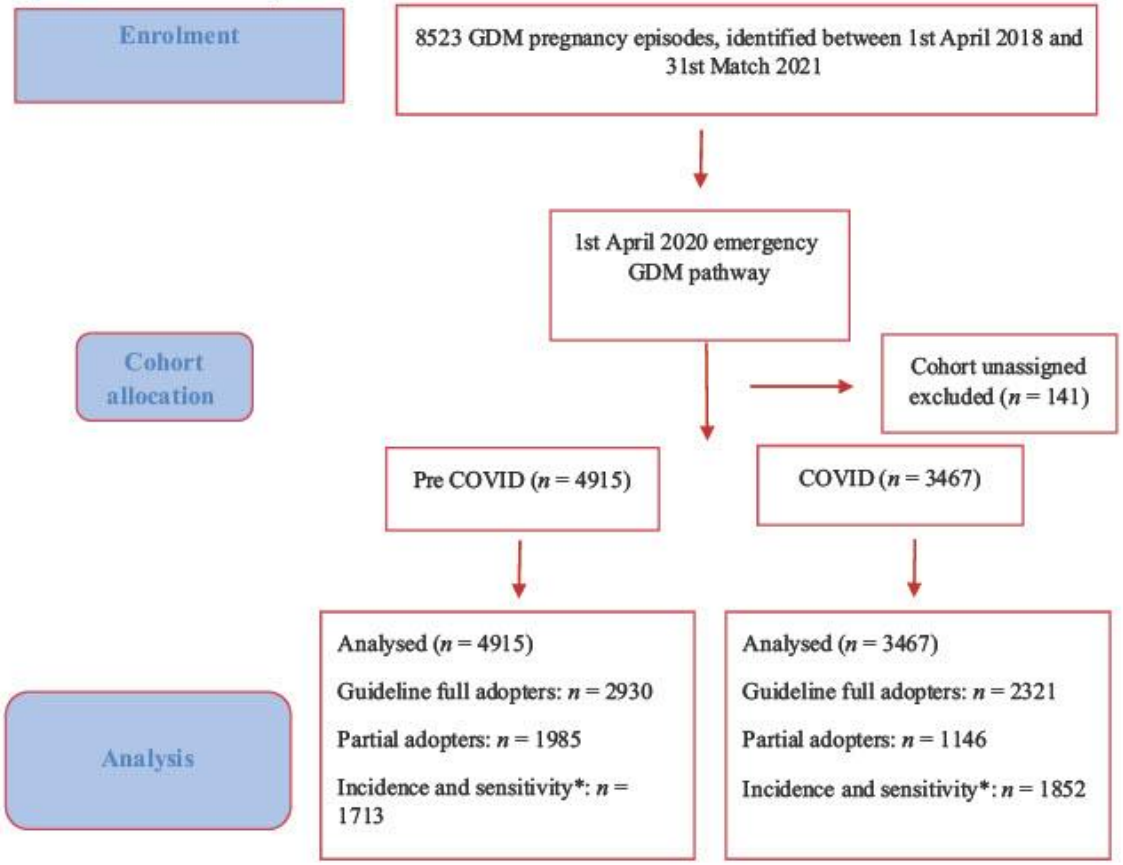

FIGURE 2 CONSORT flow chart of participants. *GDM incidence before and during COVID-19 was estimated using time-matched cohorts between April and December 2019 and 2020; Sensitivity analysis was undertaken to account for changes in practice over time and seasonal variation in GDM by comparing data from April 2019 to April 2020, with those from April 2020 to April 2021.

In the sensitivity analysis, comparing women diagnosed with GDM in only 2019 and 2020, we identified similar patterns (Table 1).

3.4 | Screening and diagnostic tests for GDM

At the eight sites which adopted the emergency GDM care recommendations, women were diagnosed, on average, 9 days later during versus pre-pandemic (183 [47.4] versus 173 [50.1] days, $p < 0.001$), respectively. Data on HbA1c at antenatal booking was available for 906/2321 (39%) women and data on RPG was available for 490/2321 (21.1%) women. Thirty-two women were managed as having type 2 diabetes, based on 26/906 (2.9%) women with HbA1c ≥48 mmol/mol and 6/490 (0.1%) having an RPG ≥11.1 mmol/L. A total of 183 women were managed as having GDM, based on 166/906 (17.8%) with HbA1c 41–47 mmol/mol, and 17/490 (3.5%) having an RPG 9.0–11 mmol/L. There was a significant increase in mean fasting glucose level at 24–28 weeks of 0.3 mmol/L.

At the one site which maintained diagnostic OGTT testing, women were diagnosed an average of 7 days earlier during versus pre-pandemic (182 [35.3] versus 189 [32.9] days, $p < 0.001$), respectively. Although at 24–28 weeks' gestation, there were minor decreases in both HbA1c and fasting glucose during the OGTT, the 2-h value did not differ.

3.5 | Impact of implementation of the emergency GDM care pathway on key maternal and neonatal outcomes

Table 2 shows that at the eight sites which implemented the emergency GDM care pathway criteria, there were no differences during versus Pre-COVID in the key maternal outcomes of operative deliveries or caesarean section. There were also no differences in perinatal mortality, LGA or neonatal unit admission.

At the Trust where no changes in the GDM diagnostic pathways were made, there were no differences in the incidence of adverse outcomes (Tables 2 and 3).

TABLE 1 Demographics of women diagnosed with GDM.

	All (data from all 9 trusts), $n=8382$				Full adoption of emergency GDM pathway (data from 8 trusts), $n=5251$				Partial adoption of emergency GDM pathway (data from 1 trust), $n=3131$			
	Pre-COVID	COVID	Total	*p*-Value	Pre-COVID	COVID	Total	*p*-Value	Pre-COVID	COVID	Total	*p*-Value
n	4915	3467	8382		2930	2321	5251		1985	1146	3131	
Age	32.5 (5.4)	32.3 (5.3)	32.4 (5.4)	0.238	32.1 (5.4)	31.9 (5.3)	32.0 (5.4)	0.259	33.0 (5.5)	33.1 (5.2)	33.1 (5.4)	0.513
Parity												
Nulliparous	1938 (40.9)	1334 (38.7)	3272 (40.0)	**0.043**	1027 (37.4)	813 (35.3)	1840 (36.4)	0.141	911 (45.9)	521 (45.5)	1432 (45.7)	0.844
Multiparous	2759 (59.1)	2113 (61.3)	4908 (60.0)		1721 (62.6)	1488 (64.7)	3209 (63.6)		1074 (54.1)	625 (54.5)	1699 (54.3)	
Missing	182 (3.7)	20 (0.6)	202 (2.4)		182 (6.1)	20 (0.9)	202 (3.8)		0 (0.0)	0 (0.0)	0 (0.0)	
Ethnicity												
White	2474 (56.8)	1831 (55.0)	4401 (56.0)	0.252	1906 (69.8)	1452 (66.1)	3358 (68.2)	**0.015**	568 (34.9)	379 (33.5)	947 (34.3)	0.132
Asian	926 (21.3)	756 (22.7)	1734 (21.9)		543 (19.9)	490 (22.3)	1033 (21.0)		383 (23.6)	266 (23.5)	649 (23.5)	
Black	626 (14.4)	470 (14.1)	1171 (14.3)		160 (5.9)	163 (7.4)	323 (6.6)		466 (28.7)	307 (27.1)	773 (28.0)	
Other	329 (7.6)	274 (8.2)	625 (7.8)		120 (4.4)	93 (4.2)	213 (4.3)		209 (12.9)	181 (16.0)	390 (14.1)	
Missing	560 (11.4)	136 (3.9)	785 (9.0)		207 (7.0)	123 (5.3)	330 (6.2)		359 (18.1)	13 (1.1)	372 (11.9)	
BMI (kg/m^2)												
<25	1180 (25.7)	766 (23.7)	1946 (24.9)	**0.002**	550 (19.5)	386 (17.3)	936 (18.5)	**0.012**	630 (35.4)	380 (38.1)	1092 (31.9)	0.402
25–30	1254 (27.3)	874 (27.1)	2128 (27.2)		730 (25.9)	582 (26.1)	1312 (26.0)		524 (29.4)	292 (29.3)	816 (29.4)	
30–40	1721 (37.4)	1193 (37.0)	3001 (37.2)		1189 (42.2)	922 (41.4)	2111 (41.8)		532 (29.9)	271 (27.2)	803 (28.9)	
>40	462 (9.6)	393 (12.2)	855 (10.7)		348 (12.4)	339 (15.2)	687 (13.6)		95 (5.3)	54 (5.4)	149 (5.4)	
Missing	386 (7.4)	241 (7.0)	627 (7.2)		113 (3.8)	92 (4.0)	205 (3.9)		204 (10.3)	149 (13.0)	353 (11.3)	
Deprivation												
Low	673 (14.8)	447 (13.5)	1120 (14.2)	**0.006**	492 (20.9)	333 (15.3)	838 (15.8)	**<0.001**	145 (7.4)	114 (10.1)	282 (8.2)	**0.017**
Middle	1782 (38.3)	1185 (35.9)	2967 (37.3)		844 (35.9)	710 (32.7)	1554 (34.3)		810 (41.3)	475 (42.1)	1285 (41.6)	
High	2189 (46.9)	1670 (50.6)	3859 (48.5)		1017 (43.2)	1130 (52.0)	2147 (47.4)		1007 (51.3)	540 (47.8)	1547 (50.0)	
Missing	605 (11.5)	165 (4.8)	770 (8.8)		577 (19.4)	148 (6.4)	725 (13.7)		23 (1.2)	17 (1.5)	40 (1.3)	
Smoking												
Non smoker	4818 (92.1)	3180 (92.7)	7998 (92.3)	0.314	2578 (88.8)	2066 (90.4)	4644 (89.5)	0.067	1922 (96.8)	1114 (97.2)	3036 (97.0)	0.623
Smoker	404 (7.9)	251 (7.3)	655 (7.7)		325 (11.2)	219 (9.6)	544 (10.5)		63 (3.2)	32 (2.8)	95 (3.0)	
Missing	27 (0.5)	36 (1.0)	63 (0.7)		27 (0.9)	36 (1.6)	63 (1.2)		0 (0.0)	0 (0.0)	0 (0.0)	
Essential hypertension												
Yes	37 (0.7)	24 (0.7)	61 (0.7)	0.697	26 (0.9)	18 (0.8)	44 (0.8)	0.577	11 (0.6)	6 (0.5)	17 (0.5)	1.000
No	4428 (90.1)	3033 (88.2)	7461 (89.0)		2631 (89.8)	1963 (84.6)	4594 (87.5)		1974 (99.4)	1140 (99.5)	3114 (99.5)	
Missing	450 (9.2)	410 (11.8)	860 (10.3)		273 (9.3)	340 (14.6)	613 (11.7)		0 (0.0)	0 (0.0)	0 (0.0)	
Previous GDM[a]												
Yes	725 (25.6)	409 (19.4%)	1134 (23.1)	**<0.001**	500 (28.5)	336 (22.5)	836 (25.8)	**0.018**	229 (21.3)	73 (11.7)	302 (17.8)	**<0.001**

Note: Data are mean (SD) or number (%), and *p*-values <0.05 in bold text. Differences between groups were tested using the Student *t*-test (for continuous normally distributed), Mann–Whitney *U*-test (for non-normally distributed variables) and χ^2 test (for categorical variables).

[a]Figure derived from multiparous women in dataset.

TABLE 2 Key maternal and neonatal outcomes during versus Pre-COVID.

Key maternal and neonatal outcomes	Full adoption of emergency GDM care pathway ($n = 5251$ pregnancy episodes, 8 trusts)			Partial adoption of emergency GDM care pathway ($n = 3131$ pregnancy episodes, 1 trust)		
	aOR	95% CI	*p*-Value	aOR	95% CI	*p*-Value
Operative vaginal delivery	1.21	0.85–1.72	0.285	0.85	0.55–1.29	0.440
Emergency caesarean section	1.19	0.94–1.50	0.141	0.92	0.68–1.23	0.562
Elective caesarean section	1.08	0.76–1.25	0.843	1.06	0.74–1.51	0.735
Perinatal mortality[a]	0.48	0.04–6.26	0.573	2.40	0.58–8.41	0.218
Large-for-gestational age infants[b]	1.02	0.83–1.24	0.884	0.93	0.65–1.34	0.713
Neonatal unit admission[c]	1.07	0.78–1.46	0.672	1.26	0.74–2.11	0.395

Note: All models adjusted for maternal characteristics (age, BMI, parity, ethnicity, deprivation, previous GDM, hypertensive disorder), induction of labour and gestational age at birth.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

[a]Additionally adjusted for mode of birth, birthweight centile, Apgar score at 5 min, neonatal unit admission, respiratory distress.

[b]Additional adjustment for mode of birth.

[c]Additional adjusted for birth weight centile, mode of birth.

TABLE 3 Secondary study outcomes.

Secondary maternal and neonatal study outcomes	Adoption of emergency GDM care pathway ($n = 5251$ pregnancy episodes, 8 trusts)			Partial adoption of emergency GDM care pathway ($n = 3131$ pregnancy episodes, 1 trust)		
	aOR	95% CI	*p*-Value	aOR	95% CI	*p*-Value
Hypertensive disorders	2.13	1.47–3.08	**<0.001**	0.37	0.06–1.46	0.207
Pharmacological treatment—insulin	0.76	0.42–1.32	0.351	NA	NA	NA
Pharmacological treatment—metformin	1.33	0.85–2.09	0.215	NA	NA	NA
Induction of labour[a]	0.87	0.68–1.12	0.292	1.13	0.86–1.49	0.379
Post-partum haemorrhage > 1500 mL[b]	0.65	0.42–1.02	0.059	0.90	0.61–1.32	0.610
Obstetric anal sphincter injury[b]	0.60	0.27–1.31	0.197	0.67	0.35–1.26	0.225
Shoulder dystocia[b]	0.64	0.26–1.59	0.337	1.03	0.25–3.82	0.968
Preterm birth (<37 weeks)[a]	1.10	0.78–1.55	0.573	0.71	0.44–1.14	0.167
Respiratory distress[c]	1.65	0.84–3.23	0.145	1.05	0.55–1.95	0.881
Small-for-gestational-age (SGA)[a]	1.27	0.76–2.13	0.367	1.23	0.76–1.95	0.392
Apgar score at 5 min <7[b]	0.87	0.53–1.43	0.583	0.55	0.28–1.09	0.085
Neonatal hypoglycaemia[c]	0.98	0.66–1.43	0.905	NA	NA	NA

Note: All models adjusted for maternal characteristics (parity, maternal age, BMI, smoking status, ethnicity, deprivation and previous GDM) (bold).

[a]Additional adjustment for essential hypertension.

[b]Additional adjustment for mode of birth.

[c]Additional adjustment for gestation at birth, neonatal unit admission, birthweight, sex and birth outcome, antenatal exposure to insulin and metformin.

3.6 | Impact of implementation of the emergency GDM care pathway on secondary outcomes

Table 3 shows that at the eight sites which implemented the emergency GDM care pathway criteria, there was an increase during versus Pre-COVID in the risk of maternal hypertensive disorders (aOR 2.13, 95% CI 1.47–3.08) among women diagnosed with GDM; these findings remained significant in the 2019–2020 sensitivity analysis. There were no other differences in maternal GDM treatment or in other outcomes.

In the Trust which continued OGTT and rolled out only virtual care, there were no differences in maternal or neonatal outcomes during versus Pre-COVID.

The unadjusted maternal and neonatal outcomes are shown in Tables S2 and S3.

3.7 | Impact of implementation of the emergency GDM care pathway on women from ethnic minority backgrounds and from the lowest socio-economic groupings

Maternal and neonatal outcomes were similar among women from non-white ethnicity backgrounds to those for the whole study population (Table S4). At sites where the emergency guideline was adopted, there was an increase during versus Pre-COVID in emergency caesarean section (aOR 1.69, 95%

CI 1.07–2.68) in women with GDM. No differences in key maternal and neonatal outcomes were seen; the only change made to GDM care pathways during the COVID pandemic was implementation of remote antenatal care for all women (Table S4).

Maternal and neonatal outcomes for women with GDM from the most deprived socio-economic backgrounds (women from IMD and SIMD decile groups 1–3) were similar during versus Pre-COVID (Table S5), except for emergency caesarean sections, where an increase was seen (aOR 1.61, 95% CI 1.01–2.57) (Table S5).

3.8 | Birthweight centiles in the whole maternity population (England and Scotland)

Among 1 204 593 term births in England and Scotland between April 2018 and April 2021, the proportion of infants in each birth centile category (LGA, SGA, AGA) was not significantly different during versus Pre-COVID-19 ($p = 0.81$, LGA 12.2% [46, 348/378, 315] versus 11.4% [98, 319/862, 278], respectively; and SGA during 5% [42, 797/862, 278] versus 4.6% [17, 575/378, 315]).

4 | DISCUSSION

4.1 | Main findings

We used observational, routinely collected data to examine the experience of screening, diagnosing and managing GDM in the UK during the COVID pandemic. We were able to explore two different strategies, one where diagnostic pathways remained similar (including use of OGTT), but antenatal GDM care was delivered largely remotely, and another where HbA1c and random glucose were the predominant diagnostic tests alongside remote antenatal care delivery. Our findings suggest that where the emergency GDM care pathway recommended by RCOG was adopted for screening and diagnosing GDM, a higher risk GDM population was identified, with an increased proportion of women from Asian and black backgrounds, from lower socio-economic groupings, with higher BMI and higher fasting glucose values. Women were also diagnosed with GDM at a later gestational age. Nevertheless, GDM care resulted in similar key maternal and neonatal clinical outcomes. Where the GDM diagnostic pathway was unaltered and virtual antenatal care was adopted for all GDM women, there were also no differences in outcomes.

4.2 | Clinical interpretation

Among women who underwent biochemical screening for hyperglycaemia at antenatal care booking, the 3.0% prevalence of hyperglycaemia suggestive of type 2 diabetes supports a practice of offering HbA1c screening in early pregnancy to women with GDM risk factors.[25]

The higher risk population identified using the emergency GDM care pathway could reflect improved uptake of GDM screening when offered at the time of routine antenatal appointments. Women from higher risk ethnic groups, with obesity, and lower socio-economic status are known to have poorer uptake of the OGTT.[3,26] Common reasons include inability to tolerate the test protocol, social/mental health issues, difficulty keeping track of multiple antenatal appointments, negative perceptions of the 'sugar drink test', needing time off work and organising childcare, travel costs and reduced health literacy.[26,27] Although women were diagnosed with GDM an average of 9 days later during versus before the pandemic, the majority of maternal and neonatal outcomes were not different over time, suggesting that offering alternative testing with HbA1c aligned with routine antenatal booking and 28-week appointments, may be a simple, effective way to improve the detection of GDM.

In the GDM population identified at sites adopting the emergency GDM care pathway diagnostic approach, an increase was seen in development of a hypertensive disorder, without differences in other major maternal or neonatal morbidities. Overall, our findings of an increase in maternal morbidity seen during the pandemic may have been driven, at least in part, by the identification of a higher risk population, rather than being solely a consequence of a change in diagnostic approach or delivery of remote antenatal care.

Across the UK, we saw variation in GDM incidence, with a trend towards an increase during 2020 compared with 2019. The published literature is inconsistent for this record. In one UK maternity unit, a 45% reduction in GDM cases was reported using emergency criteria retrospectively over a sampling period of 6 weeks.[14] Another study analysed retrospective data collected over a 6-year period and showed a potential for a decrease in GDM of 29%.[15] The incidence of GDM also increased in the partial adopter site, although they continued with their pre-pandemic pathway for screening and diagnosing women. We were not able to explain this; it is possible that the lockdown changed the mode of transport available for women to attend for screening and this contributed to the findings, but this is speculation. Other studies have reported an increase in GDM prevalence, particularity associated with the first lockdown.[28,29] One explanation for an increase in GDM diagnosis during COVID-19 may relate to lockdown behaviours, such as increased consumption of snacks and carbohydrates[30,31] and reduced exercise,[32] leading to weight gain,[33] an independent risk factor for GDM.[34]

4.3 | Strengths and limitations

A strength of our study is that we demonstrate contemporary, UK-wide representation of GDM population demographics, screening strategies and maternal and neonatal outcomes. Many sites 'hand-collected' data, overcoming the problems of poor national coding of GDM and the lack of linked data collection systems that would facilitate national audit, as possible for pre-gestational diabetes in pregnancy.[35]

We chose a before-and-after comparison analysis, which is well-suited for evaluating changes in clinical practice in real-world settings.[36] As the national guidelines that are published by RCOG are typically interpreted in the UK as guidance rather than being mandatory, there was variation in uptake of the guidelines during the pandemic, allowing us to report on centres where there was little change in clinical pathways, as well as centres where care pathways were changed.

Limitations of our study include our before-after study design, as the heavy data collection burden precluded collection of data at multiple time points; however, we did adjust for known confounders of the GDM-outcome relations. We could not determine incidence at all sites and the findings need to be interpreted with caution, given the possibility of lack of data ascertainment. We were also unable to identify women whose diagnosis of GDM was potentially 'missed', because of the altered diagnostic approach during COVID. As in the pre-pandemic epoch in the UK, there was no universal biochemical screening for GDM during COVID, so confirming that the whole population was screened using clinical risk factors was not possible; we could only include women diagnosed and treated for GDM from among those tested based on clinical risk factors, demonstrating that these women do not appear to be at significant risk of poor obstetric outcomes, unlike women with raised glucose levels in pregnancy who are not treated.[37] Our findings do not support retrospective studies that modelled pregnancy outcomes associated with the emergency GDM care pathways, and suggested that adverse outcomes may be increased because women who would have normally been diagnosed with GDM may be 'missed'.[16] Consistent with our findings is a prospective study in Spain that found that the rate of missed diagnoses of GDM did not substantially change when comparing conventional criteria used before the pandemic with alternative diagnostic criteria used during the pandemic.[38] A nationwide cohort study of 948 020 singleton births in England, comparing maternal and neonatal outcomes for the general maternity population during COVID-19 and in the year prior, found an increase in obstetric intervention.[39] We had no information about whether women were included in both Pre- and COVID populations and so were not able to adjust for this in our analyses. Finally, some outcomes had high degrees of missingness, which increased or decreased during versus Pre-COVID, highlighting the need for high-quality, routine clinical audit of GDM and related outcomes.

5 | CONCLUSION

Despite major changes to antenatal care pathways during the pandemic, maternal and neonatal outcomes for women diagnosed and treated for GDM were similar to those pre-pandemic and/or were accounted for by identification of a higher risk population. This emphasises the need for large-scale trials to evaluate different screening and management strategies and their impact on clinical care outcomes, healthcare provider workload, and cost. Of particular interest are various combinations of clinical risk factor screening and biochemical diagnostic testing, as well as combinations between any of these approaches and universal biochemical screening. Approaches introduced during the COVID-19 pandemic are particularly worthy of evaluation; alternative screening tools of HbA1c and random plasma glucose facilitate early identification of GDM among higher risk women who may also fail to attend for OGTT, and remote and virtual antenatal care for glucose management provide alternative models of care.

AUTHOR CONTRIBUTIONS

This study was designed by the Diabetes in Pregnancy Working Group. The data analysis was conducted by N-MM with contributions from RMR, LAM, PD, SLW, PS and RL. N-MM wrote the first draft and RMR, LAM, PD, SLW, SP and RL edited it. All other authors contributed to data collection. All authors approved the final version of the paper. RMR is guarantor for the work.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Ethical approval was obtained from the National Research Ethics Committee (REC 21/SS/0031). Prior to data-sharing, all data were de-identified by individual NHS Trusts, in accordance with local information governance for patient confidentiality and data protection.

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REFERENCES

1. Saravanan P, Diabetes in Pregnancy Working Group, Maternal Medicine Clinical Study Group, Royal College of Obstetricians and Gynaecologists, UK. Gestational diabetes: opportunities for improving maternal and child health. Lancet Diabetes Endocrinol. 2020;8(9):793–800.
2. Ye W, Luo C, Huang J, Li C, Liu Z, Liu F. Gestational diabetes mellitus and adverse pregnancy outcomes: systematic review and meta-analysis. BMJ. 2022;377:e067946.
3. Knight M, Bunch K, Tuffnell D, Patel R, Shakespeare J, Kotnis R, et al., editors. Saving lives, improving mothers' care: lessons learned to inform maternity care from the UK and Ireland confidential enquiries into maternal deaths and morbidity 2017–19. 2021 [cited 2022 July 17]. Available from: https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/maternal-report-2020/MBRRACE-UK_Maternal_Report_Dec_2020_v10_ONLINE_VERSION_1404.pdf
4. Excellence NIfHaC. Diabetes in pregnancy: management from preconception to the postnatal period. London: NICE; 2015 [updated 16 Dec 2020; cited 2022 July 23]. Available from: https://www.nice.org.uk/guidance/ng3
5. Royal College of OaG. Guidance for maternal medicine services in the evolving coronavirus (COVID-19) pandemic. London: RCOG; 2020 [updated 9 Dec 2020; cited 2022 July 17]. Available from: https://www.rcog.org.uk/media/nkpfvim5/2020-12-09-guidance-for-maternal-medicine-services-in-the-coronavirus-c.pdf
6. Jardine J, Relph S, Magee LA, von Dadelszen P, Morris E, Ross-Davie M, et al. Maternity services in the UK during the coronavirus disease 2019 pandemic: a national survey of modifications to standard care. BJOG. 2021;128(5):880–9.
7. Steering DCCPG, Canada CatSoOaGo. Urgent update – temporary alternative screening strategy for gestational diabetes screening during the COVID-19 pandemic 2020 [cited 2022 July 17]. Available from: https://www.waterloowellingtondiabetes.ca/userContent/documents/Newsflash/Canadian%20Alternative%20GDM%20Guidelines%20COVID-19.pdf
8. Australasian Diabetes in Pregnancy Society (ADIPS) tADSA, the Australian Diabetes Educators Association (ADEA), Diabetes Australia (DA). Diagnostic testing for gestational diabetes mellitus (GDM) during the COVID 19 pandemic: antenatal and postnatal testing advice 2020 [cited 2022 July 17]. Available from: https://www.adips.org/documents/COVID-19GDMDiagnosis030420ADIPSADSADEADAforWebsite.pdf
9. Tennant P, Doxford-Hook E, Flynn L, Kershaw K, Goddard J, Stacey T. Fasting plasma glucose, diagnosis of gestational diabetes and the risk of large for gestational age: a regression discontinuity analysis of routine data. BJOG. 2022;129(1):82–9.
10. Shah BR, Sharifi F. Perinatal outcomes for untreated women with gestational diabetes by IADPSG criteria: a population-based study. BJOG. 2020;127(1):116–22.
11. Nachtergaele C, Vicaut E, Pinto S, Tatulashvili S, Bihan H, Sal M, et al. COVID-19 pandemic: can fasting plasma glucose and HbA1c replace the oral glucose tolerance test to screen for hyperglycaemia in pregnancy? Diabetes Res Clin Pract. 2021;172:108640.
12. Meek CL, Lindsay RS, Scott EM, Aiken CE, Myers J, Reynolds RM, et al. Approaches to screening for hyperglycaemia in pregnant women during and after the COVID-19 pandemic. Diabet Med. 2021;38(1):e14380.
13. Curtis AM, Farmer AJ, Roberts NW, Armitage LC. Performance of guidelines for the screening and diagnosis of gestational diabetes mellitus during the COVID-19 pandemic: a scoping review of the guidelines and diagnostic studies evaluating the recommended testing strategies. Diabet Epidemiol Manag. 2021;3:100023.
14. van-de-l'Isle Y, Steer PJ, Watt Coote I, Cauldwell M. Impact of changes to national UK guidance on testing for gestational diabetes screening during a pandemic: a single-centre observational study. BJOG. 2021;128(5):917–20.
15. van Gemert TE, Moses RG, Pape AV, Morris GJ. Gestational diabetes mellitus testing in the COVID-19 pandemic: the problems with simplifying the diagnostic process. Aust N Z J Obstet Gynaecol. 2020;60(5):671–4.
16. McIntyre HD, Gibbons KS, Ma RCW, Tam WH, Sacks DA, Lowe J, et al. Testing for gestational diabetes during the COVID-19 pandemic. An evaluation of proposed protocols for the United Kingdom, Canada and Australia. Diabetes Res Clin Pract. 2020;167:108353.
17. Gov.uk. English indices of deprivation 2019. 2019 [cited 2022 July 17]. Available from: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019
18. Gov.scot. Scottish index of multiple deprivation 2020 [cited 2022 July 17]. Available from: https://www.gov.scot/collections/scottish-index-of-multiple-deprivation-2020/
19. Egan AM, Bogdanet D, Griffin TP, Kgosidialwa O, Cervar-Zivkovic M, Dempsey E, et al. A core outcome set for studies of gestational diabetes mellitus prevention and treatment. Diabetologia. 2020;63(6):1120–7.
20. The International Fetal and Newborn Growth Consortium for the 21st Century I-s. The International Fetal and Newborn Growth Consortium for the 21st century online. 2009 [updated 2022]. Available from: https://intergrowth21.tghn.org/
21. Scotland PH. Births in Scotland technical report 2021 [cited 2022 July 17]. Available from: https://publichealthscotland.scot/media/10491/2021-11-30-births-technical.pdf
22. Audit NMP. NMPA methods for births occurring from 1 April 2018. 2018. Available from: https://maternityaudit.org.uk/FilesUploaded/NMPA%20Methods%20for%20births%20from%201%20April%202018.pdf
23. Cauldwell M, van-de-L'Isle Y, Watt Coote I, Steer PJ. Seasonal and SARS-CoV-2 pandemic changes in the incidence of gestational diabetes. BJOG. 2021;128(11):1881–7.
24. Ayman G, Strachan JA, McLennan N, Malouf R, Lowe-Zinola J, Magdi F, et al. The top 10 research priorities in diabetes and pregnancy according to women, support networks and healthcare professionals. Diabet Med. 2021;38(8):e14588.
25. Simmons D. Paradigm shifts in the management of diabetes in pregnancy: the importance of type 2 diabetes and early hyperglycemia in pregnancy: the 2020 Norbert Freinkel Award Lecture. Diabetes Care. 2021;44(5):1075–81.
26. Lachmann EH, Fox RA, Dennison RA, Usher-Smith JA, Meek CL, Aiken CE. Barriers to completing oral glucose tolerance testing in women at risk of gestational diabetes. Diabet Med. 2020;37:1482–9.
27. Chepulis L, Papa V, Morison B, Cassim S, Martis R. Barriers to screening for gestational diabetes mellitus in New Zealand following the introduction of universal screening recommendations. Womens Health Rep (New Rochelle). 2022;3(1):465–72.
28. He Z, Lv Y, Zheng S, Pu Y, Lin Q, Zhou H, et al. Association of COVID-19 lockdown with gestational diabetes mellitus. Front Endocrinol (Lausanne). 2022;13:824245.
29. Zanardo V, Tortora D, Sandri A, Severino L, Mesirca P, Straface G. COVID-19 pandemic: impact on gestational diabetes mellitus prevalence. Diabetes Res Clin Pract. 2022;183:109149.

30. Dun Y, Ripley-Gonzalez JW, Zhou N, You B, Li Q, Li H, et al. Weight gain in Chinese youth during a 4-month COVID-19 lockdown: a retrospective observational study. BMJ Open. 2021;11(7):e052451.
31. Ghosh A, Arora B, Gupta R, Anoop S, Misra A. Effects of nationwide lockdown during COVID-19 epidemic on lifestyle and other medical issues of patients with type 2 diabetes in North India. Diabetes Metab Syndr. 2020;14(5):917–20.
32. Martínez-Vizcaíno V, Sanabria-Martínez G, Fernández-Rodríguez R, Cavero-Redondo I, Pascual-Morena C, Álvarez-Bueno C, et al. Exercise during pregnancy for preventing gestational diabetes mellitus and hypertensive disorders: an umbrella review of randomised controlled trials and an updated meta-analysis. BJOG. 2023;130(3):264–75.
33. Cao W, Sun S, Danilack VA. Analysis of gestational weight gain during the COVID-19 pandemic in the US. JAMA Netw Open. 2022;5(9):e2230954.
34. McLennan NM, Hazlehurst J, Thangaratinam S, Reynolds RM. Endocrinology in pregnancy: targeting metabolic health promotion to optimise maternal and offspring health. Eur J Endocrinol. 2022;186(6):R113–26.
35. Murphy HR, Howgate C, O'Keefe J, Myers J, Morgan M, Coleman MA, et al. Characteristics and outcomes of pregnant women with type 1 or type 2 diabetes: a 5-year national population-based cohort study. Lancet Diabetes Endocrinol. 2021;9(3):153–64.
36. Craig P, Cooper C, Gunnell D, Haw S, Lawson K, Macintyre S, et al. Using natural experiments to evaluate population health interventions: new Medical Research Council guidance. J Epidemiol Community Health. 2012;66(12):1182–6.
37. Stacey T, Tennant PWG, McCowan LME, Mitchell EA, Budd J, Li M, et al. Gestational diabetes and the risk of late stillbirth: a case-control study from England, UK. BJOG. 2019;126(8):973–82.
38. Molina-Vega M, Gutierrez-Repiso C, Lima-Rubio F, Suarez-Arana M, Linares-Pineda TM, Cobos Diaz A, et al. Impact of the gestational diabetes diagnostic criteria during the pandemic: an observational study. J Clin Med. 2021;10(21):4904.
39. Gurol-Urganci I, Waite L, Webster K, Jardine J, Carroll F, Dunn G, et al. Obstetric interventions and pregnancy outcomes during the COVID-19 pandemic in England: a nationwide cohort study. PLoS Med. 2022;19(1):e1003884.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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3.3 Conclusions

This chapter presents findings from the first part of a two-part multi-method evaluation of emergency care pathways for screening, diagnosing, and managing GDM during the COVID-19 pandemic. The key findings are discussed in relation to recent literature and are connected to the broader research presented in this thesis.

3.3.1 Literature review

The findings of this study are consistent with other reports, which confirm similar pregnancy outcomes under the emergency guidance for GDM screening and diagnosis. Pregnancy outcomes were modelled using UK data from 2018, showing comparable rates of LGA infants, Caesarean births, preterm deliveries, and stillbirths among women diagnosed via NICE criteria compared to those diagnosed using HbA1c ≥39 mmol/mol or fasting plasma glucose (FPG) ≥5.6 mmol/L (130).

Notably, in maternity care settings where GDM diagnostic pathways remained unchanged but virtual antenatal care was adopted, no differences in key pregnancy outcomes were observed. This finding is supported by international evidence. A Canadian cohort study reported no significant increase in maternal or fetal complications following the introduction of virtual antenatal care during the first year of the pandemic (131). Similarly, in Australia, a publicly funded health system replaced 46% of in-person antenatal consultations with telehealth visits, reporting no changes in adverse pregnancy outcomes compared to conventional care (132). Furthermore, a feasibility study of "DiabCare", a telemonitoring platform for remote GDM care, demonstrated significant improvements in glycaemic control (133).

These findings contribute to a growing body of evidence supporting the feasibility of remote GDM care (134-137). However, it remains unclear how many healthcare providers in the UK have adopted remote or hybrid care models since the pandemic. Anecdotal evidence suggests that remote clinical care has become an integral part of GDM management, and findings from subsequent parts of this multi-method study,

particularly qualitative insights from healthcare professionals, are likely to inform the continuation or expansion of such care models.

3.3.2 GDM incidence

A key finding of this study was the increased incidence of GDM during the COVID-19 pandemic compared to pre-pandemic levels. Across sites where diagnostic criteria (NICE 2015) remained unchanged, GDM incidence rose from 8.5% to 11.2%. This trend is consistent with national data, which reported a 33% increase in GDM incidence during the pandemic (138). Globally, reports have documented similar increases in GDM incidence during the pandemic, ranging from 13% to 34% (139-145). For example, in the United States, national statistics recorded a 30% rise in GDM rates, reaching 7.8 cases per 1,000 births (144). Contributing factors may include reductions in physical activity, increased sedentary behaviour, and weight gain during lockdowns (146-149).

Some studies suggest that a gradual increase in the risk profile of pregnant populations, such as rising maternal age, body mass index (BMI), and gestational weight gain (GWG), may partly explain the higher GDM detection rates. A multicentre retrospective cohort study in Australia involving 28,207 pregnancies compared GDM detection rates during two pre-pandemic years with the first and second years of the pandemic. GDM incidence increased across the pandemic periods (21.2% vs. 22.9% vs. 24.8%; $p < 0.001$), coinciding with rises in maternal age, BMI, obesity prevalence, and GWG. However, after adjusting for maternal baseline characteristics and GWG, only the second year of the pandemic was independently associated with an increased risk of GDM (OR 1.17 [1.06, 1.28], $p = 0.01$) (143).

Other studies, however, present contrasting findings. A UK cohort study observed a significant increase in GDM detection during the pandemic compared to pre-pandemic levels but found no significant change in the overall proportion of women undergoing risk-based screening between 2006-2020 and 2020-2021 (63.75% vs. 69.45%; $p = 0.526$ (138) Similarly, in another cohort study comparing 5,245 pre-pandemic pregnancies with 4,843 pregnancies during the pandemic, GDM prevalence rose by 22.2% (from 9.9% to

12.2%), yet no significant increase in GWG, even among women with obesity, was noted (150).

The increase in GDM detection may partially reflect gradual changes in the risk profile of pregnant populations over time. However, the close temporal proximity of pandemic cohorts suggests that pandemic-specific factors likely played a significant role. Potential contributors include physiological stress caused by prolonged lockdowns, social isolation, economic hardship, and a rise in mental health conditions such as anxiety and depression. Notably, only one study reporting an increase in GDM incidence included data on COVID-19 infection. This study observed higher rates of COVID-19 infection during the second year of the pandemic, which coincided with an adjusted increase in GDM detection (143). Current evidence on the effects of SARS-CoV-2 infection during pregnancy highlights common placental histological changes, such as vascular injury (malperfusion and thrombosis) and inflammation (151, 152). However, no clear correlation has yet been established between maternal infection, placental lesions, and the development of GDM, as research in this area remains extremely limited.

3.3.3 Evaluation of alternative diagnostic tools

The data from this study indicate that women diagnosed with GDM during the pandemic using HbA1c and fasting plasma glucose in routine antenatal care were a higher-risk population compared to those diagnosed before the pandemic. This group included a greater proportion of women from Asian and Black ethnic backgrounds, younger age groups, lower socioeconomic statuses, and with higher BMIs and fasting plasma glucose levels. The shift in population characteristics is likely multifactorial.

Firstly, HbA1c may have identified higher-risk women, as suggested by Saravanan et al., who demonstrated its utility as a diagnostic tool for GDM in low-resource settings (79). Secondly, using a single non-fasted blood test during routine antenatal appointments may have captured women who, pre-pandemic, might not have attended an OGTT or been missed by risk-factor-based screening. This is significant, as these women represent a high-risk group with an increased risk of stillbirth (40).

The OGTT, while widely used, is resource-intensive and often poorly tolerated. Evidence from a pragmatic randomised clinical trial involving 23,792 women demonstrated that adherence was higher in a two-step screening approach (92%) compared to a one-step OGTT strategy (66%), suggesting a preference among patients and care providers for simpler, single, non-fasting blood tests (50). Studies further emphasise that women perceive the OGTT as inconvenient, unpleasant, and time-consuming, making it a barrier to effective GDM screening (153, 154).

HbA1c demonstrates inadequate sensitivity for detecting GDM compared to the OGTT(81) , its potential role, either alone or as part of a composite risk score, warrants further evaluation.

This study, along with others, supports the exploration of alternative diagnostic tests to improve acceptability and uptake.

3.3.3.1 Continuous glucose monitoring

The role of continuous glucose monitoring (CGM) as an alternative diagnostic tool to the OGTT has been recently evaluated. CGM involves the use of a disposable subcutaneous electrochemical sensor to measure interstitial glucose levels. The sensor is connected to a receiver, enabling continuous recording and storage of glucose data, which can be captured as frequently as every 5 minutes, depending on the technology used (155).

While CGM has traditionally been studied in the context of GDM for its insights into glucose regulation during pregnancy (156), recent research has focused on its utility in diagnosing GDM (155, 157, 158). Studies comparing CGM to OGTT have demonstrated CGM can identify significant differences between women with GDM and those with normal glucose tolerance in terms of blood glucose variability and time spent in, below, or above the recommended glucose range for pregnancy (155, 158).

An Australian study further explored the acceptability of CGM as a diagnostic tool. Quantitative assessment revealed that CGM was significantly more acceptable to women than the OGTT, with 81% rating CGM as highly acceptable compared to 27% for OGTT ($p < 0.001$)(155). Similarly, a UK-based qualitative study evaluated CGM and home OGTT, identifying key themes of reassurance and convenience. Women reported that

CGM was painless, had few adverse events, and expressed strong recommendations for its use in diagnosing GDM (159).

These findings highlight the significant promise of CGM as a diagnostic tool for GDM. However, further research is needed to refine CGM metrics for identifying GDM and to evaluate its potential for predicting adverse pregnancy outcomes.

3.3.3.2 Updated SIGN guidelines 2024

The SIGN guidance for the management of diabetes in pregnancy was updated in 2024, introducing significant changes to the diagnostic thresholds for gestational diabetes mellitus (GDM). Diagnosis is based on a single-step 75 g OGTT for women with risk factors, using the following thresholds:

- **Fasting plasma glucose:** ≥5.3 mmol/l
- **Two-hour post 75 g glucose load:** ≥9.0 mmol/l
- **One-hour post 75 g glucose load (where used):** ≥10.6 mmol/l

These updates were largely informed by emerging evidence from a recent large RCT that compared lower and higher diagnostic thresholds. The trial found no significant improvement in outcomes at the population or whole-study level with lower thresholds (61). However, subgroup analyses showed that lower criteria were beneficial in certain cases, with a number needed to diagnose and treat of 4 (95% CI 2 to 17) to prevent one large-for-gestational-age (LGA) infant.

The guideline committee considered practical challenges in making this decision, including the high volume of women with risk factors requiring OGTT and the fact that some centres in Scotland had been unable to offer OGTT to all eligible women. Current evidence suggests that raising the diagnostic thresholds will result in fewer women being diagnosed with GDM in Scotland. A population level evaluation of this will be urgently required.

3.3.4 Summary

The findings from this study underscore the potential for telehealth and alternative diagnostic methods to improve access to GDM care, particularly for underserved populations. However, further research is needed to evaluate the long-term impact of these approaches on maternal and neonatal outcomes. Additionally, studies investigating the interplay between COVID-19 infection, maternal physiology, and GDM development are essential to better understand the pandemic's influence.

Chapter 2 presents the second part of a multi-method study evaluating changes in GDM care delivery during the SARS-CoV-2 pandemic. This study examines healthcare professionals' perceptions and experiences of providing remote antenatal care to women with GDM during this time.

4 Results Chapter 2

4.1 Introduction

This chapter begins with a review of the literature on remote antenatal care for GDM. The literature presented includes a summary of studies, before and during the first wave of the SARS-CoV-2 pandemic, which informed the research question and design of my study. Past literature relevant to the implementation of remote care for GDM within the NHS is addressed, and the rationale for undertaking a qualitative interview study of UK HCPs is then presented.

The remainder of this chapter is structured into four sections. Section one outlines the aims and key research questions of the study. Section two provides a discussion of the study's methodological approach, including sampling, recruitment, data collection, analysis, and sociological framework adopted. The main findings of the study are presented in section three. The themes identified through thematic analysis are presented under three inter-connected research questions. Finally, section four explores the findings in relation to the existing literature, considers the wider implications of my research. There are 2 appendices at the end of the thesis related to this chapter: the participant information sheet (Appendix 2.1) and interview topic guide (Appendix 2.2).

4.1.1 Remote clinical care

Remote clinical care is a healthcare model that delivers complete episodes of care without the need for face-to-face interactions (NHS England) (160). This approach uses telecommunication and electronic information technologies, commonly known as telemedicine or e-health, to replace in-person interactions between healthcare providers and patients (161, 162). By leveraging these technologies, remote clinical care can deliver a broad range of services, including consultations, monitoring, and patient education (162). A key component in this model is remote patient monitoring, also known as telemonitoring, where patients monitor their health conditions and relay data to

healthcare professionals for evaluation and action, all from outside conventional medical settings (160, 161). In this study, the terms "remote care" and "remote monitoring" are used to describe these practices.

4.1.1.1 The landscape of remote GDM care before SARS-CoV-2

For several years, remote clinical care has been proposed as a potential solution to the increasing demand that GDM places on maternity services (163-165). Remote care systems offer a wide range of services, including monitoring blood glucose levels, providing dietary advice, promoting physical activity, managing blood pressure, and offering post-natal interventions (165). Despite the growing demand and development of remote care services, their use in GDM antenatal care remained low and infrequent before the SARS-CoV-2 pandemic—a trend observed across many medical disciplines and healthcare systems worldwide. The limited adoption of remote clinical care for GDM was due to several factors, including concerns about patient safety given the high-risk nature of the condition. Technological limitations, challenges in data integration, and the comfort of both providers and patients with traditional care models also played a significant role. Additionally, regulatory restrictions, particularly regarding data security and privacy, along with limited reimbursement frameworks, further reinforced the preference for traditional, in-person management methods (166)

Although remote care delivery has not been routinely offered in the clinical management of GDM, it has been extensively evaluated in clinical trials, leading to the publication of several systematic reviews addressing concerns about patient safety. The largest review, published in 2020, analysed outcomes from 32 RCTs involving 5,108 women with GDM (134). This study assessed a wide range of remote care interventions, including hardware, software, mobile apps, and web-based systems for education, dietary interventions, physical activity, and remote blood glucose monitoring. Overall, compared to standard care, remote care interventions resulted in a small but significant improvement in maternal glycaemic outcomes. Additionally, a meta-analysis of pooled data from 19 trials showed a reduction in Caesarean birth rates in the remote care group compared to standard care. Two more recent systematic reviews, including studies published up to 2021, reported similar findings, with remote interventions linked to improvements in glycaemic control, lower maternal weight gain during pregnancy, and a

reduced need for Caesarean births (135, 136). Overall, the pooled evidence suggests that remote care interventions have small but positive effects on maternal and glycaemic outcomes.

4.1.1.2 Remote glycaemic monitoring interventions

Some of the most widely used tools in remote GDM care are those that provide remote access to women's home blood glucose readings, enabling them to monitor their levels at home with results transmitted in real-time to healthcare providers. Early innovations in this field utilised web-based platforms (165, 167-171) . However, there has been a recent shift toward mobile health (mHealth), where smartphones are used to transfer data and run applications, facilitating remote blood glucose monitoring and communication between patients and healthcare providers. In the UK, Mackillop et al. developed a digital blood glucose management system called "GDm-health", which operates on a mobile app platform to enable monitoring and bidirectional digital communication. A randomized trial found the "GDm-health" app to be safe, with no differences in maternal and neonatal outcomes compared to standard care, except for a reduction in caesarean births (172). Similarly, researchers in Australia, China, Israel, Norway, Singapore and Spain have developed smartphone applications that integrate remote blood glucose management with digital dietary, exercise, and weight management tools, alongside communication features (173-180). Overall, these integrated remote glycaemic management tools demonstrate modest improvements in glycaemic outcomes with no safety concerns (134-136).

4.1.1.3 Evaluation of remote care interventions

To date, most research on remote clinical care models for GDM has followed a traditional approach, focusing on predefined clinical outcomes and objective endpoints, essentially asking the question, "Does it work?" (134-136). However, in accordance with the Medical Research Council (MRC) guidance on evaluating complex interventions, effectiveness assessments must consider the full spectrum of effects and how they vary among recipients and providers across different sites and over time (124).

To address this, some researchers have expanded their evaluations to explore the processes involved in implementing remote GDM care, asking, "How and why does it work?" These questions are essential for evaluating complex interventions, as the same intervention may be perceived and implemented differently across various settings.

Studies have examined adherence as well as the acceptability and satisfaction of both women and healthcare providers with remote interventions. A mix of quantitative and qualitative methods has been employed to explore these factors. Reports indicate that women's participation in and adherence with remote GDM care are higher compared to those receiving standard care (167, 170, 181-184). Similarly, researchers have noted high levels of satisfaction among women receiving remote clinical care (163, 165, 167, 173, 175, 181, 182, 184-187). In the UK, Hirst et al. assessed women's satisfaction with the "GDm-health" mobile app, finding that 57 out of 60 women reported they would use it again, with significantly higher satisfaction compared to standard care (172, 185). Another UK study found that women were willing to self-manage GDM from home and be monitored remotely during pregnancy, with 78% to 90% of participants finding smartphones acceptable for managing their GDM (188).

Qualitative studies examining women's experiences with remote clinical care have identified themes such as convenience, particularly in reducing hospital visits for women living far away or those with childcare and work commitments (168, 175, 187, 189, 190). The ease of use, especially with digital blood glucose management compared to paper diaries, was also commonly reported (168, 187, 191). Accessibility emerged as a common theme, with women appreciating the ability to access information and data at any time due to the widespread availability of mobile phones (191-193). These studies also reported improved GDM self-management, facilitated by the visualization and easy access to data (189, 190, 192). Women described how remote blood glucose technologies helped them better understand the relationship between blood glucose levels and dietary intake. The usability of technology, particularly the quality and personalization of information, was highly valued. Overall, women's feedback was positive, though some issues were raised, particularly technical difficulties related to data transfer and concerns about the privacy of personal health information (168, 192, 193).

A smaller number of studies have included healthcare professionals' experiences in their evaluation of remote GDM care. Similar to studies gathering women's insights, many researchers focused on quantitative evaluations using satisfaction and acceptability scores. Healthcare providers generally viewed remote care interventions as suitable and appropriate for women with GDM (168, 182, 189, 193, 194). In studies using interviews or focus groups, themes relating to convenience emerged, particularly the ability to remotely access women's blood glucose readings (194). Effects on workload were commonly discussed, with some healthcare providers noting that remote care improved efficiency by allowing more time for interaction during consultations and facilitating quicker responses to episodes of hyperglycaemia (163, 181). However, other studies reported an increased workload for healthcare providers, driven by the longer duration of telephone consultations compared to face-to-face visits and additional administrative tasks (168, 194). Communication challenges were also highlighted, with providers noting that remote interactions made it difficult to gauge patients' emotions and led to missed opportunities to talk to patients directly (181, 193). Lastly, technical issues were identified as potential barriers to the future use of remote clinical care (193).

4.1.1.4 A gap in the literature

An existing body of evidence supports the use of remote care delivery for GDM. Reviewing the literature offers some insights into usability and satisfaction. However, reviewing these studies highlight significant gaps in our understanding of delivering remote care for women with GDM.

To date most studies are small, single-centre trials, often pilot studies conducted in controlled research settings. These studies typically restrict participation to native language speakers with access to the necessary technology (12, 27, 34, 38). As a result, they offer little insight into how remote care interventions would be received and implemented in real-world settings or among more complex patients. To my knowledge, only one study has focused on evaluating remote care for lower-income women (195). Such biases significantly limit the generalizability and depth of the findings. This limitation was emphasised in one study where healthcare providers noted that the

remote care model only appeared effective for typical GDM patients, yet the study did not include high-risk patients (193).

The emphasis on quantitative rather than qualitative inquiry has prevented researchers from fully exploring the broader impacts of remote care and understanding how these interventions are perceived and implemented. Furthermore, most studies focus on women's engagement and satisfaction, often excluding the perspectives of healthcare providers and other stakeholders. In studies where these views were solicited, researchers included fewer than five participants, sampling from a narrow range of disciplines (168, 181, 182, 193, 194). The very small sample sizes in these studies make it highly unlikely that the authors achieved data saturation, limiting the robustness of their conclusions.

A recent conference consensus on patient engagement in healthcare emphasizes the critical role of healthcare providers' commitment, identifying it as a key factor in fostering patient engagement (196). Graffigna et al. highlight that the adoption and delivery of remote care systems will have significant impacts on healthcare providers' roles, influencing job satisfaction, commitment, and efficiency (196, 197) . These factors, in turn, directly affect patient engagement. Therefore, the perspectives and experiences of those delivering healthcare are essential in studies aimed at evaluating remote clinical care (168).

4.1.2 SARS-CoV-2 and remote GDM care

At the outset of the pandemic, the UK Government classified pregnant women as being at higher risk of severe illness if infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Pregnant women were advised to adhere strictly to public health measures such as social distancing and self-isolation to reduce their risk of exposure. The Royal College of Obstetricians and Gynaecologists (RCOG) provided guidance suggesting that GDM clinics could be effectively conducted via telephone or video consultations instead of in-person where appropriate (118). This recommendation led to the widespread adoption of remote antenatal services, with over 80% of antenatal

appointments conducted remotely across the NHS in 2020 (198), and up to 70% of GDM consultations being delivered remotely during the first wave of the pandemic (199).

The transition to remote clinical care was considered a necessary response to the unprecedented challenges posed by the pandemic, despite the absence of formal evaluations or a robust evidence base. The guidance from the RCOG acknowledged the limited evidence underpinning many of its recommendations (118).

In Chapter 1, I examined the impact of changes to the screening, diagnosis, and management of GDM on maternal and neonatal outcomes in the UK. Across the cohort study sites, various approaches to care delivery were adopted. At one site, remote care was implemented while pre-pandemic screening and diagnostic protocols were maintained, resulting in no significant changes to maternal and neonatal outcomes (200). Similar findings were reported in Australia, where integrating telehealth into antenatal care reduced in-person consultations by 50% without adversely affecting pregnancy outcomes (201). Comparable results were observed in studies conducted in Spain, Poland, and the USA (201-204). While these studies provide evidence supporting the feasibility of remote care for women with GDM, they fail to explore the mechanisms behind its implementation. This gap leaves an incomplete understanding of how and why remote care was delivered and its overall effectiveness during the pandemic.

During the first wave of the pandemic, a limited number of studies examined the impact of remote care delivery in the NHS by exploring the experiences of women and HCPs (199, 205). Most studies and published protocols focused on women's experiences with GDM and general antenatal care (192, 206-208).

As discussed earlier, pre-pandemic studies on remote GDM care rarely included HCPs, and this trend continued in the early pandemic research. In cases where HCPs were included, studies primarily examined the acceptability of remote care using quantitative and qualitative survey methodologies (205, 209, 210). These studies reported that virtual clinics reduced unnecessary visits and enabled the safe management of low-risk pregnancies from home. In one study, 89% (n=32) of qualitative survey respondents reported a positive experience with telehealth, and 94% (n=34) believed it improved patient access to care (210). However, concerns were raised about the training of junior

doctors in virtual clinics compared to face-to-face clinics. Additionally, some participants reported better team cohesion, and that remote care facilitated colleague discussions (210). Notably, these studies predominantly included doctors, with one study comprising 96% (n=26) doctors and only 4% (n=1) midwives, thus limiting representation from the broader antenatal multidisciplinary team (205).

These studies were conducted early in the pandemic at a time when HCPs were still adapting to the novel demands of the situation and anticipating a swift "return to normal." As a result, it is uncertain whether enough time had passed for clinical pathways to become fully established and embedded in practice, which may limit the depth and generalisability of the findings.

4.1.3 Rationale for the study

In response to the pandemic, the RCOG COVID-19 GDM antenatal guidelines introduced remote consultations with the multidisciplinary team for education and glycaemic control monitoring (118). This paradigm shift in care delivery required significant behavioural and attitudinal changes from healthcare providers.

Qualitative inquiry is the most effective method to capture the underlying reasons for behaviour, social interactions, and the ways people interpret the events around them (211). To investigate the impact of the pandemic on GDM care delivery, this study aimed to explore HCPs' experiences of, and views about, delivering remote care through qualitative methods, specifically semi-structured interviews. The study sought to gather perceptions and insights from a broad spectrum of HCPs involved in multidisciplinary care across the NHS in the UK.

Qualitative research is particularly well-suited for exploring why certain strategies succeed or fail, and it is valuable in identifying unexpected consequences or outcomes (211). The literature indicates a scarcity of well-designed studies evaluating service providers' perspectives on remote care delivery. The SARS-CoV-2 pandemic presented a unique opportunity to examine the impacts of remote care interventions outside of a controlled research environment, offering findings through a "real-world" lens across

various NHS care settings, among ethnically and socioeconomically diverse populations.

4.2 Aims and Objective

The aim of this study was to explore the perspectives and experiences of HCPs involved in delivering multidisciplinary care in the early phases of the SARS-CoV-2 pandemic. The key objectives were to understand the rationale and processes behind the implementation of remote care within the NHS, and to offer learning and insights that could inform future care delivery.

4.2.1 Research questions

The specific research questions this study sought to address were:

RQ 1 What did HCPs at individual sites do to reconfigure their services to provide remote multidisciplinary antenatal care and why?

RQ2 What did HCPs find successful and unsuccessful when delivering multidisciplinary care during the early phases of the pandemic and why?

RQ 3 What lessons can be learnt from delivering remote multidisciplinary GDM care during the pandemic and which aspects of pandemic GDM care delivery do HCPs think should be retained in the longer-term, and why?

4.3 Methods

This section begins with a discussion of the sociological theory underpinning the study. This is followed by a description of the processes involved from study design to data analysis. It concludes with a reflexivity statement, where I reflect on how my unique positionality has shaped and informed the research process.

4.3.1 Epistemology and theoretical framework

Epistemology in clinical qualitative research is centred on understanding how knowledge is constructed and interpreted within the context of health. In this study, the epistemological approach adheres to the principles of Normalization Process Theory (NPT), which provides a framework for understanding the factors that influence the implementation, embedding, and integration of innovations in healthcare settings (212). NPT is particularly concerned with how interventions become normalized—that is, how they are so thoroughly integrated into routine practice that they become invisible or taken for granted.

NPT is well suited to clinical studies focused on developing and evaluating complex medical interventions, as it examines not only the initial stages of implementation but also the long-term sustainability and integration of these interventions (212, 213) . In this study, NPT is used to explore the work that HCPs and multidisciplinary teams (MDTs) undertook to implement and embed remote practices into clinical care during the early stages of the SARS-CoV-2 pandemic. The theory guided both the study design and the analysis of the data, ensuring that the research questions were aligned with the core components of NPT.

NPT comprises four key components: **coherence** (sense-making), **cognitive participation** (engagement), **collective action** (the work done to enable the intervention), and **reflexive monitoring** (appraisal of the benefits and costs of the intervention) (214). These components were directly mapped to the research questions to provide a structured analysis of the data.

- **Coherence and Cognitive Participation:** What did individual sites do to reconfigure their services to provide remote multidisciplinary antenatal care (ANC) and why?
- **Collective Action and Reflexive Monitoring:** From the HCPs' perspective, what aspects of remote multidisciplinary antenatal care were successful or unsuccessful, and why? What lessons can be learned from delivering remote GDM care during the pandemic, and which elements of this care delivery should be retained in the longer term?

Several study design decisions were guided by the principles of NPT and are highlighted throughout this chapter.

4.3.2 Study design

This qualitative study utilised individual semi-structured interviews to collect data from HCPs involved in delivering GDM care following the reconfiguration of services due to SARS-CoV-2. The HCPs were drawn from selected study sites across the UK. Conducted in accordance with the consolidated criteria for reporting qualitative research (COREQ) (215), the study aimed to capture participants' experiences and perspectives in depth and detail. Semi-structured interviews were chosen as they are well suited for exploring personal experiences and the interaction between individual views and external factors (216-218). This method allows for in-depth, rich insights in a setting that encourages participants to discuss social and personal matters and express their opinions freely, without the influence of professional hierarchies or group dynamics (218, 219). In contrast, group interviews or focus groups, while effective for capturing group dynamics and potentially offering insights into MDT care delivery, present logistical challenges, particularly when coordinating the schedules of busy healthcare professionals. These challenges were further compounded by the constraints of the pandemic.

Due to the constraints imposed by the SARS-CoV-2 pandemic, interviews were conducted via the video conferencing platform Microsoft Teams. At the time, physical distancing measures were in place, making remote interviewing the only feasible option. Previous research indicates that remote interviews conducted by telephone are a viable

alternative to face-to-face interactions, with no significant differences in the quality or content of the data collected (220, 221). Although there is less research on video interviews, recent studies suggest that video conferencing is a cost-effective and practical alternative to in-person interviews, effectively overcoming geographical and time barriers (222).

While challenges such as lack of internet access or digital skills may limit participation, researchers have noted that these issues can be mitigated, making virtual interviewing a preferred option in many cases (223).

Remote interviewing also offered additional advantages. It eliminated the need for local Research and Development approvals from individual healthcare trusts, improving the efficiency of data collection. Moreover, it reduced the logistical burden on participants and healthcare units by removing the need to host interviewers, while also saving on travel costs and time.

4.3.3 Study setting(s)

This study aimed to explore the experience of delivering MDT care remotely. To gain comprehensive insights into MDT care during the pandemic, HCPs from all disciplines within the MDT were interviewed. Capturing diverse perspectives was crucial for understanding the impact of remote care on team dynamics and overall service delivery, enabling a detailed and nuanced exploration of the subject. This decision to include input from the entire team aligns with the four principles of NPT, enhancing the study's ability to demonstrate the effects of remote service delivery on multidisciplinary care.

While interviewing HCPs from a single site would have allowed for detailed insights, it would have limited the generalisability of the findings. To balance depth with breadth, the study included three distinct MDTs across different locations. The research was conducted at one NHS site in Scotland and two in England. To maintain confidentiality, the sites have been anonymised and labelled Sites A, B, and C.

These sites were purposefully chosen to represent diverse GDM populations, covering a range of ethnic and sociodemographic backgrounds, varying geographical settings, and different types of healthcare environments, including tertiary and district general care

facilities. Additionally, one site with prior experience using remote antenatal care before the pandemic was included, alongside sites that had rapidly transitioned to remote care during the SARS-CoV-2 pandemic. All sites were subject to national lockdowns during the study period, providing a consistent context for data collection.

4.3.4 Sampling

HCPs were eligible to participate in the study if they were currently providing GDM care within the NHS and had experience delivering care both before and during the SARS-CoV-2 pandemic.

4.3.4.1 Sampling Strategy

Purposive sampling was employed to ensure representation from diverse GDM multidisciplinary teams (MDTs). The study aimed to include teams that had adopted remote monitoring during the pandemic, as well as those with differing approaches to care delivery before the pandemic. Drawing on my knowledge of UK practice and a review of the literature, I was aware that Sensyne Health plc had offered one year of free use of GDm-Health™, a remote monitoring system for managing diabetes in pregnancy, at the onset of the pandemic. Therefore, I specifically sought to include a site using this technology.

Individual MDTs were identified with assistance from a national diabetes-in-pregnancy network, of which I am a member. Recruitment began on November 15, 2020, and was initiated through direct, personalised email contact with the clinical lead for each service.

4.3.4.2 Recruitment Approach

A maximum variation sampling approach was applied at each study site to capture shared patterns and unique perspectives across different teams. The aim was to recruit HCPs from all disciplines involved in GDM care, including doctors, nurses, midwives, dieticians, and additional site-specific staff such as specialist midwives and healthcare assistants. This ensured a wide range of experiences and opinions were represented. Recruitment materials, including a standard email flyer, emphasised the voluntary nature of participation and the importance of circulating the invitation to all team members to reduce potential pressure or bias.

The recruitment timeline for this study was initially determined by the time required to obtain approvals, which were granted in August 2020. However, I deliberately postponed recruitment until late 2020. This decision was made to allow recruitment to take place after the initial waves of the pandemic, with the aim of gaining a more comprehensive understanding of the long-term integration of remote practices. This approach aligned with NPT's emphasis on evaluating interventions beyond their initial implementation phase.

4.3.4.3 Sample Size and Saturation

The target sample size was 20–30 participants from three clinical teams. This was based on prior qualitative studies involving HCPs, where this range was sufficient to achieve theoretical saturation—the point at which no new themes or data emerge during analysis (219). In total, 23 HCPs from three units consented to participate, representing all key MDT roles.

4.3.5 Ethical approval and Sponsorship

Ethical approval was granted by the Edinburgh Medical School Research Ethics Committee (EMREC) on 04 /08/20 (20-EMREC-001). The study was co-sponsored by NHS Lothian and the University of Edinburgh through the Academic and Clinical Central Office for Research and Development (ACCORD).

An amendment was submitted to extend recruitment and approved on 06/05/21.

4.3.6 Consent

All potential participants were provided with a participant information sheet and a data protection information sheet (Appendix 2.1). They were given at least 48 hours to review the materials and ask any questions before deciding to participate. Oral consent was then obtained and audio-recorded at the start of each interview using a predefined script (Appendix 2.4).

Using oral, audio-recorded consent over the phone has been successfully implemented in previous qualitative studies involving HCPs and pregnant women (220, 224). For this study, this approach was chosen to minimize the burden on participants by reducing the following:

Time commitment: Participants did not have to wait for written consent forms to be mailed, filled out, and returned before the interview could take place. This also avoided the inconvenience of going to a post-box when social distancing or shielding measures were in place.

Administrative tasks: The need for participants to complete and return consent forms via pre-paid envelope was eliminated, along with the potential need for follow-up if forms were delayed or lost

4.3.7 Data collection

An interview topic guide with open-ended questions was developed using insights from the literature, my clinical expertise, and feedback from both clinical and non-clinical supervisors. The questions were designed to align with the research objectives while allowing participants the flexibility to share their personal experiences. The guide was piloted with three HCPs across two study sites. Transcripts from these pilot interviews were reviewed by my supervisor (JL), and minor revisions were made to the guide based on their feedback. The pilot interviews provided data of sufficient depth and quality to be included in the final study.

As the interviews progressed, the topic guide was adapted to reflect emerging findings, ensuring new themes were explored in subsequent interviews.

To ensure a conducive interview environment, interviews were scheduled at times convenient for participants. I conducted interviews from a quiet, secure home office, and participants were asked in advance to minimise background noise and interruptions where possible. However, the practical realities of healthcare settings meant that occasional interruptions were unavoidable.

Interviews were conducted via Microsoft Teams and audio-recorded using an encrypted digital recorder. Recordings were transcribed verbatim by an independent transcription service (1st class secretarial services). Each transcript was carefully checked for accuracy, and any identifiable information was removed to safeguard participant confidentiality. Finalised transcripts were securely stored on university servers, in accordance with my data management plan.

At the beginning of each interview, descriptive information about participants—including professional role, age and years of experience—was collected. Interviews were conducted concurrently across study sites and continued until data saturation was reached, defined as the point at which no new themes or insights emerged from the analysis of additional data.

All interviews were conducted between November 2020 and April 2021. Each interview was transcribed and initially analysed, with preliminary codes assigned immediately after the interview. By the 23rd interview, representation from all MDT roles had been achieved, and data saturation was confirmed.

4.3.7.1 Pilot Interviews

The pilot interviews served not only to evaluate and refine the topic guide but also to prompt a minor adjustment to the sampling strategy. During these interviews, participants consistently highlighted the involvement of community midwives (CMWs) in GDM care, revealing a gap in the initial recruitment approach, which had been focused solely on tertiary settings. As a result, CMWs were included in the study and recruited from all three study sites.

4.3.8 Data analysis

A thematic analysis was undertaken, following the stages outlined by Braun and Clarke (225)

1. Familiarisation with the data
2. Generating initial codes and searching for themes
3. Reviewing, defining and naming themes
4. Writing the report

These stages were designed to overlap, in an iterative process, that began during data collection.

4.3.8.1 Familiarisation with the data

The analysis started with familiarization, where I repeatedly read and cross-compared the interview transcripts to identify primary patterns across and within the data—a

process known as "pattern coding." This initial stage was crucial for immersing myself in the data and gaining a comprehensive understanding of the content.

Generating initial codes and searching for themes

At this stage, I adopted a deductive, or a priori, approach to categorise data in alignment with my research questions. This initial step involved creating broad categories based on my theoretical framework and research objectives. Subsequently, I transitioned to an inductive, or emergent, approach known as "open coding." During this phase, themes and concepts were allowed to emerge organically from the data through iterative readings of the transcripts, aiming to capture insights that arose during data collection or were unanticipated at the outset. To support this process, I maintained a reflective journal to document decision-making, including references to specific quotes, which helped to contextualise and make sense of the data

4.3.8.2 Reviewing defining and naming themes

Following the initial coding, I undertook a second cycle of "pattern coding" to develop an initial coding framework. This framework was applied to a sample of three interviews, which were then thoroughly reviewed and discussed with my supervisor (JL). These discussions led to the refinement of the identified themes and the coding framework.

Further refinements were made through additional discussions, ultimately resulting in consensus on the final themes. Representative quotations were selected to illustrate each theme. This collaborative process, involving multiple coders, is recognised as essential in qualitative research for ensuring rigour and credibility.

To support the coding and management of the qualitative data, QSR Nvivo-14 qualitative data analysis software was used. This software facilitated data organisation and ensured the systematic application of the coding framework.

4.3.9 Reflexivity

Unlike quantitative research, which seeks to uncover objective truths free from bias, qualitative research embraces subjectivity. Reflexivity is a key component of this approach, involving the ongoing process of recognising and critically examining the

researcher's role, biases, and influence throughout the study. By engaging in reflexivity, researchers can enhance the rigour, credibility, and ethical integrity of their findings. In this section, I reflect on how my background, experiences, and motivations shaped this research, both positively and negatively, and outline the measures taken to mitigate potential biases.

At the time of this study, I was a 34-year-old, white British female with 8 years of NHS experience, including 5 years of specialist training in Obstetrics and Gynaecology, where I developed a specific interest in maternal medicine. Prior to the SARS-CoV-2 pandemic, I was part of the team delivering GDM care at Study Site A.

My clinical background and connections within the diabetes in pregnancy network, along with those of my supervisor (RR), were instrumental in facilitating recruitment, providing valuable access during a time when engaging healthcare professionals was particularly challenging (226). While my clinical role helped build rapport and encouraged participants to provide rich, detailed accounts, it also presented potential challenges. Allied health professionals may have felt hesitant to disclose certain experiences due to perceived power dynamics. Similarly, senior medical colleagues might have withheld responses they were uncomfortable sharing with a peer or someone they viewed as a more junior.

Additionally, my expertise in diabetes in pregnancy meant participants sometimes communicated complex ideas implicitly, assuming shared understanding. This tacit knowledge occasionally led to incomplete verbalisation of key concepts. To address this, I consciously asked participants to explain ideas as if speaking to a non-clinical audience, prompting further elaboration when necessary. I also presented myself primarily as a researcher rather than a doctor to reduce hierarchical barriers, particularly when interviewing both senior colleagues and allied HCPs.

In Study Site A, where I had prior professional relationships, maintaining neutrality was particularly challenging. To mitigate this, I removed references to my clinical role (e.g., email signatures), conducted interviews from a neutral home office, and wore casual clothing to minimise hierarchical perceptions. These strategies aimed to create a comfortable, open environment, encouraging participants to share candidly.

As a novice qualitative researcher, I undertook formal training in qualitative methods through the Edinburgh Wellcome Trust Clinical Research Facility and Oxford University's courses. I further enhanced my skills through active participation in qualitative research reading group and mentorship from my supervisor, JL, an experienced qualitative researcher. These efforts equipped me to navigate the complexities of qualitative data collection and analysis with greater confidence and rigour.

4.4 Results

The results section begins with an overview of the three study sites and the participants involved. This is followed by three sections, addressing each of the research questions.

4.4.1 Study site description

Site A is a large urban tertiary centre in Scotland, providing GDM clinics across three hospital locations. The population primarily reflects the broader Scottish maternity demographic, being predominantly white Scottish, with a smaller proportion of women from various ethnic backgrounds, many of whom are second-generation British.

Site B is a medium sized maternity unit operating within a mixed urban and rural setting in England. Healthcare professionals deliver care in both tertiary and district general hospital environments, catering to a multi-ethnic population spanning diverse socioeconomic groups.

Site C is a single-centre medium sized maternity unit within district general hospital in England. It serves a predominantly ethnic population, primarily of Southeast Asian heritage, with a significant representation of lower socioeconomic and immigrant communities.

4.4.2 Characteristics of study participants

Table 2.1 presents the characteristics of the 23 interview participants, who were recruited from three sites across England and Scotland. It includes details on their professional roles, ages, years of clinical experience, and workplace site. The participants represent typical members of a multidisciplinary team managing GDM. All participants were employed in medium-sized maternity units (2,500–5,000 births per year) or large-sized units (over 5,000 births per year), as classified by delivery data from the national maternity audit. (https://maternityaudit.org.uk/). Participant ages ranged from 28 to 62 years, with clinical experience ranging from 1 to 23 years.

Participant	*Professional role*	*Age*	*Years experience*	*Site*
SA CM1	Community midwife	57	13	A
SA CM2	Community midwife	56	9	A
SA DC1	Consultant Diabetologist	48	7	A
SA DC2	Consultant Diabetologist	62	23	A
SA DSN1	Diabetes specialist nurse	55	17	A
SA MW1	Midwife	53	15	A
SA OC1	Obstetric Consultant	43	2.5	A
SA OC2	Obstetric Consultant	53	19	A
SA OR1	Obstetric Registrar	38	7	A
SB CM1	Community midwife	28	7	B
SB D1	Dietician	43	11	B
SB DC1	Consultant Diabetologist	44	5	B
SB DSN1	Diabetes specialist nurse	57	20	B
SB MW1	Midwife	35	3	B
SB OC1	Obstetric Consultant	37	2	B
SB OR1	Obstetric Registrar	30	6	B
SC CM1	Community midwife	35	1	C
SC D1	Dietician	41	19	C
SC DC1	Consultant Diabetologist	59	22	C
SC DSN1	Diabetes specialist nurse	54	12	C
SC HCA1	Healthcare assistant	56	6	C
SC OC1	Obstetric consultant	39	3	C
SC OC2	Obstetric consultant	49	10	C

Table 2 *Characteristics of study participants.*

4.4.3 How was care delivered before the SARS-CoV-2 pandemic?

To provide context on how antenatal care changed during the pandemic, I present themes identified through a thematic analysis of antenatal care provision before the pandemic.

4.4.3.1 Multidisciplinary team

Prior to the SARS-CoV-2 pandemic, all three sites delivered an MDT model of care. A range of HCPs fed into each individual MDT with participants describing their teams as *"cohesive"*, with HCPs appraising the MDT approach as offering a "shared understanding of the priorities" (SB DC2) and improving patient care and outcomes.

> "I think that the obstetrician learns about diabetes; the diabetologist learns about obstetrics; and in that way they are much better placed to counsel the patient… they're able to pick up on things that have been missed or perhaps misinterpreted, or slightly poorly explained to the patient." SA OC2

The delivery of MDT care varied both across and within sites. Some MDTs adopted a joint approach to consultations, whilst others saw patients individually.

> "We do it slightly differently across both clinics…at one site, we have the MDT in one room everyone sits together, and they see the woman together. But at the other site everybody's separate. So, they see the obstetrician with a midwife first, then they'll be called in to see the diabetes team after. And there's a dietitian as well in clinic". SB MW1

Across all but one site, HCPs reported that GDM care was predominantly led by medical staff "It was the preference of the clinicians that cover the clinics" (SB MW1). However, one clinic had a nurse-led service.

4.4.3.1.1 Remote consultations

Before the pandemic, all sites had traditional face-to-face appointments at frequent intervals, except one hospital at study site A which had already introduced remote care. This nurse-led "virtual" clinic used a web-based platform to access patients' blood

glucose readings for remote, telephone-based consultations focused on glycaemic review and medication management

> "They ran twice a week… if the doctors started them on metformin, they would book them into the virtual clinic, which is run by a DSN. We would phone these women up to review their blood glucose levels, and then decide if their metformin tablets needed to be increased or decide whether they needed to go onto insulin". SA DSN1

However, all sites had experience with telephone communication between face-to-face appointments. HCPs described this workload as "ad hoc," and as being handled by nurses.

> "We'd always say to patients that, if you've any issues, you know, then you can always ring us. So, we put the onus on the fact that the patients would ring us if they'd got an issue. So, we didn't have a specific clinic, but patients would ring throughout the week". SB MW1

4.4.3.1.2 Community midwife involvement

HCPs, including CMWs, noted that women often stopped receiving CMW care after a GDM diagnosis.

> "When they got diagnosed with GDM…their community midwifery care would stop because they would, in effect, transfer to the hospital base". SC D1

HCPs also described how the midwifery care received in the clinic took a medical rather than a holistic approach.

> "When they got diagnosed with GDM they'd see the clinic midwives…and didn't get a chance to get the touchy/feely, how are you? It's very much taking measurements…rather than the discussions and the conversations." SC CM1

4.4.3.2 Drivers of clinical practice

4.4.3.2.1 Population needs

Pre-pandemic, several key clinical drivers of care were identified, key amongst these being the needs of the population served. At study site C, for example, the patient population was described as comprising "*a lot of ethnic backgrounds, and lots of different cultures within the ethnic backgrounds*" (SC DC1) According to staff at this site, the need for language support at this site led to the decision to embed an interpreter into the clinical team:

> "The interpreter we have is Urdu-speaking. We use her in a dual role, where she educates patients on blood monitoring as well as providing language support." SC DSN 1

Additionally, this site delivered education sessions one-on-one rather than in groups to accommodate the large numbers of non-native English speakers:

4.4.3.2.2 Physical Space

HCPs widely agreed that physical space in the clinics partly dictated how MDT care was delivered.

> “the area where we do the clinic, there isn’t necessarily enough rooms to do all the consultations…so it was really based purely on room size, and what we could accommodate” SB DSN1

Furthermore, constraints on clinic space were described as leading to delays and then lengthy clinic appointments.

> “I think a lot of it was about, why can’t I have seen you all together in one room, it would have saved me a lot of time, I’ve been here since nine o'clock this morning. It was all about the logistics about the clinic room…it’s just situational”. SC DC1

4.4.3.3 Services under pressure

A prominent theme across HCPs accounts was the strain on GDM services before the pandemic. HCPs at the different study sites described overlapping causes and effects of this strain; and differences were seen in how individual sites adapted.

4.4.3.3.1 Too many patients

HCPs described a gradual increase in GDM cases over time. Despite allocating more resources to GDM, demand continued to outpace the service's capacity.

> “when we look back over the last 15 years, we just see our numbers rising and rising and rising.” SA DC1

The clinic environment was described as "*very crowded*," with HCPs noting frequent complaints from patients “*always asking, is it me next?" SB DSN1*

4.4.3.3.2 Inefficiencies

Many HCPs also highlighted inefficiencies in the care pathways, wherein, “the clinics are inefficient and cumbersome…they don’t always have the right people in the right places” SC DC1. Some HCPs felt inefficiency lay in the MDT model of care. This kind of approach resulted in their time not always being used optimally.

> “when we’re all in a room together, if a woman hasn’t had a scan or doesn’t necessarily need any input from an obstetrician, there’s not a lot we’re doing whilst they’re looking at the blood sugars”. SB OC1

Another issue reported across the sites were inefficiencies stemming from disjointed electronic documentation systems.

> “There are technological documentation issues between the two services because diabetes uses a different database to record information than the obstetric team. And so, it has required us to use two different computers, at least two different electronic patient record formats. And in terms of summarising the clinic documentation, that is also done in two different ways”. SA DC2

HCPs outlined how overcrowded services impacted the quality of care they could provide with numerous descriptions of cuts and compromises having been made.

> "we hit a point pre-COVID where we were so overwhelmed with patients with gestational diabetes that we had to reduce the frequency of clinic appointments just to be able to manage the sheer volume…care probably hasn’t been quite as we had originally intended”. SB MW1

HCPs further described how consultations had been limited to providing basic care which at times was felt to be substandard.

> "The time wasn't there to have those general conversations with the ladies, it was very 'get to the crux of the matter now'. And sometimes the ladies might just want to talk about their concerns". SB MW1

One HCP suggested that constricting their care provision had led to the overtreatment of women.

> "Unfortunately, due to numbers, we would not review patients unless they had a particular question…In terms of a routine review then we just didn't have the capacity…So for example if they came back in two weeks' time and all their results were high they may have automatically just started on Metformin when actually it may have been beneficial to look at that and make some other changes". SBD1

Several HCPs across all sites also described resultant dissatisfaction with their care provision.

> "It was very difficult to have those handovers between MDT colleagues about a patient because you just didn't have time to go and do that. It was literally on to the next one". SC D1

Together, oversubscribed, inefficient clinics and subsequent effects on care provision were described as having had a negative impact on staff wellbeing with several HCPs reporting unpleasant working environments and low morale.

> "We were struggling…because we just had so many ladies to get through. It wasn't a pleasant clinic for staff necessarily." SB MW

> "There's no let up. The clinic would start at nine o'clock…you'd would then be having patients back-to-back, no gaps. So you might then be finishing clinic at half two/three o'clock, and that's when you'd then get your lunch…it was really difficult". SC D1

4.4.3.3.3 Solutions

Prior to the pandemic HCPs described acknowledging that problems with their GDM clinics needed addressing but also that they were facing problems with funding to address these.

> "So pre-COVID, we were already at a position of, we need to do something about this as an MDT, but quite what, because how do we get the additional funding? How do we change?" SC D1

As previously described, one site (Site A) had already introduced some virtual clinics with HCPs at this site describing the need to reduce demand on the service as having been the main driver.

> "We developed a pilot scheme of virtual clinics....the intention of that was partly to offload the pressures on the clinic and it did have a massive impact on making the numbers manageable in clinics". SA DC1

4.4.4 RQ1. What did HCP do to reconfigure their services to provide remote ANC care and why?

4.4.4.1 Introduction of remote antenatal care

4.4.4.1.1 Variation in MDT approach

HCPs at all sites reported pivoting to remote ANC at the start of the SARS-CoV-2 pandemic, but their approaches varied. Some, for example, described maintaining their pre-pandemic MDT approach, while others conducted 1-1 consultations.

> "the biggest change has been by seeing women remotely, so not seeing them face to face in clinic but by speaking to them on the telephone…the clinic runs in the same way…the endocrinologist and I would telephone the patient and run through the consultation in exactly the same way as we would normally, both taking turns to speak to the patient." SA OR1

In some sites HCPs also described conducting consultations remotely from home.

> "when the pandemic first hit, we were advised from our department to do all our consultations remotely. So to not attend the clinic". SB D1

4.4.4.1.2 New technologies and communication methods

To deliver remote care, HCPs at all sites described using digital technology to access women's blood glucose readings by linking home blood glucose monitors to a smart phone-based app or web platform. For communication, HCPs primarily used telephones, with some using a written tool in the app.

> "we quickly got involved and we actually got remote monitoring brought in for our gestationals" SB DSN1

> "the main thing that we've changed, is there's a lot more telephone consultations now" SB CM1

4.4.4.1.3 The beginning of the hybrid model

In the first wave of the pandemic HCPs described making a pragmatic decision to allocate glycaemic reviews to allied HCPs (nurses, midwives and dieticians) and delivering these via remote consultations.

> "We've moved to virtual clinics...the virtual clinics being run by the diabetes specialist nurses, because they've not necessarily needed to be seen by the joint obstetrics diabetes clinic, and instead they've been getting interim appointments with the diabetes specialist nurse, by virtual clinic." SB OC1

HCPs at all sites reported rolling out remote glycaemic clinics for all patients, with those at Site A which had a virtual service in place reporting a rapid expansion of their service.

> "we would say from a DSN point of view...our virtual clinics absolutely took off. There was far more women and there are far more women being referred to the virtual clinics". SA DSN1

In addition to nurses delivering remote glycaemic reviews, some HCPs described hosting MDT consultations remotely whilst others continued to offer a reduced volume of face-to-face consultations and adopted a hybrid model of care.

> "The DSNs and consultants will see them only when they're coming back for scans. We will tie in the face-to-face with them then, and in between it's telephone. Now that's helped in terms of reducing footfall in the clinic" SC D1

One consistent finding was the number of consultations between patients and doctors reduced and the role of the allied health professionals in GDM care dominated during this time period.

> "We introduced an app, which means that they don't need to come in between their scans. So in the olden days they'd come, have their scan, then they'd come back in two weeks for us to see them. So now they don't come for that in-between visit. And then the nurses ring them in between" SB OC1

4.4.4.2 Shifts in HCP roles

HCPs further noted how during the early stages of the pandemic, delivering remote care had been made possible by expanding the team of allied health professionals through redeployment.

> "they had some community staff that were redeployed in COVID times. So the nurses and dieticians, we had more than we should have had, because they weren't doing their normal community job. So that was a positive in COVID" SB DC2

Another significant shift, according to these HCPs was the involvement of CMWs in GDM care.

"In the past, a gestational diabetic I would not see face-to-face from about 28/30 weeks because she would be seen so regularly at the diabetic clinic. Whereas now with virtual appointments, I would obviously have to see them face-to-face for their clinical check". SA CM2

4.4.4.3 Safeguarding patients and HCP

4.4.4.3.1 Spread of infection

Unsurprisingly, HCPs explained the primary motivator for moving to remote care delivery was to minimise the risk of spreading SARS-CoV-2 infection.

> "we were all quite frightened by the COVID pandemic and keen to make sure that we protected pregnant women...there was real anxiety around trying to be sure that we were doing the best for patients" SC D1

Additionally, HCP also talked about fear for their own health and safety and, more notably, concern for their families.

> "I have a vulnerable child so he went to live with my mum for three months... that was really hard...you knew you needed to protect". SB MW

> One of my consultants stopped all face-to-face contact until she'd had both vaccines. So that was difficult. I understand. She was in a high-risk group and was very worried about it". SB DSN1

Hence, the transition to remote care was described as allowing HCPs to continue providing essential services while safeguarding both their patients and themselves, addressing immediate health risks and demonstrating resilience to the uncertainties they faced.

4.4.4.3.2 Balancing risk

HCPs also described pressure from senior leadership to reduce patient contact.

> "We were asked to reduce numbers coming into the actual clinic face to face and do it all via video link or telephones". SB DSN1

However, this also resulted in several HCPs feeling a loss of autonomy and concern for some women's wellbeing.

> "The message coming from on high was one of panic and you mustn't see patients... it was quite difficult to ensure that we do deal with a high-risk group of patients and that their care wasn't compromised because that clearly wasn't appropriate for a lot of the people we saw. So, at the outset, we had to get that across, that we have to see people" SA DC1

Indeed, several HCPs explained how, at times, they had to fight against this pressure to protect the health of their patients.

> "As a team, we made the clinical decision it's inappropriate for women to wait that long between seeing us...Because there's a lot of things happening in ten weeks of pregnancy". SA CM2

4.4.4.3.3 Communication barriers

HCPs described that one of the main drivers for fighting to see at least some women face-to-face was the communication barriers they faced with women who did not speak English.

> "the interpreting service that we use is huge. Say I have ten patients diagnosed with GDM, minimum six will require interpreters... We could not have done this all remotely. So we earmark these women and actually bring them back to clinic. So not everyone is suitable. You triage them, you figure out who is suitable for

telephone consultations and who are suitable for face-to-face consultation". SC OC1

HCP reported that assessing women's suitability for remote care was more often nuanced, extending beyond a simple assessment of English-speaking ability to include elements such as comprehension and capacity.

"its not just communication but our ability to evaluate their understanding of what they should be doing is more challenging." SA DC1

HCPs described how accessing remote interpretation services presented another barrier, finding the process technically difficult and raising concerns around confidentiality.

"It became evident that we couldn't effectively use interpreters over the telephone, those three-way conversations did not work…Either we had difficulty connecting with the interpreting service, or the big word, or just having a three-way phone call; but we found that to be absolutely unworkable. So those women have all had to be seen face to face, or we have suboptimal virtual consults". SA OC1

"You would have an interpreter coming in on the call and then you've got the issue of confidentiality, who's in the room with the interpreter, you just don't know". SB MW1

4.4.4.4 Availability of technology

As HCPs noted, arguably the most fundamental thing that helped enable and drive delivery of remote care during the early stages of the pandemic was their ability to remotely access women's home blood glucose readings. While one site already had the technology in place to undertake remote monitoring and expanded the access to all women, HCPs at the other two sites reported how this technology had been provided free of charge by an external provider, for one year.

"they said we'll give you a year's free trial of this. And we thought, okay, well, it's a good time to try it out because we just cannot accommodate all these patients

face-to-face, then let’s give it a go. So we have moved a lot to remote diabetes consulting”. SC DC1

Themes	Subthemes	Key quotes
Delivery of remote Antenatal care	Change to MDT care provision	"Not seeing them face to face in clinic but by speaking to them on the telephone …the endocrinologist and I would telephone the patient and run through the consultation in exactly the same way as we would normally" SA OR1
	New technologies and communication	
	• Remote glycaemic management	"We quickly got involved and we actually got remote monitoring brought in for our gestationals" SB DSN1
	• Telephone consultations	"The main thing that we've changed, is there's a lot more telephone consultations now" SB CM1
	• Free provision	"They said we'll give you a year's free trial of this. And we thought, okay, well, it's a good time to try it out because we just cannot accommodate all these patients face-to-face, then let's give it a go" SC D1
	The beginning of the hybrid model	"We've moved to virtual clinics…the virtual clinics being run by the diabetes specialist nurses, because they've not necessarily needed to be seen by the joint obstetrics diabetes clinic, and instead they've been getting interim appointments with the diabetes specialist nurse, by virtual clinic." SB OC1
Shifts in HCP roles	Expansion of allied health care professionals	"They had some community staff that were redeployed in COVID times. So the nurses and dieticians, we had more than we should have had" SB DC2
Safeguarding patients and HCP	Spread of infection	"I have a vulnerable child so he went to live with my mum for three months… that was really hard…you knew you needed to protect" SB MW

	Balancing risk	"It was quite difficult to ensure that we do deal with a high-risk group of patients and that their care wasn't compromised because that clearly wasn't appropriate for a lot of the people we saw…we had to get that across, that we have to see people" SA DC1
	Remote communication	
	• Assessment of comprehension and capacity	"its not just communication but our ability to evaluate their understanding of what they should be doing is more challenging." SA DC1
	• Face to face care needed with language barriers	"It became evident that we couldn't effectively use interpreters over the telephone, those three-way conversations did not work" SA OC1

Table 3 Summary of themes and subthemes, identified during thematic analysis, with illustrative quotes for RQ1 What did HCP do to reconfigure their services to provide remote ANC care and why?

4.4.5 RQ2. What did healthcare professionals find successful and unsuccessful when delivering remote antenatal care, and why?

This section presents the findings from research question two: What did healthcare professionals find successful and unsuccessful in delivering remote antenatal care, and why? It begins with aspects of remote care delivery that HCPs found effective, before moving to the aspects that HCPs considered less successful. It also reports on strategies HCPs employed to address the challenges of remote care delivery.

4.4.5.1 What aspects of GDM care delivery were successful

4.4.5.1.1 Engagement

HCPs observed how most women had appeared to be actively engaged with remote care (e.g. telephone consultations and the use of app-based technology for blood glucose monitoring). They further observed how most such women had appeared to be happy and comfortable with remote consultations and had actively prepared for them e.g. by downloading the required software prior to an appointment.

> "they were more than happy, they were delighted, they were like, oh, great, I don't need to come to the hospital, that's great, I'm absolutely happy to speak with you on the phone". SA DSN 1

> "On the whole, it was a very motivated group, so they did engage on the phone. I got more patients ringing me or texting me with questions when I wasn't in clinic than I'd get when I was in clinic". SB D1

HCPs described how remote care delivery had been beneficial for women by avoiding lengthy hospital appointments (which were often accompanied by lengthy travel times) or spending money on childcare and travel. As they pointed out, this shift to remote care

aligned with women's changing needs and preferences, offering convenience and flexibility whilst managing their healthcare needs.

> "I think for the women like it because they don't have to come to hospital, it's a big thing for them. It takes a lot of time out their day coming to hospital all afternoon. A lot of them have got children and they weren't allowed to bring their children to hospital, so they needed to get childcare. So, I think a lot of them are quite happy with it." SA CM1

4.4.5.1.2 Independent decision-making

As reported above, HCPs noted how the introduction of remote antenatal diabetes clinics had resulted in a significant portion of the clinical workload being shifted to allied medical staff, such as DSNs and midwives. As they further pointed out, this transition had resulted in the latter taking on new roles and responsibilities within the GDM care pathway including the adoption and development of independent clinical decision-making. Participants suggested that by taking on greater responsibilities and being directly involved in the delivery of remote diabetes care, these professionals had gained confidence in making clinical decisions autonomously. They further suggested that this change had helped enhance the efficiency of the GDM care pathway as well as emphasising the value of allied medical staffs' expertise in delivering high-quality care.

> "we've trusted, if you like, our nurses to know at what point to escalate treatment." SA DC1

> "For some ladies I have been the one who they speak to the whole way through…I do the call at the start for their education…We start them on treatment if they need and when they needed insulin I saw them in the clinic for that…We can always ask the consultant if we need, but we rarely do, between us we just get on with it". SB MW1

HCPs further noted how the introduction of remote antenatal care had enabled DSNs and midwives to initiate medication via remote contact, a practice which had been uncommon prior to the start of the SARS-CoV-2 pandemic. They described several

benefits arising from this approach, including expediting treatment and facilitating dose titration. As they pointed out, by being able to start medications remotely, nurses and midwives had been able to address problems with glycaemic management without the delay which could arise from women having to attend in-person appointments.

> "Metformin is easy because all that's required with metformin is that we tell the patient that we are starting it and tell them how to take it over the phone. And we can send a message directly to the GP surgery…And within a day or two, they can get started on it." SC DC1

4.4.5.1.3 Forced evaluation of practice

HCPs described how transitioning to a remote model of care during the early stages of the pandemic had prompted an evaluation of existing clinical practices. In doing so, HCPs across all three sites identified historical idiosyncratic practices that were time-inefficient and lacked clear clinical benefit. One example was women attending weekly for fetal monitoring.

> "For GDMs, they would have a growth scan at 36 weeks and then CTGs weekly from 38 weeks until delivery. So, it is quite a big workload, and we did kind of feel that what were we gaining out of doing these CTGs. What reassurance was it giving us for the women? Is it worth doing or is it not worth doing? And then obviously when COVID came, they decided that they weren't going to do that anymore because they felt that it was something that perhaps wasn't needed. And so, we stopped doing the CTGs." SA MW1

Another common finding was a lack of available space in the clinic's pre-pandemic. At one site, limited space in the clinic led to consultations in an open bay area, raising concerns around confidentiality

> "You have just curtains between, so you've got a privacy issue there. You can hear what the other one is doing in the other bed, next door. Yeah, it was just messy." SC OC2

By introducing remote care HCPs described having been able to address some of their practices, streamline care delivery processes and optimise resource allocation.

4.4.5.1.4 Introducing technology

HCPs found additional advantages in using technology for GDM care. Including facilitating identification of women who were not engaging in self-management practices.

> "I think they probably cheated a bit more in the olden days because they would just fill the book in the day before they came to clinic, probably, make up some results. Whereas they can't cheat with this. It's better". SC OC2

HCPs further noted how they were better placed to detect women not engaging with care, more and offer greater support.

> "sometimes on a list I will jump back and forward, so there are certain women that you know, there's no point in me phoning them at nine o'clock in the morning because, actually, they won't be up at nine o'clock in the morning, so I know I won't get hold of them, so I might go, right, I'm going to phone them instead because I know that I'll speak to them now, because you get to know the women quite well." SA DSN 1

Additionally, HCPs reported a confidence in prescribing, due to their increased confidence in the reliability of the data there were able to use to base prescribing decisions on.

> "I think it gives you more security, because obviously they can't fudge the readings, so hopefully my prescribing decisions can be made more reliable". SB DSN

One tool, the GDM Health App, adopted at two study sites, was described as offering several features that were beneficial for women and HCPs.

1. **Traffic light tool for visualizing glucose levels**: This feature was described as providing a straightforward way for women to interpret their blood glucose readings. HCPs suggested that by using a color-coded system women could

easily understand whether their blood glucose levels were within acceptable limits or required attention. They further suggested that this visual representation could help those individuals who had previously struggled to interpret numerical readings.

"Most of the women I've met seemed to like the app. It's got, a green if it's normal, red if it's high, blue if it's low. I think they like the visual, like, knowing, what their sugars are and a visual reminder of, I've been high all day, I need to... Rather than just writing down numbers". SB CM1

2. **Recording of dietary intake**: HCPs found women engaged well with this feature and suggested that it promoted greater awareness of dietary habits and helped empower women to adopt healthier food choices.

"I find that if they are writing down what they've eaten, then they have a better understanding of why their levels are going up or not going up... I'm finding more are putting the food into the app and therefore they are more engaged because they've got a greater understanding." SB D1

The function to record dietary intake along with blood glucose readings was described as a valuable tool for HCPs, particularly dieticians. By having access to these data, dieticians described being better able to correlate dietary habits with blood glucose levels, enabling them to identify trends, triggers, and potential areas for intervention. Dietitians expressed that this technology allowed them to offer personalised dietary guidance and support that helped to address women's unique circumstances and needs.

"it feels that actually we are managing to make a difference with these ladies. Seeing what (dietary) changes they have made already, and then being able to have a discussion with them and, okay, and if we do this as well and we tweak this a little bit further, let's give you another week. Let's review it again next week. We let the nurse review it again next week. And actually if we do these couple of changes, we can probably get your levels to a point where you can continue on diet control rather than it being you need to start medication now." SC D1

3. **Free text/chat function for communication and documentation**: HCPs reported how the chat function within the App had provided a convenient and quick platform for communicating and had further help to reduce barriers to receiving prompt and timely care:

   "We could just text them back on the app, so we didn't necessarily always need to speak to them face to face." SB DSN 1

   "They can request for a call back if they want to discuss their blood sugars…that's the positive of the technology…we can communicate with the patient without waiting for them to come to clinic and tell us what problems they're having". SC DSN1

4.4.5.1.5 Relieving the burdensome GDM clinics

Introducing remote care was described as having dramatically reduced the number of women physically attending GDM clinics.

"overnight our numbers in the clinic dropped by at least 70%". SB OC1

While this approach aligned with efforts to minimise exposure to the SARS-CoV-2 virus HCPs noted how it has also helped address pressures within GDM care provision that the health service experienced before the onset of the pandemic. Furthermore, by reducing the number of in-person visits HCPs described having more time to allocate to women, especially those requiring additional support:

"I had a little extra time, I was able to then actually follow up those ladies more. They had my telephone number, because I was contacting them. So I actually found that if they had any problems they contacted me directly a little bit more frequently than they did before. And I actually had that extra time to spend." SB D1

4.4.5.1.6 Improved job satisfaction

Delivering remote antenatal care appeared to improve HCP's job satisfaction. HCPs described providing better quality of care whist at the same time as making the service more convenient for women. One HCP described how remote care facilitated delivering personalised care, which gave them a greater sense of fulfilment and job satisfaction.

> "I think with the GDM Health app you feel more satisfied because you're physically being able to tailor your advice more effectively and you're being able to see whether it actually works or not". SC D1

Other accounts highlighted how tools for delivering remote care had made day-to-day tasks easier, improving efficiency and enhancing the overall quality of their working day.

> "it's always nice having a less horribly busy clinic, so that's definitely got advantages in terms of not feeling like you're rushing everyone and not keeping people late, because we did often run late, and obviously that makes patients and staff quite unhappy". SB OR1

4.4.5.2 What aspects of GDM care delivery was less successful?

4.4.5.2.1 Women's availability

During the early stages of the pandemic, HCPs observed a high level of participation in remote consultations due to the increased availability during lockdown periods. However, they went on to raise concerns about women's availability once physical distancing measures were no longer in place:

> "now that people are a bit freer and more mobile, sometimes getting hold of them is tricky…". SB CM1

HCPs also voiced concerns about support networks for women when delivering care remotely. They suggested that the presence of a support person (such as a partner), during clinic appointments could greatly enhance the effectiveness of care and noted that this component could thus be lost when providing care remotely.

> "We found that when partners came, they maybe had some unrealistic expectations of the lady or there was some blame for getting gestational diabetes. We were very clear to say you've not caused this. And that helped to settle any disputes at home, whereas now they're not getting the chance to hear that." SC D1

4.4.5.2.2 Delivering remote education

HCPs also described encountering challenges in delivering education remotely through telephone consultations. Across all three sites, HCPs reported attempting this method

but finding it to be universally unsuccessful. They unanimously agreed that group delivery is preferable citing reasons such as efficiency and shared learning from group involvement.

> "So they would have a two hour session, they'd get eight women done. It takes quite a long time to deliver that one-to-one for eight women…so doing one-to-one virtual education for every patient is quite a challenge for our team." SA DC1

> "I think we gave a better service when we were doing it as a group session together…there is definitely a benefit of having a group because I think the women gain from each other when they're meeting together in a group." SA DSN1

Hence, at all three sites, HCPs described having already returned to or planning to return to face-to-face group education sessions.

4.4.5.2.3 Decline in antenatal care provision

As previously noted, prior to SARS-Co-2 pandemic the majority of midwifery care for GDM was delivered by staff at the antenatal diabetes clinic, often weekly in later pregnancy. During the early stages of the pandemic, visits to the antenatal diabetes clinic decreased and women were advised to attend their community midwife for antenatal reviews. However, HCPs reported that women's general antenatal needs had been compromised as a consequence.

> "We kept reminding women to make contact and see their midwife and often we would phone again in another couple of weeks and they had not been seen by the community team." SB OC1

HCPs further observed that community midwives' workloads had increased during the early phases of the pandemic, due to these individuals taking on additional tasks previously carried out by other HCPs.

> "we would have to do extra because the GP wasn't seeing patients or their health visitor couldn't do it, so we would have to do it. And because the health visitors were trying not to go in to see the women so much it seemed that we were doing everyone else's work for them. We also had to do extra training so that we could

> do all the vaccines as well to stop women having to go to the doctors for the vaccinations." SC CM1

4.4.5.2.4 Shifting the GDM workload

Across all study sites, HCPs reported how moving to a remote model of care had placed increased demands on allied health professional resources, caused by large a proportion of the GDM workload moving onto the nursing and dietetics team.

> "What it has meant is that we've had to pick up additional work. We've now got this additional telephone clinic and the nurse that got the additional telephone clinic on top of everything else that we're doing as well.

Several of the allied healthcare providers, notably nursing and midwifery staff, described difficulties they faced taking on this additional workload, examples included feeling overwhelmed by having to take on extra work, particularity with hidden elements of care provisioning such as administrative tasks. HCPs described examples where this had led to stress and, in extreme cases to staff needing to take time off work:

> "we had one member of staff that was off for months, that obviously had a big knock-on effect for the rest of us as well, who were already stressed and then had to pick up the pieces. I definitely had a meltdown one day on the phone, I phoned my boss and she talked me down. But there was one of the other midwives went off for weeks too." SC CMW 1

While, overall, nurses, midwives, and dieticians described having been determined to make the remote care model successful because "*we all agreed it actually makes sense*" *(SA MW1)* they also raised additional negative issues aside from staff sickness, including being uncomfortable and unprepared for their new clinical duties.

> "I rang a lady last week, I could see that there's no blood glucose levels, so I was asking her, is there an issue?...And she told me, I've just lost my baby. So, you're getting those conversations, which we never had before...It's hard especially when my midwifery background was zilch". SC DSN 1

4.4.5.2.5 Disconnected multidisciplinary team

When describing their experiences of remote care, HCPs reported feeling isolated and disconnected from their team and missing the camaraderie and friendly contact with their colleagues.

> "I don't think we will we ever go back to full face to face consultations, and it's a shame because it's changed the dynamics in the team as well so we don't see the medical staff... before they would drop in for a chat, it's just a different working environment". SA DSN1

Many also indicated the potential negative impacts on women's care which had resulted from them missing out on opportunities to share clinical knowledge and expertise in face-to-face team settings.

> "I think there's definitely benefits for us to be more cohesive as a team if we're all seeing a patient together, and we can bounce ideas off each other and interact. That's more difficult if the diabetologist is on the phone to the patient." SB OR1

HCPs also noted how communicating clinical information to other team members was more difficult and cumbersome, raising concerns about clinical error making. As they pointed out, while previously, important information could be easily communicated during clinic conversations, this now had to be communicated by ineffective electronic patient record systems.

> "I would be writing on an electronic system for our records, which they don't have access to in that clinic. So I would message to the lead, and say these are the ladies I've seen, these are the issues, these would be my recommendations. And then they would have to make sure that information got cascaded to whoever was seeing that lady. So I think there was a big gap there". SC D1

4.4.5.2.6 IT infrastructure and equipment

While embedding technology to remotely access women's blood glucose readings was widely regarded as successful by HCPs, other technologies aimed at facilitating remote consultations were considered to have been less successful. Across all three sites, HCPs reported encountering challenges with equipment for conducting remote

consultations, including poor internet connections and shortages of computing equipment, such as laptops and telephone/video communication devices. HCPs also reported having to use their own mobile phones to contact women. This makeshift approach enabled communication but, as they suggested, did not provide an appropriate platform for delivering comprehensive care remotely.

> "the clinic phone doesn't have a speaker phone facility and therefore people have had to use their own personal mobile phone in order to conduct a work consultation, which I think is completely unacceptable because our employer should provide the means to be able to deliver the way that you're delivering care". SA OR1

Themes	Subthemes	Key quotes
Engagement	Women engaged in remote care	"it was a very motivated group… they did engage on the phone. I got more patients ringing me or texting me with questions when I wasn't in clinic than I'd get when I was in clinic" (SB D1)
	Women's availability reduced over time	"Now that people are a bit freer and more mobile, sometimes getting hold of them is tricky…" SB CM1
	Remote education didn't work	"I think we gave a better service when we were doing it as a group …there is definitely a benefit of having a group because I think the women gain from each other." SA DSN1
	Remote medication	"Metformin is easy because all that's required with metformin is that we tell the patient that we are starting it and tell them how to take it over the phone" SC DC1
	Technology	"I'm finding more are putting the food into the app and therefore they are more engaged because they've got a greater understanding." SB D1
	• Simple tools for visualization and data capture	".It's a green if it's normal, red if it's high, blue if it's low. knowing what their sugars are and a visual reminder of, I've been high all day, I need to call.. Rather than just writing down numbers". SB CM1
	• Facilitating communication	
Allied health professional led care	Independent decision-making	"For some ladies I have been the one who they speak to the whole way through…I do the call at the start for their education…We start them on treatment if they need …We can always ask the consultant if we need, but we rarely do, between us we just get on with it." SB MW1
	Shifting the GDM workload	So there's an additional 60 ladies to ring each week." SC D1
	Unprepared	"I rang a lady last week with no blood glucose levels, I was asking her, is there an issue?…And she told me, I've just lost my baby. So, you're getting those conversations, which we never had before." SC DSN 1

A disconnected MDT	Isolation	"I don't think we will we ever go back to full face to face consultations, and it's a shame because it's changed the dynamics in the team as well so we don't see the medical staff… before they would drop in for a chat, it's just a different working environment". SA DSN1
	Loss of shared clinical knowledge	"Benefits for us to be more cohesive as a team if we're all seeing a patient together, and we can bounce ideas off each other and interact." SB OR1
	Lack of IT infrastructure and equipment	"I would be writing on an electronic system for our records, which they don't have access to in that clinic." SC D1
	Decline in antenatal care provision	"We kept reminding women to make contact and see their midwife and often we would phone again in another couple of weeks and they had not been seen by the community team." SB OC1
Forced an evaluation of practice	Inefficient and non-evidenced based practices identified	"when COVID came, they decided that they weren't going to do that anymore because they felt that it was something that perhaps wasn't needed. And so, we stopped doing the CTGs." SA MW1
	No capacity for community midwifes to deliver GDM care	"We kept reminding women to make contact and see their midwife and often we would phone again in another couple of weeks and they had not been seen by the community team." SB OC1
	Relieving burdensome GDM clinics	"I had a little extra time, I was able to then actually follow up those ladies more. They had my telephone number, because I was contacting them. So I actually found that if they had any problems they contacted me directly a little bit more frequently than they did before. And I actually had that extra time to spend." SB D1

Table 4 Summary of themes and subthemes, identified during thematic analysis, with illustrative quotes for RQ2. What did HCPs find successful and unsuccessful when delivering multidisciplinary care during the early phases of the pandemic and why?

4.4.6 RQ 3. What lessons can be learnt from delivering remote multidisciplinary GDM care during the pandemic and which aspects of pandemic GDM care delivery do HCPs think should be retained in the longer-term, and why?

The final results section will address the third research question: What lessons can be learnt from delivering multidisciplinary GDM care during the pandemic and what aspects of care do HCPs think should be retained in the longer term, and why?

4.4.6.1 A hybrid model of care is best

HCPs reported many advantages to delivering GDM care remotely; in particular they highlighted the advantageous role it played in management of glycaemia. However, when one site (Site A) transitioned to a fully remote service at the beginning of the pandemic, HCPs described being concerned women were not receiving adequate care; specially, that obstetric examinations had been neglected.

> "end of the bed clinical appearance and whether someone looks like they have a macrosomic bump on board or polyhydramnios, things like that. Other things in clinical examination, subtle things like oedema, features of preeclampsia, things like that." SA OR1

Consequently, HCPs at this site agreed that some degree of face-to-face interaction was vital for ensuring comprehensive care for all women with GDM.

Other study sites (sites B and C) transitioned less dramatically, moving from a face-to-face to a hybrid model. In these sites, HCPs also concluded that the optimal model for GDM care should utilise remote care alongside face-to-face appointments timed to take place at key points in women's GDM journey, including at the time of diagnosis and near to delivery.

> "I don't think everything should be dealt with over the phone, because they have a lot of questions, they usually see the dietitian, they get to meet the people that they're speaking to on the phone. I think it's probably quite important to still keep

> at least one appointment at the start, but there is scope to cut down how frequently we're bringing people up to the hospital". SB DSN 1

Indeed, HCPs appeared committed and motivated to use a hybrid model moving forwards. This was demonstrated by various HCPs describing how they planned to overcome the problems they had experienced with remote consultations by, for instance, securing appropriate funding and staffing arrangements.

> "we are pleased with it...We are looking into how their activity could be captured and job-planned". SC OC1

Some HCPs also described seeking evidence which would give them the guidance and support they needed to continue delivering care using a hybrid model.

> "I potentially would like to continue doing the gestationals the way we're doing it. I'd like to see some audit results from pre- and post-COVID and then as a team we could make a decision and hopefully put forward a case to continue the model" SB D1

4.4.6.2 Change in practice requires a "driver"

During the interviews HCP discussed GDM care provision beyond the first wave of the pandemic. They emphasised the need to properly consolidate the temporary changes hurriedly introduced during the first wave, ensuring that a hybrid care model becomes the standard approach moving forward. Additionally, they highlighted the importance of having a 'driver' within the team—someone responsible for advocating and pushing for further changes in the future."

> "You need to get a group of people together to look at what's available. You need someone with good technology experience to drive the team, to say this is what we're going to do. And I think it's probably taken that long because there hasn't been anybody with that drive to do it". SB D1

They acknowledged that, without this, future GDM services would be slow to evolve and could potentially stagnate.

> "I think it is down to that person who drives it. Because I wouldn't be a person who went oh look, this is around. I'd be the person who thought I need to go on a million

> courses to know how to use that. Whereas some people do really drive things forward and get stuff done. And without a person like that on your side things could slip back to the old ways, of not really looking at, or trying new things." SC D1

Despite recognising the need for a motivator, many HCPs, especially doctors, felt it was not their role to be the driver for change.

> "Clinicians are consumed with delivering clinical care and don't have time to think about different ways of doing that. I don't think that clinicians are the people necessarily to drive that forward. But I think that they would be willing to embrace it." SB DC1

Several HCPs attributed the success of their transition to remote delivery to the diabetes nursing staff who most readily and quickly adapted to taking on new technology and adopting and developing new working arrangements.

> "It basically worked because of the nursing staff. Because they took on that role of ringing the women up...that took the App, figured it all out and ran with it". SC DC1

4.4.6.3 Remote antenatal care will not fix the GDM workload

As highlighted earlier, during the early stages of the SARS-CoV-2 pandemic, allied health professionals took on a significant portion of the remote care delivery workload. As also indicated earlier, these individuals reported a general willingness to take on the additional workload because it made sense to do so at the time and had helped alleviate some of the pressure faced in the clinics.

However, despite these positive descriptions, HCPs raised concerns that moving the workload into remote clinics merely diverted rather than reduced the workload problem they had faced before the pandemic. This concern was expressed by both medical and allied health professionals in the GDM MDT.

> “The two clinics a week was becoming overwhelmed before we went to the telephone model. But in a way, all the telephone model has achieved is to put those patients into a less conspicuous place”. SB DC1

HCPs further noted how the workload had been absorbed by existing and redeployed staff during the first wave of the pandemic, without any extra funding or additional resources. Hence there was a unanimous view that, in order to deliver remote care effectively, there would need to be a substantial uplift in staff resourcing.

> “we need more virtual DSN time to do the virtual clinics. If we’re going to then adjust the frequency with which we see women and allow more of the glycaemic reviews to be virtual, that needs additional resource” SA DC1

> “if I had more time in my job plan, I could use the app and target the ladies… Because it actually tells you who is out of target. I could definitely improve their sugars if we could work like that”. SB D1

When they shared these opinions and views, HCPs also identified a need for investment beyond additional clinical staff to include greater administrative support:

> “we desperately need administrative support to oversee in what way patients are booked in to clinics, making sure that their education session happen in the right order. Having an oversight of which results then need to be followed up, for example, in the postnatal period. And I think an administrator would be really valuable”. SA DC1

When they offered these kinds of suggestions, HCPs also noted the challenges posed by wider staff shortages within the NHS, particularly when it came to achieving a workforce which was equipped to deliver a remote GDM service. In doing so, HCPs tried to identify solutions, including creating new roles in the MDT, but also acknowledged that some of their suggestions would be difficult to achieve, and might require time, effort and a need to compromise:

> "A specialist midwife would take on some of our role (medical consultant) and some of the diabetes nurse specialist roles. But maybe I’m wrong; maybe it's harder to get midwives these days than nurses, so maybe we should get the

> nurses to do what nurses can do and leave the midwives to concentrate on giving midwifery care. A specialist midwife would be good. Although you probably need more than one." (SC OC2)

4.4.6.4 Technology was not perceived to be a barrier

At the start of the pandemic, HCPs raised their concerns about women struggling to navigate the technology required for remote care. However, many reported women readily adapted, realising a greater level of digital literacy than initially expected.

> "At the beginning, there was a lot of anxiety about whether patients would get on board. But in practice, we actually found our women were generally downloading and used the app... with minimal issues. Majority were quite tech-savvy or had support from a family member to get them going." SB D1

They reported that it was unusual to encounter women without access to or an understanding of how to use technology. This was even the case at the site (site C) serving a highly deprived population, where access to technology was described as remarkably high.

> "I think the main concern people had was that people wouldn't have their own phones, that they shared phones or it was, the husband's phone and things like that. But I would say over the last year it's really not very often. I don't think it's been a big issue." SC OC2

Based on these experiences, HCPs suggested that it was feasible and realistic to expect that most women will have access to, and be able to use, technology to support remote care delivery in the future.

Other accounts offered examples of where remote care had overcome a perceived barrier to receiving remote care. The former included a Doctor at site C who offered the following reflections:

> "Telephone consultations with an interpreter, so you're having a three-way telephone conversation, actually I think works remarkably well. I was surprised at just how successful three-way telephone consultations were there....it's more

> convenient than having an interpreter come physically to the clinic. And that would be an obvious expected weakness that's proved not to be the case". SC DC1

HCPs outlined how they made adaptions for women who had limited access to technology to allow them to receive remote care. One example included always calling women rather than expecting women to make contact, acknowledging that many women may have phones but may not be in a position to use phone credit to make calls.

> "and there have been certain other things I have done, for people who have been a bit disadvantaged…we tend to phone women…they are usually able to take calls" SA DCN1

However, amongst these reports of successful integration of technology into GDM care HCPs also acknowledged problems with providing equitable care for all women using a remote model.

> "There needs to be equity of care. The virtual access with the technology is brilliant, but what about those people that it doesn't suit? We need to make sure that they're getting…it might not be the same service but it needs to be equitable. We can't be missing those ladies out because their care is important too, and their outcomes are important to. I do think we are getting the right balance for them now". SC D1

4.4.6.5 Developing technologies and IT

When they reflected upon their experience of using web or App based tools, many HCPs expressed the need for technology to be user friendly for patients, describing this as a key determinant for the success of remote care.

> "Its got to be the future that we've got remote access to data, preferably with minimum effort on the part of the patients. Because at the beginning of the pandemic when we were trying to get people to upload their data, they couldn't bothered, you know, they couldn't find or they couldn't be bothered to ask the manufacturers for a USB cable, or they didn't have an appropriate computer, they

> just couldn't be bothered. So we were back to the bad old days when we said what have your blood sugars been like and they say fine. And that was about as much information as you could realistically get". SC DC1

Across all sites HCP described problems integrating new technologies into existing IT infrastructure. All sites described using multiple systems for documentation and HCPs described how remote technology added another layer into an existing complex network of digital systems. HCPs identified to deliver a hybrid MDT model of care effectively, a unified IT system would be required.

> "The doctors and midwives in maternity use one system. The rest of the hospital use a different system. And then the diabetes team use neither; they use something else which is an outpatient setting system. So I can't see what they've written…sometimes it looks like nobody's seeing these women, because people haven't documented. They say well we haven't got time to document here because we're documenting on all these other systems.. We really need a single system". SC D1

4.4.6.6 Less medical focused model of care

HCPs uniformly shared a vision for GDM care beyond the acute phase of the pandemic. This vision included fewer appointments with doctors and continuation of remote glycaemic management led by Allied health professionals

> "I think it would possible with appropriate staffing to expand the virtual service and to make sure that we really only bring people up to clinic face-to-face where necessary. So I imagine that compared with pre-pandemic, there might be a more streamlined appointment schedule for women with more virtual reviews. But those virtual reviews could be done by the diabetes educators rather than by the joint consultants in diabetes and obstetrics." SA OC2

Medical staff expressed confidence that allied health professionals were capable of performing this role.

> "I think it's absolutely brilliant. I think it's the way forward, and I think post-pandemic, if there is a post-pandemic, we should do more of that. The DSNs are very, very thorough, they're very, I would say proactive with the women." SB DC2

However, for this to be feasible, they anticipated a need for expansion and upskilling of roles alongside existing staff.

> "I think there would be a role for a specialist midwife who could see women with either the diabetes specialist nurse or the diabetologist in place of the obstetrician, when there wasn't obstetric input required.... it would be very valuable if we could have one." SA OC1

Medical staff described being better placed to support allied health professionals and manage high risk patients or complications when they arose, noting times where they had facilitated the continuation of remote care by providing support and guidance.

> "We realised things weren't working, I think we needed to have more joined up communication with them (nurses). We then developed a flow sheet for them which we agreed that patients who needed insulin therapy should return to our clinic." SA DC1

HCPs perceived remote care delivered by AHPs could feasibly resolve the burden GDM is placing on antenatal services

> "We could have potentially far fewer labour and cost intensive hospital-based appointments, and instead we move the care to other individuals who have appropriate training and know at what point they need to then refer them back in for specialist care." SA DC1

Some HCPs outlined a model of care where women without complex needs could be co-cared for by specialist diabetes AHPs and community midwifes. They caveated this by underscoring the need for options for escalation when required.

> "So for example, we would not be able to take on the blood sugar monitoring. So that should be done by the diabetic team. And if that remains normal then we could see the women from an obstetric point...or from a midwifery point of view,

so that the diabetes aspect is dealt with by diabetic nurses.... we would need robust guidelines but I could see that working for straightforward ladies." SC CM1

Other HCPs felt this model would need rigid guidelines to be feasible.

"to manage the risk and we would need guidelines for us to tell the woman what risks there is or there isn't." SA MW1

Other perceived advantages of an allied health professional led model of care included involvement with community midwifery teams who could offer continuity of care for women.

"A lot of diabetic women miss out on the community side of the care, because they come into clinic appointments. I think it's nice for the women to have a named midwife who they can see in their diabetes care and they know they've got someone to go to if they've got any questions. They've got an extra phone number to ring as well. If they're having problems with their meter or with anything else, they can contact us. So I think it does benefit the women in a lot of ways." SA MW1

Themes	Subthemes	Key quotes
A hybrid model of care is best	Some degree of face-to-face is vital	"I don't think everything should be dealt with over the phone, I think it's probably quite important to still keep at least one appointment at the start, but there is scope to cut down how frequently we're bringing people up to the hospital". SB DSN 1
	Committed to continue • Remote glycaemic monitoring technologies	"we are pleased with it...We are looking into how their activity could be captured and job-planned". SC OC1
	Technology was not a barrier	"I think the main concern people had was that people wouldn't have their own phones...But it's really not very often. I don't think it's been a big issue." SC OC2
Change in practice requires a driver	Progress could easily stagnate	"You need someone with good technology experience to drive the team, to say this is what we're going to do. And I think it's probably taken that long because there hasn't been anybody with that drive to do it". SB D1
Remote antenatal care will not fix the GDM workload	Investment needed in Allied health professionals	"We need more virtual DSN time to do the virtual clinics. If we're going to then adjust the frequency with which we see women and allow more of the glycaemic reviews to be virtual, that needs additional resource" SA DC1
Less medical focused model of care	Allied health professionals leading care	"We could have potentially far fewer labour and cost intensive hospital-based appointments, and instead we move the care to other individuals who have appropriate training and know at what point they need to then refer them back in for specialist care." SA DC1
	Identification of suitable patients is a challenge	"We realised things weren't working, we then developed a flow sheet for them (nurses) which we agreed that patients who needed insulin therapy should return to our clinic." SA DC1

Table 5 Summary of themes and subthemes, identified during thematic analysis, with illustrative quotes for RQ3. What lessons can be learnt from delivering remote multidisciplinary GDM care during the pandemic

4.5 Discussion

This discussion summarises the key findings in relation to the study's research questions and the existing literature. Finally, it considers areas for future research and connects the qualitative study findings to the broader research presented in this thesis.

4.5.1 Summary of findings

4.5.1.1 Pre-pandemic care

The enforced changes in practice during the pandemic provided HCPs with a unique opportunity to evaluate and reflect on GDM care provision before the pandemic. HCPs noted that GDM services were traditionally shaped by local population needs and advocated for a multidisciplinary care model. However, the growing GDM population, combined with inefficient clinic structures, strained the delivery of care. This strain was evident in accounts of dissatisfaction with care provision, which revealed sobering insights into the neglect of general antenatal care, outdated practices, and potential over-medicalization. These concerns align with findings from national inquiries, such as the Ockenden Review, highlighting numerous failings in maternity care (227).

A 2020 government report noted a decline in maternity care quality over the previous five years, while the Care Quality Commission's 2019 report found 6% of maternity units inadequate and 33% needing improvement (228). High burnout rates and a decline in experienced midwives were central issues (229). A 2020 Royal College of Midwives (RCM) survey found that over half of midwives considered leaving their jobs, with 57% planning to leave the NHS within a year, citing staffing shortages and dissatisfaction with care quality (230).

These findings underscore the significant issues with general antenatal services in the NHS prior to the pandemic. The perspectives and experiences of HCPs delivering remote multidisciplinary care to women in the early phases of the pandemic, as presented in this study, must be viewed within this broader context.

4.5.1.2 The evolution of services

At the onset of the pandemic, HCPs described swiftly pivoting their approach to delivering remote GDM care. They were driven by concern for patient safety and a

profound sense of duty to protect themselves, their family and their colleagues. This paradigm shift in antenatal care provision was seen in the NHS (198) and globally with increases in virtual or remote antenatal care and decreases in the numbers of antenatal clinic visits occurring in both high and low resource settings (231, 232).

4.5.1.3 Adoption of remote glycaemic management

HCPs adopted and expanded remote care primarily through technology to manage women's blood glucose levels, significantly altering their roles in GDM care. Whereas doctors and nurses previously shared responsibility in face-to-face multidisciplinary clinics, remote glycaemic management became predominantly the responsibility of allied health professionals, leading to fewer medically-led consultations. This shift resulted in a substantial workload increase for allied health professionals. Despite this, many allied health professionals expressed satisfaction and gratification with their new roles, citing increased autonomy in clinical decision-making, improved efficiency and a perceived preference for remote care among women. This study did not evaluate women's experience of receiving virtual care during the pandemic, however findings indicate high satisfaction and a preference for remote glycaemic management with studies in Canada and Australia reporting women favoured the improved organization and reduced appointment wait-times, supporting the perceptions of HCPs in this study (131, 226, 233, 234).

Overall, both allied health professionals and medical staff viewed the shift to remote glycaemic management and the reconfiguration of roles positively. These findings are consistent with the ASPIRE-COVID-19 Collaborative study examining the impact of the pandemic on NHS maternity staff experience. They reported how an influx of staff and resources, along with a sense of camaraderie, public support, and professional pride, contributed to an unexpectedly positive work environment (235). Similarly, in Canada, the evaluation of virtual care for GDM during the pandemic revealed that HCPs were generally satisfied with the transition to virtual care, despite initial concerns from nurses about an increased workload (234).

4.5.1.4 HCP fatigue

Amidst positive experiences of delivering remote GDM care, concerns were voiced about the sustainability of virtual clinical care. HCPs noted that while remote care had seemingly improved some pre-existing issues, such as long waiting times, it had only served to shift the workload burden rather than truly addressing it. In the ASPIRE study, researchers found that in the early pandemic protective factors that initially created a positive work environment eventually waned, leading to unmanageable workloads for HCPs (235). Reports of "compassion fatigue," poor staff recruitment and retention, and soaring workloads painted a picture of extreme burnout among antenatal care providers in the NHS.

While my findings do not indicate severe burnout among GDM care providers, early signs of fatigue were evident across all study sites. A key responsibility of healthcare professionals (HCPs) is to drive improvements in clinical care. However, my findings revealed that many HCPs felt it was either not their responsibility or that they lacked the time and energy to initiate changes. These observations point to emerging fatigue among HCPs.

The difference between my findings and those of the ASPIRE research team may be due to the timing of data collection. The ASPIRE study, which continued recruiting until October 2021—nearly two years into the pandemic—was better positioned to capture longer-term impacts.

Interestingly, fatigue has not been reported in studies examining remote care in non-NHS settings. This could reflect the timing of those studies, most of which were conducted during the first wave of the pandemic. Alternatively, it might highlight longstanding inadequacies in antenatal care provision that participants identified as pre-dating the pandemic.

4.5.1.5 Clinical activities not suited to virtual delivery

Not all aspects of remote GDM care were perceived to be as effective as remote glycaemic management, particularly in the delivery of education. HCPs expressed a preference for traditional group-based, face-to-face education over one-on-one virtual

sessions. Similar findings were observed in a Canadian study, where nursing staff reported greater difficulty gauging patient engagement during video sessions compared to in-person interactions(234). This preference for group education was recognised even before the SARS-CoV-2 pandemic, as studies suggested that group settings not only helped manage increasing workloads more efficiently but were also perceived by women as more beneficial (236, 237).

4.5.1.6 Embedding technology into GDM care

HCPs working in the NHS reported the benefits of remote glycaemic management, emphasising its convenience and efficiency. Beyond reducing clinic visits, HCPs noted unexpected advantages, such as quickly identifying women not engaging with GDM care. Other studies exploring the acceptability and experience of receiving diabetes and antenatal care via telehealth during the pandemic reported that it improved access to care (238), particularly for "hard-to-reach" women who might otherwise miss appointments (226).

Initially, HCPs were concerned about women's ability to use technology, but adoption was more successful than expected, due to factors including:

1. **Access to technology**: Most women had the necessary technology, reducing but not eliminating concerns about digital poverty in the particular sites involved in this study.
2. **Patient Adaptability**: Many women were described as more "tech-savvy" and adaptable than initially thought.
3. **Support Systems**: Women often received help from family or friends to navigate the technology.
4. **User-Friendly Design**: The tools, such as GDM health apps, were user-friendly, making them accessible to a wide range of users.

This ease of adoption for many women was seen as contributing to the overall success of remote GDM care, countering fears and highlighting technology's potential to enhance healthcare delivery. However, HCPs recognised that remote care was not suitable for women who did not have the language skills needed to participate in remote

consultations or for the small population of women who did not have access to a smart phone, or the data required to utilize glycaemic monitoring apps. These findings are similar across studies exploring the use of remote clinical care in antenatal services during the pandemic (226, 234, 239-241).

HCPs further identified a lack of digital infrastructure affecting their ability to deliver care. Similarly Australian researchers reported that while telephone consultations posed few technology barriers for women, clinicians noted challenges with access to private consultation rooms, headphones, and hands-free phones. Another major concern was the lack of integration between existing IT systems. This was identified as a major barrier to delivering effective and safe remote care and a key obstacle to future digital technology integration. This concern was also identified in a systemic review of digital solutions for GDM care published before the pandemic (242). Additionally, unified and integrated electronic records could help address aspects of professional isolation experienced when delivering remote care, as reported in this study and others (226, 241).

4.5.1.7 Evolution of hybrid GDM care

The introduction of remote glycaemic management and remote consultations presented HCPs with challenges, particularly in ensuring equitable access for women who do not have smart phones or have good command of English. Whilst HCPs recognized that these groups were at risk of being further disadvantaged, they acknowledged only a small minority could not effectively receive remote care. For these women, HCP pivoted to offering alternative care pathways including traditional face-to-face care.

Over the first year of the pandemic, HCPs naturally transitioned to a “hybrid” model of care for all women, which allowed them to meet the physical needs of patients, while alleviating the strain on clinics by delivering glycaemic management remotely. However, HCPs noted challenges with this hybrid approach, particularly in identifying women with hidden care needs such as mental illness. In one study, the reduced number of consultations and the transactional nature of telephone and digital communications were reported to be detrimental to providing relational care, for example in safeguarding

against domestic violence (243). Similar findings were reported across health care sectors (240, 241).

The hybrid model allowed HCPs to deliver a more personalized model of care and HCPs proposed a vision for future care pathways offering a hybrid model of care for low-risk women with GDM, led by allied health professionals and community midwives. They emphasized such an approach would require an investment in human resources, workflows and investment in technology infrastructure.

4.5.2 Implications for current GDM care delivery

The integration of remote clinical care, initially adopted during the pandemic, has continued to play a significant role in the management of GDM (131, 132, 205). To ensure the sustainability of this mode of care, it will be essential to address several critical challenges raised by HCPs.

First, the workforce needs to be developed with a focus on skill specialization. Remote GDM care demands a unique combination of medical, nursing, and midwifery expertise, making it challenging to find professionals who can efficiently fulfil these roles. Additionally, the administrative complexity involved in managing remote GDM care necessitates not only administrative skills but also clinical knowledge, underscoring the need for experienced healthcare personnel. Finally, there is a high level of responsibility and accountability associated with remote care, as errors in administrative or clinical tasks can directly affect patient outcomes. This highlights the importance of investing in comprehensive training programs and resources to cultivate a capable workforce adept at managing the nuances of remote GDM care.

In addition to workforce development, improving existing IT infrastructure should be prioritized before adopting new digital tools. Strengthening these foundational aspects will help ensure that remote GDM care can be sustained effectively and safely, benefiting both patients and healthcare providers.

4.6 Conclusion

This study, based on interviews with 23 NHS healthcare providers, offers an in-depth analysis of the reconfiguration and delivery of GDM care in the NHS during the early stages of the SARS-CoV-2 pandemic. It highlights pre-existing inadequacies in GDM care provision and examines the benefits and limitations of remote antenatal care from the perspective of HCPs.

While these findings provide valuable insights into the evolution of remote care for GDM, they are limited to the experiences of HCPs during the early pandemic.

A key finding is the enthusiasm of HCPs for hybrid remote care models for women with uncomplicated GDM. Dietitians, diabetes specialist nurses, and midwives reported positive engagement with women during remote consultations. They found that digital tools for remote glycaemic monitoring, combined with virtual consultations, enabled more effective education and dietary optimization compared to traditional in-person care pathways. Remote care was seen as particularly well-suited for women at lower risk.

However, no tools currently exist to help HCPs identify which women would benefit most from allied health professional-led remote care models. Stratifying women based on risk profiles could be a valuable strategy for developing tailored and effective remote care pathways for GDM.

In the final chapter of this thesis, I address this gap by presenting two systematic reviews that evaluate precision markers for predicting women's responses to lifestyle interventions and treatment. These findings could support the stratification of women into low- and high-risk groups, enabling the creation of personalized and effective care pathways informed by HCPs' experiences with remote care during the pandemic

5 Results Chapter 3

5.1 Introduction

In Chapter 1 of this thesis, I highlighted a concerning trend: the incidence of GDM increased during the COVID-19 pandemic compared to pre-pandemic levels. This rise is particularly striking given the adoption of diagnostic criteria that would typically be expected to lower the number of diagnosed cases. This growing incidence presents significant challenges for the NHS in planning and providing care for an increasing number of affected women

HCPs in the NHS, shared serious concerns about GDM care provision before and during the pandemic, citing overbooked clinics and subsequent inadequacies in care delivery. Despite these challenges, the adoption of remote clinical care, supported by technology for glycaemic management, was widely regarded as a positive step toward addressing the increasing workload. To build on this progress, comprehensive cost-effectiveness and cost-benefit assessments are essential. These should evaluate the number and type of women who could benefit from remote care models and include workforce forecasting to ensure sustainable, long-term implementation.

Interviews conducted with HCPs in 2021 revealed the absence of an optimal strategy for determining which women are suitable for remote care and which require early, intensive input from a medical-led multidisciplinary team (MDT) in a high-risk setting. A potential solution for the NHS is to stratify care for women with GDM into low- and high-risk categories. Such an approach could help manage the growing GDM population effectively, preserving care quality without overburdening resources. One promising method for achieving this stratification is through precision medicine approaches.

In 2024 The Precision Medicine Diabetes Initiative (PMDI), commissioned by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD), developed a second international consensus statement. This

document comprehensively addresses the pillars of precision medicine—prevention, diagnosis, treatment, and prognosis—across diverse forms of diabetes, including monogenic diabetes mellitus (MDM), GDM, type 1 diabetes (T1DM), and T2DM.

The primary objectives of the PMDI are:

1. To identify areas where current evidence supports the application of precision approaches in diabetes prevention and care.
2. To highlight key gaps where additional or higher-quality evidence is required to enable the broader implementation of precision medicine in diabetes.

During my PhD studies, I was invited to join the research team contributing to the GDM theme within the PMDI. This international collaboration included researchers from Canada, Germany and the UK. My contributions to this body of work form the final chapter of my thesis.

The findings of our research were published in *Communications Medicine* under the title: "Precision Medicine in Diabetes Initiative: Gestational Diabetes Mellitus", authored by Jamie L. Benham, Véronique Gingras, Niamh-Maire McLennan, Jasper Most, Jennifer M. Yamamoto, Catherine E. Aiken, Susan E. Ozanne, Rebecca M. Reynolds, and the ADA/EASD PMDI.

All study authors were recognized as equal contributors. My specific contributions included designing the study, formulating search strategies, screening abstracts and full-text articles, collating and analysing data and preparing the first draft of the manuscript under the guidance of Rebecca Reynolds and Susan E. Ozanne.

5.1.1 Background and rationale

The first randomised trials on the treatment of GDM demonstrated that effective glycaemic management during pregnancy significantly reduces the risk of serious neonatal outcomes (59, 60). Today, GDM treatment includes behavioural and pharmacological therapies. Women diagnosed with GDM are offered lifestyle interventions, including tailored dietary and exercise guidance. However, when these measures fail to adequately control blood glucose levels, pharmacological treatments, including oral hypoglycaemic agents and insulin, are introduced. This process may take several weeks during which women and their baby continue to be exposed to hyperglycaemia.

A critical unanswered question remains: which women will respond sufficiently to behavioural interventions alone, and which will require escalation to pharmacological therapies? Efficient care relies on timely initiation of efficacious treatment. Identifying these women is crucial for determining those at the greatest risk.

Research on GDM focuses on identifying and treatment women and their babies at the highest risk of complications. To date, most studies have adopted a glucose-centric perspective, using levels of glycaemia as the primary determinant of risk, which lacks a strong evidence base. Notably, in an attempt to identify women and offspring at highest risk, the recent TOBOGM trial found no overall benefit from early diagnosis and treatment of GDM (73).

Currently, the clinical management of GDM is largely standardised, applying a uniform approach to all diagnosed women (38, 92). While this strategy has been effective in reducing complications associated with GDM, it may over-medicalise pregnancies at lower risk and fail to provide timely intervention for those at the greatest risk. Emerging evidence highlights the heterogeneity among individuals with GDM, suggesting that distinct phenotypes, characteristics, and associated risk factors exist within the condition (112, 114, 244). This diversity supports the need for a precision approach to GDM treatment.

It is not known whether precision treatment—tailored to individual patient characteristics—could improve outcomes for mothers and their offspring. To address this gap, a systematic review was proposed by the PMDI, to explore potential precision markers for predicting GDM treatment success. One promising approach involves identifying patient-level characteristics that predict the need for or escalation of treatment.

Adopting a precision approach to GDM management has broad implications. It could optimise resource allocation in lower-resource settings, where the burden of GDM is rapidly increasing, and improve care efficiency in higher-resource settings. facing the rising prevalence of GDM. As discussed in Chapter 2, the challenges faced in delivering GDM care in NHS settings demonstrate the need for innovative strategies to streamline GDM management to improve maternal and neonatal outcomes.

The following section presents the findings in a publication format. The full paper can be accessed at: https://doi.org/10.1038/s43856-023-00371-0

5.2 Precision gestational diabetes treatment

communications medicine

ARTICLE

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Precision gestational diabetes treatment: a systematic review and meta-analyses

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Abstract

Background Gestational Diabetes Mellitus (GDM) affects approximately 1 in 7 pregnancies globally. It is associated with short- and long-term risks for both mother and baby. Therefore, optimizing treatment to effectively treat the condition has wide-ranging beneficial effects. However, despite the known heterogeneity in GDM, treatment guidelines and approaches are generally standardized. We hypothesized that a precision medicine approach could be a tool for risk-stratification of women to streamline successful GDM management. With the relatively short timeframe available to treat GDM, commencing effective therapy earlier, with more rapid normalization of hyperglycaemia, could have benefits for both mother and fetus.

Methods We conducted two systematic reviews, to identify precision markers that may predict effective lifestyle and pharmacological interventions.

Results There was a paucity of studies examining precision lifestyle-based interventions for GDM highlighting the pressing need for further research in this area. We found a number of precision markers identified from routine clinical measures that may enable earlier identification of those requiring escalation of pharmacological therapy (to metformin, sulphonylureas or insulin). This included previous history of GDM, Body Mass Index and blood glucose concentrations at diagnosis.

Conclusions Clinical measurements at diagnosis could potentially be used as precision markers in the treatment of GDM. Whether there are other sensitive markers that could be identified using more complex individual-level data, such as omics, and if these can feasibly be implemented in clinical practice remains unknown. These will be important to consider in future studies.

Plain language summary

Gestational diabetes (GDM) is high blood sugar first detected during pregnancy. Normalizing blood sugar levels quickly is important to avoid pregnancy complications. Many women achieve this with lifestyle changes, such as to diet, but some need to inject insulin or take tablets. We did two thorough reviews of existing research to see if we could predict which women need medication. Firstly we looked for ways to identify the characteristics of women who benefit most from changing their lifestyles to treat GDM, but found very limited research on this topic. We secondly searched for characteristics that help identify women who need medication to treat GDM. We found some useful characteristics that are obtained during routine pregnancy care. Further studies are needed to test if additional information could provide even better information about how we could make GDM treatment more tailored for individuals during pregnancy.

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Gestational diabetes (GDM) is the most common pregnancy complication, occurring in 3–25% of pregnancies globally[1]. GDM is associated with short- and long-term risks to both mothers and babies, including adverse perinatal outcomes, future obesity, type 2 diabetes and cardiovascular disease[1–3]. The landmark Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) demonstrated that effective treatment of GDM reduces serious perinatal morbidity[4].

Current treatment guidelines for management of GDM assume homogeneous treatment requirements and responses, despite the known heterogeneity of GDM aetiology[5–8]. Standard care includes diet and lifestyle advice at a multi-disciplinary clinic, home blood glucose monitoring at least four times per day, clinic reviews every 2 to 4 weeks, and then progression to pharmacological treatment with metformin, glyburide and/or insulin if glucose targets are not met. Around a third of women cannot maintain euglycaemia with lifestyle measures alone and require treatment escalation to a pharmacological agent[3]. Yet current treatment pathways often take 4–8 weeks to achieve glucose targets. This delay resulting in continued exposure to hyperglycaemia poses a risk of accelerated foetal growth[9,10]. Previous research has suggested that maternal characteristics including body mass index (BMI) $\geq 30\,kg/m^2$, family history of type 2 diabetes, prior history of GDM and higher glycated haemoglobin (HbA1c) increase the likelihood of need for insulin treatment in GDM[11], indicating the potential for risk-stratification of women to streamline successful GDM management. There is emerging evidence that precision biomarkers predict treatment response in type 2 diabetes, which has similar heterogeneity to GDM[12,13] and thus gives rationale to investigate whether a similar precision approach could be successful in optimising outcomes in GDM.

To address this knowledge gap, we conducted two systematic reviews of the available evidence for precision markers of GDM treatment. We aimed to determine which patient-level characteristics are precision markers for predicting (i) responses to personalised diet and lifestyle interventions delivered in addition to standard of care (ii) requirement for escalation of treatment in women treated with diet and lifestyle alone, and in women receiving pharmacological agents for the treatment of GDM. For both reviews we considered whether the precision markers predicted achieving glucose targets, as well as maternal and neonatal outcomes. The Precision Medicine in Diabetes Initiative (PMDI) was established in 2018 by the American Diabetes Association (ADA) in partnership with the European Association for the Study of Diabetes (EASD). The ADA/EASD PMDI includes global thought leaders in precision diabetes medicine who are working to address the burgeoning need for better diabetes prevention and care through precision medicine[14]. This systematic review is written on behalf of the ADA/EASD PMDI as part of a comprehensive evidence evaluation in support of the 2nd International Consensus Report on Precision Diabetes Medicine[15].

We find a paucity of studies examining precision lifestyle-based interventions for GDM highlighting the pressing need for further research in this area. We find a number of precision markers identified from routine clinical measures that may enable earlier identification of those requiring escalation of pharmacological therapy (to metformin, sulphonylureas or insulin). These findings suggest that clinical measurements at diagnosis could potentially be used as precision markers in the treatment of GDM. Whether there are other sensitive markers that could be identified using more complex individual-level data, such as omics, and if these can feasibly be implemented in clinical practice remains unknown and will be important to consider in future studies.

Methods

The systematic reviews and meta-analyses were performed as outlined a priori in the registered protocols (PROSPERO registration IDs CRD42022299288 and CRD42022299402). The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines[16] were followed. Ethical approval was not required as these were secondary studies using published data.

Literature searches, search strategies and eligibility criteria. Search strategies for both reviews were developed based on relevant keywords in partnership with scientific librarians (see Supplementary Note 1 for full search strategies). We searched two databases (MEDLINE and EMBASE) for studies published from inception until January 1st, 2022. We also scanned the references of included manuscripts for inclusion as well as relevant reviews and meta-analyses published within the past two years for additional citations.

For both systematic reviews we included studies (randomised or non-randomised trials and observational studies) published in English and including women ≥16 years old with diagnosed GDM, as defined by the study authors. For the first systematic review (precision diet and lifestyle interventions), we included studies with any behavioural intervention using any approach (e.g., specific exercise, dietary interventions, motivational interviewing) that examined precision markers that could tailor a lifestyle intervention in a more precise way compared to a control group receiving standard care only. For the second systematic review (precision markers for escalation of pharmacological interventions to achieve glucose targets), we included studies investigating women with GDM that required escalation of pharmacological therapy (e.g., insulin, metformin, sulphonylurea) compared to women with GDM that achieved glucose targets with diet and lifestyle measures only, or women with GDM treated with oral agents that required progression to insulin to achieve glucose targets. For both reviews, we included any relevant reported outcomes; maternal (e.g., treatment adherence, hypertensive disorders of pregnancy, gestational weight gain, mode of birth), neonatal (e.g., birthweight, macrosomia, shoulder dystocia, preterm birth, neonatal hypoglycaemia, neonatal death), cost efficiency or acceptability. We excluded studies with a total sample size <50 participants to ensure sufficient data to interpret the effect of precision markers. We also excluded studies published before or during 2004, in order to consider studies with standard care similar to ACHOIS[4].

Study selection and data extraction. The results of our two searches were imported separately into Covidence software (Veritas Health Innovation, Australia, available at www.covidence.org) and duplicates were removed. Two reviewers independently reviewed identified studies. First, they screened titles and abstracts of all references identified from the initial search. In a second step, the full-text articles of potentially relevant publications were scrutinised in detail and inclusion criteria were applied to select eligible articles. Reason for exclusion at the full-text review stage was documented. Disagreement between reviewers was resolved through consensus by discussion with the group of authors.

Two reviewers independently extracted relevant information from each eligible study, using a pre-specified standardised extraction form. Any disagreement between reviewers was resolved as outlined above.

Data extracted included first author name, year of publication, country, study design, type and details of the intervention when applicable, number of cases/controls or cohort groups, total

number of participants and diagnostic criteria used for GDM. Extracted data elements also included outcomes measures, size of the association (Odds Ratio (OR), Relative Risk (RR) or Hazard Ratio (HR)) with corresponding 95% Confidence Interval (CI) and factors adjusted for, confounding factors taken into consideration and methods used to control covariates. We prioritised adjusted values where both raw and adjusted data were available. Details of precision markers (mean (standard deviation) for continuous variables or *N* (%) for categorical variables) including BMI (pre-pregnancy or during pregnancy), ethnicity, age, smoking status, comorbidities, parity, glycaemic variables (e.g., oral glucose tolerance test (OGTT) diagnostic values, HbA1c), timing of GDM diagnosis, history of diabetes or of GDM, and season were also extracted.

Quality assessment (risk of bias and GRADE assessments). We first assessed the quality and risk of bias of each individual study using the Joanna Briggs Institute (JBI) critical appraisal tools[17]. A Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach was then used to review the total evidence for each precision marker, and the quality of the included studies to assign a GRADE certainty to this body of evidence (high, moderate, low and/or very low)[18]. Quality assessment was performed in duplicate and conflicts were resolved through consensus.

Statistical analysis. Where possible, meta-analyses were conducted using random effects models for each precision marker available. The pooled effect size (mean difference for continuous outcomes and ORs for categorical outcomes) with the corresponding 95% CI was computed. The heterogeneity of the studies was quantified using I^2 statistics, where $I^2 > 50\%$ represents moderate and $I^2 > 75\%$ represents substantial heterogeneity across studies. Publication bias was assessed with visual assessment of funnel plots. Statistical analyses were performed using Review Manager software [RevMan, Version 5.4.1, The Cochrane Collaboration, Copenhagen, Denmark].

As part of the diabetes scientific community, we are sensitive in using inclusive language, especially in relation to gender. However, the vast majority of original studies that the GDM precision medicine working groups reviewed used women as their terminology to describe their population, as GDM per definition occurs in pregnancy which can only occur in individuals that are female at birth. To be consistent with the original studies defined populations, we use the word 'women' in our summary of the evidence, current gaps and future perspectives, but fully acknowledge that not all individuals who experienced a pregnancy may self-identify as women at all times over their life course.

Reporting summary. Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Results

Study selection and study characteristics. PRISMA flow charts (Figs. 1 and 2) summarise both searches and study selection processes.

For the first systematic review (precision approaches to diet and lifestyle interventions), we identified 2 eligible studies ($n = 2354$ participants), which were randomised trials from USA and Singapore (Supplementary Data 1)[19,20].

For the second systematic review (precision markers for escalation of pharmacological interventions to achieve target glucose levels), we identified 48 eligible studies ($n = 25{,}724$ participants) (Supplementary Data 2)[21–68]. There were 34 studies ($n = 23{,}831$ participants) investigating precision markers for escalation to pharmacological agent(s) in addition to standard care with diet and lifestyle advice. Of these, 29 studies ($n = 20{,}486$) reported escalation to insulin as the only option[21–49] and 5 ($n = 3345$) reported escalation to any medication (metformin, glyburide and/or insulin)[50–54]. There were 12 studies ($n = 1836$ participants) investigating precision markers for escalation to insulin when treatment with oral agents was not adequate to achieve target glucose levels. Initial treatment was with glyburide in 6 of these studies ($n = 527$)[55–60] and metformin in the other 6 studies ($n = 1142$)[61–66]. A further 2 eligible studies reported maternal genetic predictors of need for supplementary insulin after glyburide ($n = 117$ participants)[67] and maternal lipidome responses to metformin and insulin ($n = 217$ participants)[68].

The majority of included studies were observational in design. Most studies reported outcomes of singleton pregnancies. The studies were from a range of geographical locations: Europe (Belgium, Finland, France, Italy, Netherlands, Poland, Portugal, Spain, Sweden), Switzerland, Middle East (Israel, Qatar, United Arab Emirates), Australasia (Australia, New Zealand), North America/Latin America (Canada, USA and Brazil) and Asia (China, Malaysia, Japan). There were a range of approaches to GDM screening, choice of diagnostic test and diagnostic glucose thresholds.

Quality assessment. Study quality assessment is presented as an overall risk of bias for the studies included in the meta-analyses in Fig. 3 and as a heat map for quality assessment for each included study in Fig. 4. Most of the studies were rated as low risk of bias, as they adequately described how a diagnosis of GDM was assigned, defining inclusion and exclusion criteria, and reported the protocol for initiation of pharmacological therapy. Not all studies reported whether women received diet and lifestyle advice as standard care. Few studies reported whether the precision marker was measured in a valid and reliable way. Using the GRADE approach, the majority of precision markers were classified as having a low certainty of evidence with some classified as very low certainty (Tables 1 and 2). No publication bias (as ascertained by funnel plot analyses) was detected.

Precision diet and lifestyle interventions in GDM. Two studies examining different precision approaches to behavioural interventions were included in the first systematic review, so we present a narrative synthesis of the findings. Neither study examined whether a precision approach to specific lifestyle interventions facilitated achievement of glucose targets during pregnancy or improved outcomes that reflect glycaemic control during pregnancy such as macrosomia, large for gestational age, or neonatal hypoglycaemia.

In one study of women with GDM[19], the intervention was distribution of a tailored letter based on electronic health record data detailing gestational weight gain (GWG) recommendations (as defined by the Institute of Medicine). Receipt of this tailored letter increased the likelihood of meeting the end-of-pregnancy weight goal among women with normal pre-pregnancy BMI, but not among women with overweight or obese pre-pregnancy BMI. This study identified normal pre-pregnancy BMI as a precision marker for intervention success.

The second study[20] used a Web/Smart phone lifestyle coaching programme in women with GDM. Pre-intervention excessive GWG was evaluated as a potential precision marker for the response to the Web/Smart phone lifestyle coaching programme in preventing excess GWG. There was no difference between study arms with respect to either excess GWG or absolute GWG

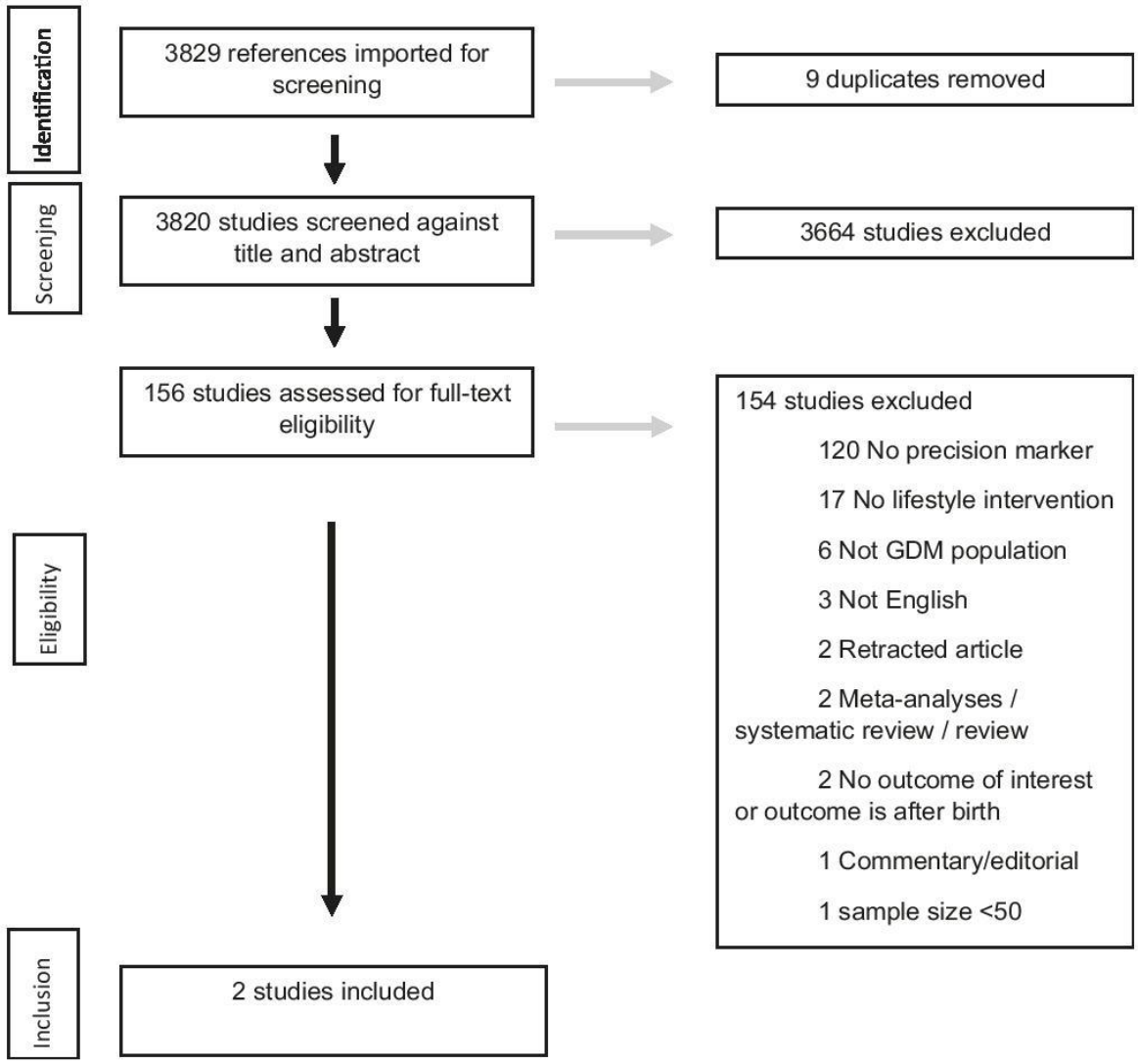

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagrams for precision approaches to enhance behavioural (diet and lifestyle) interventions. The PRISMA flow diagram details the search and selection process applied in the review.

by the end of pregnancy indicating that early GWG is not a useful precision marker with respect to this intervention.

Precision markers for escalation of pharmacological interventions to achieve glucose targets in GDM. Of the 34 studies of precision markers for escalation to pharmacological therapy to achieve glucose targets in addition to standard care with diet and lifestyle advice, 23 studies ($n = 19{,}112$ participants) were included in the meta-analysis[21–23,25,26,31–36,38,40,41,43–46,48,50–53] and 11 studies ($n = 7158$ participants) in the narrative synthesis[24,27–30,37,39,42,47,49,54].

Table 1 and Supplementary Figs. 1–13 show that precision markers for GDM to be adequately managed with lifestyle measures were lower maternal age, nulliparity, lower BMI, no previous history of GDM, lower HbA1c, lower glucose values at the diagnostic OGTT (fasting, 1 h, 2 and/or 3 h glucose), no family history of diabetes, later gestation of diagnosis of GDM and no macrosomia in previous pregnancies. There was a similar pattern for not smoking but this did not reach statistical significance.

Twelve studies ($n = 1836$ participants) of precision markers for escalation to insulin to achieve glucose targets in addition to oral agents were included in the meta-analysis[55–66].

Table 2 and Supplementary Figs. 14–25 show that precision markers for achieving glucose targets with oral agents only were nulliparity, lower BMI, no previous history of GDM, lower HbA1c, lower glucose values at the diagnostic OGTT (fasting, 1 h, and/or 2 h glucose), later gestation of diagnosis of GDM and later gestation at initiation of the oral agent. In sensitivity analyses, there were no differences in the precision markers predicting response to metformin versus glyburide (Supplementary Data 3).

Similar precision markers for escalation to pharmacotherapy to achieve glucose targets were observed in the 11 studies ($n = 7158$ participants) that were not included in the meta-analysis[24,27–30,37,39,42,47,49,54] (Supplementary Data 4). Additional precision markers including foetal sex[28], ethnicity[30,47] and season

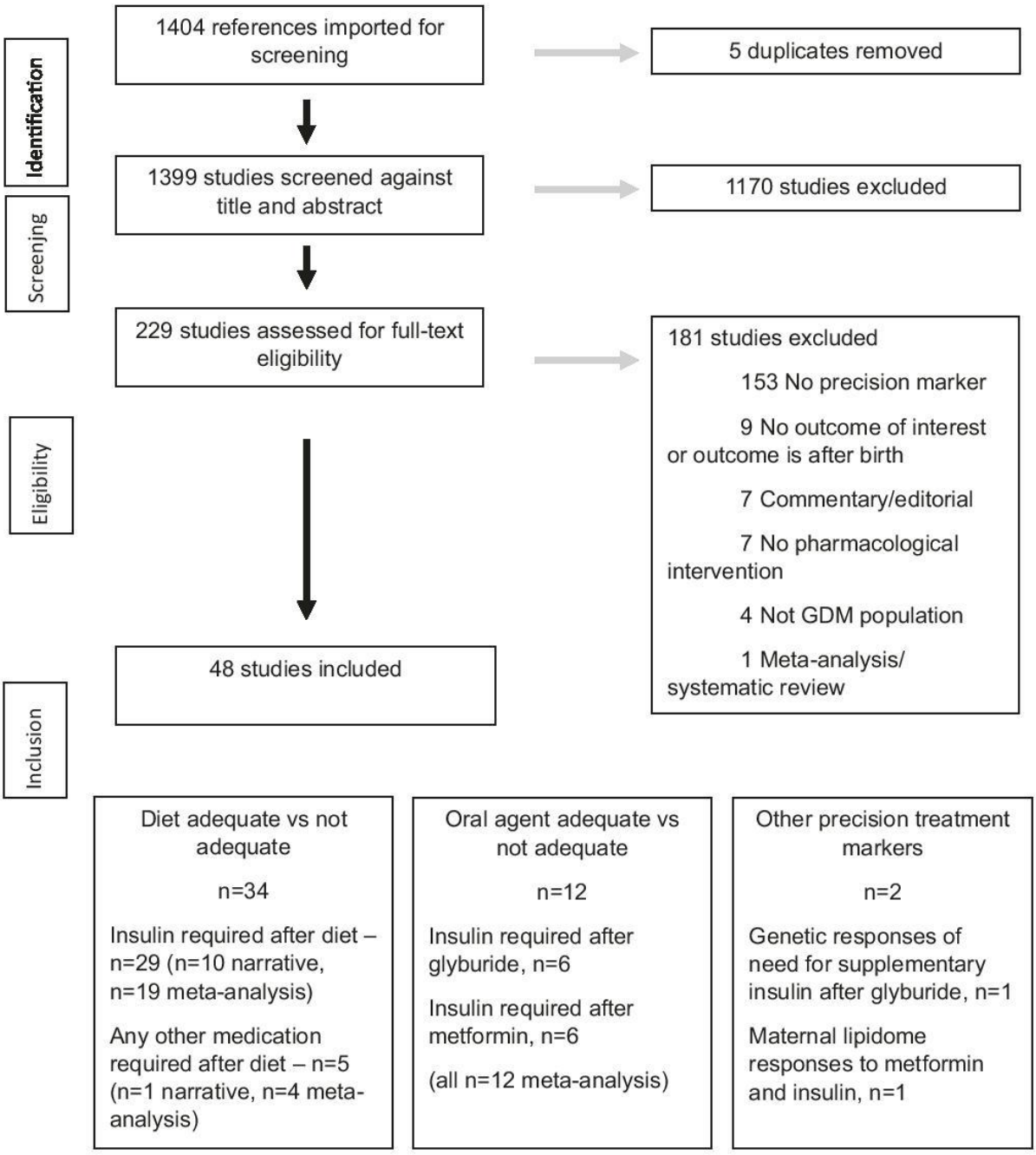

Fig. 2 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagrams for precision markers for escalation of pharmacological interventions. The PRISMA flow diagram details the search and selection process applied in the review.

of birth[37] were evaluated in some studies but there was insufficient data to draw conclusions.

There was a paucity of data in examining other precision markers with only weak evidence that the maternal lipidome[68] or genetics[67] hold potential as precision markers for escalation of pharmacological treatment (Supplementary Data 4).

Discussion

As the factors contributing to the development of GDM and its aetiology are heterogeneous[5–8], it is plausible that the most effective treatment strategies may also be variable among women with GDM. A precision medicine approach resulting in more rapid normalisation of hyperglycaemia could have substantial benefits for both mother and foetus. By synthesising the evidence from two systematic reviews, we sought to identify key precision markers that may predict effective lifestyle and pharmacological interventions. There were a paucity of studies examining precision approaches to better target lifestyle-based interventions for GDM treatment highlighting the pressing need for further research in this area. However, we found a number of precision markers to enable earlier identification of those requiring escalation of pharmacological therapy. These included characteristics

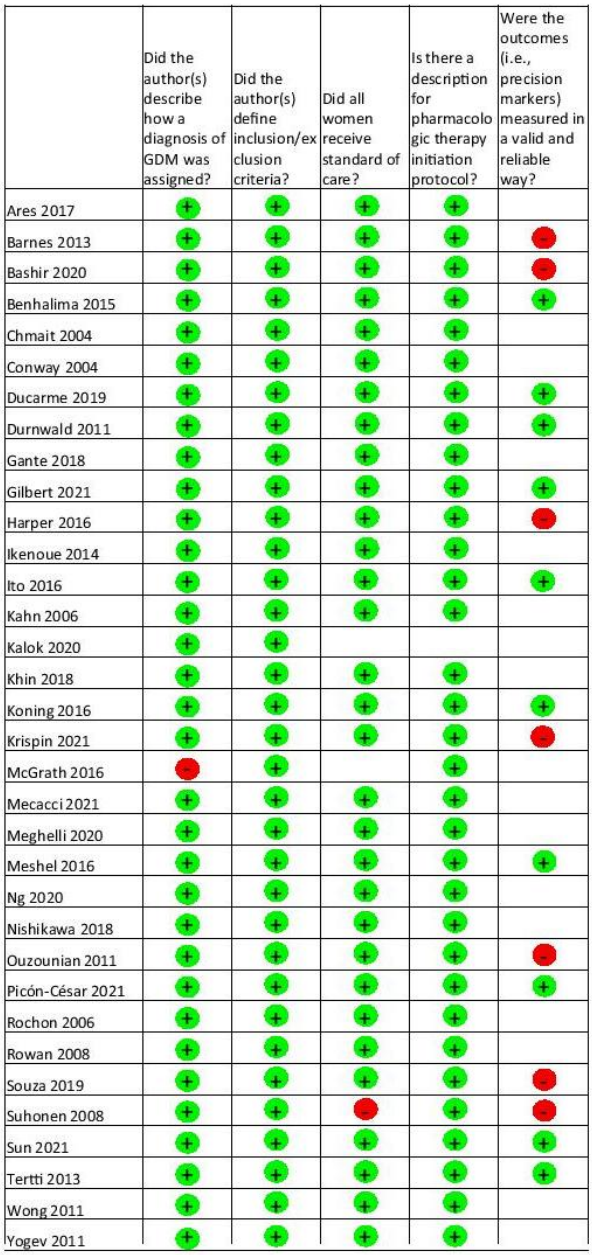

Fig. 3 Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all studies included in the meta-analyses. Green circle with + sign, Yes, Red circle with - sign, No, Blank - not described.

such as BMI, that are easily and routinely measured in clinical practice, and thus have potential to be integrated into prediction models with the aim of achieving rapid glycaemic control. With the relatively short timeframe available to treat GDM, commencing effective therapy earlier, and thus reducing excess foetal growth, is an important target to improve outcomes. Basing treatment decisions closely on precision markers could also avoid over-medicalisation of women who are likely to achieve glucose targets with dietary counselling alone.

In our first systematic review, we identified only two studies addressing precision markers in lifestyle-based interventions for GDM, over and above the usual lifestyle intervention as standard care[19,20]. In both studies, precision markers were examined as secondary analyses of the trials and only two precision markers (communication of GWG goals according to pre-pregnancy BMI; and early GWG as a precision marker for the efficacy of technological enhancement to a behavioural intervention) were assessed; it is thus not possible to conclusively identify any precision marker in lifestyle-based interventions for GDM. This gap in the literature highlights the need for more research, as also echoed by patients and healthcare professionals participating in the 2020 James Lind Alliance (JLA) Priority Setting Partnership (PSP)[69].

Our second systematic review extends the observations of a previous systematic review reporting maternal characteristics associated with the need for insulin treatment in GDM[11]. We identified a number of additional precision markers of successful GDM treatment with lifestyle measures alone, without need for additional pharmacological therapy. The same set of predictors identified women requiring additional insulin after treatment with glyburide as with metformin, despite their different mechanisms of action. However, the numbers of women included in most studies were relatively low and most studies with data in relation to need to escalation to insulin in addition to glyburide were over 10 years old[55,56,58–60]. We acknowledge that there are also differences in diagnostic criteria, clinical practices, and preferences for choice of which drug to start as first pharmacological agent in various global regions which may limit the generalisability of our findings.

Notably, many of the identified precision markers are routinely measured in clinical practice and so could be incorporated into prediction models of need for pharmacological treatment[70,71]. By identifying those who require escalation of pharmacological therapy earlier, better allocation of resources can be achieved. Additionally, some of the precision markers identified, such as BMI, are potentially modifiable. This raises the question of how women can be helped to better prepare for pregnancy[72]. Implementing interventions prior to pregnancy could help understand if these precision markers are on the causal pathway, thus providing an opportunity for prevention and improving health outcomes.

Importantly, there was a lack of data on other potential precision treatment biomarkers, with only two eligible low-quality studies reporting maternal genetic and metabolomic findings[67,68]. In the non-pregnancy literature, efficacy of dietary interventions has been reported to differ for patients with distinct metabolic profiles, for example high fasting glucose versus high fasting insulin, or insulin resistance versus low insulin secretion[73–75]. More recent evidence from appropriately designed, prospective dietary intervention studies has confirmed that dietary interventions tailored towards specific metabolic profiles have more beneficial effects than interventions not specifically designed towards a patient's metabolic profile[76–79]. Ongoing studies such as the Westlake Precision Birth Cohort (WeBirth) in China (NCT04060056) and the USA Hoosier Moms Cohort (NCT03696368) are collecting additional biomarkers which will enhance knowledge in this field. However, implementing such measures in clinical practice, if they prove informative, could be complex and expensive and thus not suitable for use in all global contexts.

Our study has several limitations: Our reviews primarily relied on secondary analyses from observational studies that were not specifically designed to address the question of precision medicine in GDM treatment and were not powered for many of the comparisons made. Prior to introduction in clinical practice, any

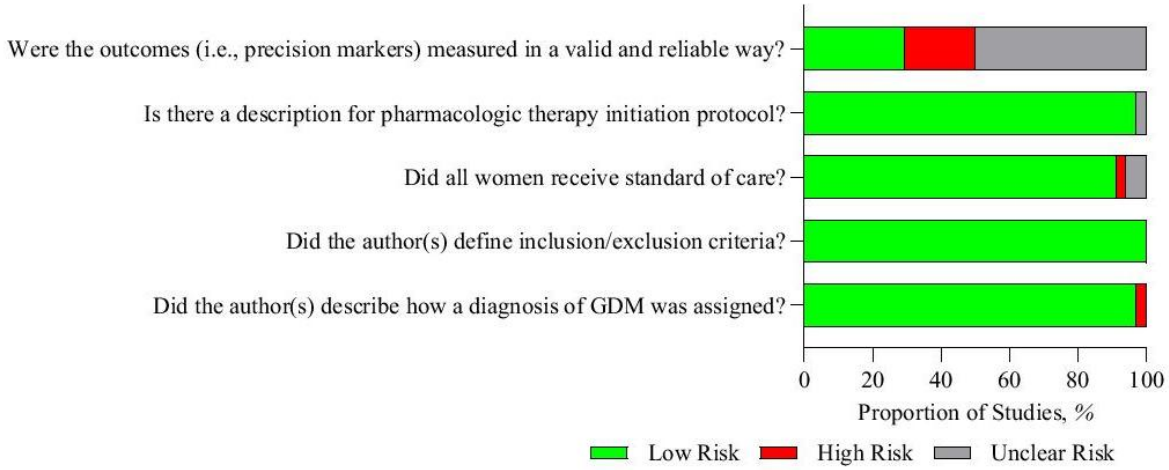

Fig. 4 Risk of bias summary: review authors' judgements about each risk of bias item for each study included in the meta-analyses. Green – low risk of bias, Grey – unclear risk of bias, Red – high risk of bias.

Table 1 Lifestyle adequate to achieve target glucose levels vs need for escalation to pharmacological agent(s) to achieve glucose targets.

Precision Marker	Studies	Participants	Statistical Method	Effect Estimate (95%CI)	GRADE
Age (years)	20	14620	Mean difference (95%CI)	−0.98 [−1.23, −0.73]	⊕⊕◯◯
Nulliparity	8	6969	Odds Ratio (95%CI)	1.53 [1.23, 1.89]	⊕⊕◯◯
Body mass index kg/m^2	16	11313	Mean difference (95%CI)	−1.83 [−2.32, −1.35]	⊕⊕◯◯
Previous history of GDM	13	9885	Odds Ratio (95%CI)	0.46 [0.37, 0.57]	⊕⊕◯◯
Haemoglobin A1C (%)	8	4825	Mean difference (95%CI)	−0.21 [−0.27, −0.14]	⊕⊕◯◯
Fasting glucose (mg/dl)	13	8663	Mean difference (95%CI)	−6.26 [−8.44, −4.08]	⊕⊕◯◯
1-h glucose(mg/dl)	10	6579	Mean difference (95%CI)	−15.33 [−20.81, −9.85]	⊕◯◯◯
2-h glucose(mg/dl)	12	8255	Mean difference (95%CI)	−9.06 [−13.55, −4.56]	⊕◯◯◯
3-h glucose(mg/dl)	3	2126	Mean difference (95%CI)	−8.56 [−12.58, −4.54]	⊕◯◯◯
Family history of diabetes	13	9256	Odds Ratio (95%CI)	0.66 [0.59, 0.75]	⊕⊕◯◯
Gestational age at GDM diagnosis (weeks)	9	5882	Mean difference (95%CI)	3.06 [2.33, 3.79]	⊕⊕◯◯
Smoking history	5	3488	Odds Ratio (95%CI)	0.80 [0.52, 1.23]	⊕⊕◯◯
Previous history of macrosomia	7	5595	Odds Ratio (95%CI)	0.63 [0.42, 0.94]	⊕⊕◯◯

Very low ⊕◯◯◯.
Low ⊕⊕◯◯.

Table 2 Oral pharmacological agent adequate to achieve target glucose levels vs need for escalation to insulin to achieve glucose targets.

Precision Marker	Studies	Participants	Statistical method	Effect Estimate (95%CI)	GRADE
Age (years)	11	1473	Mean difference (95%CI)	−1.04 [−2.10, 0.03]	⊕⊕◯◯
Nulliparity	8	1215	Odds Ratio (95%CI)	1.55 [1.17, 2.04]	⊕⊕◯◯
Body mass index (kg/m^2)	10	1692	Mean difference (95%CI)	−1.21 [−2.21, −0.21]	⊕⊕◯◯
Previous history of GDM	8	1412	Odds Ratio (95%CI)	0.43 [0.30, 0.63]	⊕⊕◯◯
Haemoglobin A1C (%)	6	1152	Mean difference (95%CI)	−0.21 [−0.29, −0.13]	⊕⊕◯◯
Fasting glucose (mg/dl)	12	1836	Mean difference (95%CI)	−8.02 [−11.87, −4.16]	⊕◯◯◯
1-h glucose (mg/dl)	8	1177	Mean difference (95%CI)	−10.64 [−18.25, −3.02]	⊕◯◯◯
2-h glucose (mg/dl)	10	1378	Mean difference (95%CI)	−7.31 [−11.38, −3.25]	⊕◯◯◯
3-h glucose (mg/dl)	6	679	Mean difference (95%CI)	0.00 [−11.79, 11.79]	⊕◯◯◯
Family history of diabetes	6	1040	Odds Ratio (95%CI)	0.79 [0.50, 1.25]	⊕⊕◯◯
Gestational age at GDM diagnosis (weeks)	11	1473	Mean difference (95%CI)	2.64 [1.42, 3.86]	⊕⊕◯◯
Gestation at oral pharmacological agent initiation (weeks)	7	967	Mean difference (95%CI)	3.79 [2.08, 5.51]	⊕⊕◯◯

Very low ⊕◯◯◯.
Low ⊕⊕◯◯.

marker would have to be rigorously and prospectively tested with respect to sensitivity and specificity to predict treatment needs. The majority of data were extracted from clinical records leading to a lack of detail, such as the precise timing of BMI measurements, and limited information about whether BMI was self-reported or clinician measured. There was marked variation in approaches to GDM screening methods, choice of glucose challenge test and diagnostic thresholds as well as heterogeneity in glucose targets or criteria met to warrant escalation in treatment. Whilst we included studies from a range of geographical settings, the majority of studies were from high income settings, and therefore our findings may not be applicable to low- and middle-income countries. Pregnancy outcomes of precision medicine strategies for GDM also remain unknown, underscoring the need for tailored interventions that account for patient perspective and diverse patient populations.

Despite these limitations, our study has several strengths. We used robust methods to identify a broad range of precision markers, many of which are routinely measured and can be easily translated into prediction models. We excluded studies where the choice of drug was decided by the clinician based on participant characteristics to avoid bias. Our study also highlights the need for further research in this area, particularly in exploring whether there are more sensitive markers that could be identified through omics approaches.

In conclusion, our findings suggest that precision medicine for GDM treatment holds promise as a tool to stream-line individuals towards the most effective and potentially cost-effective care. Whether this will impact on short-term pregnancy outcomes and longer term health outcomes for both mother and baby is not known. More research is urgently needed to identify precision lifestyle interventions and to explore whether more sensitive markers could be identified. Prospective studies, appropriately powered and designed to allow assessment of discriminative abilities (sensitivity, specificity), and (external) validation studies are urgently needed to understand the utility and generalisability of our findings to under-represented populations. This is an area of active research with findings from ongoing studies (NCT04187521, NCT03029702, NCT05932251) eagerly awaited. Consideration of how identified markers can be implemented feasibly and cost effectively in clinical practice is also required. Such efforts will be critical for realising the full potential of precision medicine and empowering patients and their health care providers to optimise short and long-term health outcomes for both mother and child.

Data availability

The included studies are detailed in Supplementary Data 1 and 2. The data underlying Tables 1 and 2 are in Supplementary Figs. 1–13 and 14–25, respectively. Additional information is available via contact with the corresponding author.

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References

1. Saravanan, P. Gestational diabetes: opportunities for improving maternal and child health. *Lancet Diabetes Endocrinol.* **8**, 793–800 (2020).
2. Vounzoulaki, E. et al. Progression to type 2 diabetes in women with a known history of gestational diabetes: systematic review and meta-analysis. *BMJ* **369**, m1361 (2020).
3. Metzger, B. E. et al. Hyperglycemia and adverse pregnancy outcomes. *N. Engl. J. Med.* **358**, 1991–2002 (2008).
4. Crowther, C. A. et al. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N. Engl. J. Med.* **352**, 2477–2486 (2005).
5. Powe, C. E., Hivert, M. F. & Udler, M. S. Defining heterogeneity among women with gestational diabetes mellitus. *Diabetes* **69**, 2064–2074 (2020).
6. Powe, C. E. et al. Heterogeneous contribution of insulin sensitivity and secretion defects to gestational diabetes mellitus. *Diabetes Care* **39**, 1052–1055 (2016).
7. Benhalima, K. et al. Characteristics and pregnancy outcomes across gestational diabetes mellitus subtypes based on insulin resistance. *Diabetologia* **62**, 2118–2128 (2019).
8. Madsen, L. R. et al. Do variations in insulin sensitivity and insulin secretion in pregnancy predict differences in obstetric and neonatal outcomes? *Diabetologia* **64**, 304–312 (2021).
9. Harrison, R. K., Cruz, M., Wong, A., Davitt, C. & Palatnik, A. The timing of initiation of pharmacotherapy for women with gestational diabetes mellitus. *BMC Preg, Childbirth* **20**, 773 (2020).
10. Tisi, D. K., Burns, D. H., Luskey, G. W. & Koski, K. G. Fetal exposure to altered amniotic fluid glucose, insulin, and insulin-like growth factor-binding protein 1 occurs before screening for gestational diabetes mellitus. *Diabetes Care* **34**, 139–144 (2011).
11. Alvarez-Silvares, E., Bermúdez-González, M., Vilouta-Romero, M., García-Lavandeira, S. & Seoane-Pillado, T. Prediction of insulin therapy in women with gestational diabetes: a systematic review and meta-analysis of observational studies. *J. Perinat. Med.* **50**, 608–619 (2022).
12. Dennis, J. M., Shields, B. M., Henley, W. E., Jones, A. G. & Hattersley, A. T. Disease progression and treatment response in data-driven subgroups of type 2 diabetes compared with models based on simple clinical features: an analysis using clinical trial data. *Lancet Diabetes Endocrinol.* **7**, 442–451 (2019).
13. Dawed, A. Y. et al. Pharmacogenomics of GLP-1 receptor agonists: a genome-wide analysis of observational data and large randomised controlled trials. *Lancet Diabetes Endocrinol.* **11**, 33–41 (2023).
14. Nolan, J. J. et al. ADA/EASD Precision Medicine in Diabetes Initiative: an international perspective and future vision for precision medicine in diabetes. *Diabetes Care* **45**, 261–266 (2022).
15. Tobias, D. K., Merino, J., Ahmad, A. & PMDI, A. E. Second international consensus report on gaps and opportunities for the clinical translation of precision diabetes medicine. Nat. Med. (in press), https://doi.org/10.1038/s41591-023-02502-5. (2023)
16. Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G. & Group, P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann. Intern. Med.* **151**, 264–269 (2009).
17. Joanna Briggs Institute (JBI) critical appraisal tools https://jbi.global/critical-appraisal-tools. Accessed 15 April 2023.
18. Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) https://guidelines.diabetes.ca/cpg/chapter2. Accessed 15 April 2023.
19. Hedderson, M. M. et al. A tailored letter based on electronic health record data improves gestational weight gain among women with gestational diabetes mellitus: the Gestational Diabetes' Effects on Moms (GEM) cluster-randomized controlled trial. *Diabetes Care* **41**, 1370–1377 (2018).
20. Yew, T. W. et al. A randomized controlled trial to evaluate the effects of a smartphone application-based lifestyle coaching program on gestational weight gain, glycemic control, and maternal and neonatal outcomes in women with gestational diabetes mellitus: the SMART-GDM study. *Diabetes Care* **44**, 456–463 (2021).
21. Ares, J. et al. Gestational Diabetes Mellitus (GDM): relationship between higher cutoff values for 100g Oral Glucose Tolerance Test (OGTT) and insulin requirement during pregnancy. *Matern. Child Health J.* **21**, 1488–1492 (2017).
22. Barnes, R. A. et al. Predictors of large and small for gestational age birthweight in offspring of women with gestational diabetes mellitus. *Diabet. Med.* **30**, 1040–1046 (2013).
23. Benhalima, K. et al. Differences in pregnancy outcomes and characteristics between insulin- and diet-treated women with gestational diabetes. *BMC Preg. Childbirth* **15**, 271 (2015).
24. Berg, M., Adlerberth, A., Sultan, B., Wennergren, M. & Wallin, G. Early random capillary glucose level screening and multidisciplinary antenatal teamwork to improve outcome in gestational diabetes mellitus. *Acta Obstetr. Gynecol, Scand.* **86**, 283–290 (2007).
25. Ducarme, G. et al. Predictive factors of subsequent insulin requirement for glycemic control during pregnancy at diagnosis of gestational diabetes mellitus. *Int. J. Gynaecol. Obstetr.* **144**, 265–270 (2019).
26. Durnwald, C. P. et al. Glycemic characteristics and neonatal outcomes of women treated for mild gestational diabetes. *Obstetr. Gynecol.* **117**, 819–827 (2011).
27. Elnour, A. A. Antenatal oral glucose-tolerance test values and pregnancy outcomes. *Int. J. Pharm Pract.* **16**, 189–197 (2008).
28. Giannubilo, S. R., Pasculli, A., Ballatori, C., Biagini, A. & Ciavattini, A. Fetal sex, need for insulin, and perinatal outcomes in gestational diabetes mellitus: an observational cohort study. *Clin. Ther.* **40**, 587–592 (2018).
29. Gibson, K. S., Waters, T. P. & Catalano, P. M. Maternal weight gain in women who develop gestational diabetes mellitus. *Obstetr. Gynecol.* **119**, 560–565 (2012).

30. Hillier, T. A., Ogasawara, K. K., Pedula, K. L. & Vesco, K. K. Markedly different rates of incident insulin treatment based on universal gestational diabetes mellitus screening in a diverse HMO population. *Am. J. Obstetr. Gynecol.* **209**, 440.e441–449 (2013).
31. Ikenoue, S. et al. Clinical impact of women with gestational diabetes mellitus by the new consensus criteria: two year experience in a single institution in Japan. *Endocr. J.* **61**, 353–358 (2014).
32. Ito, Y. et al. Indicators of the need for insulin treatment and the effect of treatment for gestational diabetes on pregnancy outcomes in Japan. *Endocr. J.* **63**, 231–237 (2016).
33. Kalok, A. et al. Correlation between oral glucose tolerance test abnormalities and adverse pregnancy outcomes in gestational diabetes: a cross-sectional study. *Int. J. Environ. Res. Public Health* **17**, 6990 (2020).
34. Koning, S. H. et al. Risk stratification for healthcare planning in women with gestational diabetes mellitus. *Netherlands J. Med.* **74**, 262–269 (2016).
35. Mecacci, F. et al. Different gestational diabetes phenotypes: which insulin regimen fits better? *Front. Endocrinol.* **12**, 630903 (2021).
36. Meghelli, L., Vambergue, A., Drumez, E. & Deruelle, P. Complications of pregnancy in morbidly obese patients: What is the impact of gestational diabetes mellitus? *J. Gynecol. Obstetr. Hum. Reprod.* **49**, 101628 (2020).
37. Molina-Vega, M. et al. Relationship between environmental temperature and the diagnosis and treatment of gestational diabetes mellitus: an observational retrospective study. *Sci. Total Environ.* **744**, 140994 (2020).
38. Ng, A., Liu, A. & Nanan, R. Association between insulin and post-caesarean resuscitation rates in infants of women with GDM: a retrospective study. *J. Diabetes* **12**, 151–157 (2020).
39. Nguyen, T. H., Yang, J. W., Mahone, M. & Godbout, A. Are there benefits for gestational diabetes mellitus in treating lower levels of hyperglycemia than standard recommendations? *Can. J. Diabetes* **40**, 548–554 (2016).
40. Nishikawa, T. et al. One-hour oral glucose tolerance test plasma glucose at gestational diabetes diagnosis is a common predictor of the need for insulin therapy in pregnancy and postpartum impaired glucose tolerance. *J. Diabetes Investig.* **9**, 1370–1377 (2018).
41. Ouzounian, J. G. et al. One-hour post-glucola results and pre-pregnancy body mass index are associated with the need for insulin therapy in women with gestational diabetes. *J. Matern.-Fetal Neonatal Med.* **24**, 718–722 (2011).
42. Parrettini, S. et al. Gestational diabetes: a link between OGTT, maternal-fetal outcomes and maternal glucose tolerance after childbirth. *Nutr. Metab. Cardiovasc. Dis.* **30**, 2389–2397 (2020).
43. Silva, J. K., Kaholokula, J. K., Ratner, R. & Mau, M. Ethnic differences in perinatal outcome of gestational diabetes mellitus. *Diabetes Care* **29**, 2058–2063 (2006).
44. Souza, A. et al. Can we stratify the risk for insulin need in women diagnosed early with gestational diabetes by fasting blood glucose? *J. Matern-Fetal Neonatal Med.* **32**, 2036–2041 (2019).
45. Suhonen, L., Hiilesmaa, V., Kaaja, R. & Teramo, K. Detection of pregnancies with high risk of fetal macrosomia among women with gestational diabetes mellitus. *Acta Obstetr. Gynecol. Scand.* **87**, 940–945 (2008).
46. Sun, T. et al. The effects of insulin therapy on maternal blood pressure and weight in women with gestational diabetes mellitus. *BMC Preg. Childbirth* **21**, 657 (2021).
47. Wong, V. W. Gestational diabetes mellitus in five ethnic groups: a comparison of their clinical characteristics. *Diabet. Med.* **29**, 366–371 (2012).
48. Wong, V. W. & Jalaludin, B. Gestational diabetes mellitus: who requires insulin therapy? *Aust. N.Z. J. Obstetr. Gynaecol.* **51**, 432–436 (2011).
49. Zawiejska, A., Wender-Ozegowska, E., Radzicka, S. & Brazert, J. Maternal hyperglycemia according to IADPSG criteria as a predictor of perinatal complications in women with gestational diabetes: a retrospective observational study. *J. Matern.-Fetal Neonatal Med.* **27**, 1526–1530 (2014).
50. Bashir, M. et al. Metformin-treated-GDM has lower risk of macrosomia compared to diet-treated GDM- a retrospective cohort study. *J. Matern.-Fetal Neonatal Med.* **33**, 2366–2371 (2020).
51. Gilbert, L. et al. Mental health and its associations with glucose-lowering medication in women with gestational diabetes mellitus. A prospective clinical cohort study. *Psychoneuroendocrinology* **124**, 105095 (2021).
52. Krispin, E., Ashkenazi Katz, A., Shmuel, E., Toledano, Y. & Hadar, E. Characterization of women with gestational diabetes who failed to achieve glycemic control by lifestyle modifications. *Arch. Gynecol. Obstetr.* **303**, 677–683 (2021).
53. Meshel, S. et al. Can we predict the need for pharmacological treatment according to demographic and clinical characteristics in gestational diabetes? *J. Matern.-Fetal Neonatal Med.* **29**, 2062–2066 (2016).
54. Zhu, S., Meehan, T., Veerasingham, M. & Sivanesan, K. COVID-19 pandemic gestational diabetes screening guidelines: a retrospective study in Australian women. *Diabetes & Metabolic Syndrome* **15**, 391–395 (2021).
55. Chmait, R., Dinise, T. & Moore, T. Prospective observational study to establish predictors of glyburide success in women with gestational diabetes mellitus. *J. Perinatol.* **24**, 617–622 (2004).
56. Conway, D. L., Gonzales, O. & Skiver, D. Use of glyburide for the treatment of gestational diabetes: the San Antonio experience. *J. Matern.-Fetal Neonatal Med.* **15**, 51–55 (2004).
57. Harper, L. M., Glover, A. V., Biggio, J. R. & Tita, A. Predicting failure of glyburide therapy in gestational diabetes. *J. Perinatol.* **36**, 347–351 (2016).
58. Kahn, B. F., Davies, J. K., Lynch, A. M., Reynolds, R. M. & Barbour, L. A. Predictors of glyburide failure in the treatment of gestational diabetes. *Obstetr. Gynecol.* **107**, 1303–1309 (2006).
59. Rochon, M., Rand, L., Roth, L. & Gaddipati, S. Glyburide for the management of gestational diabetes: risk factors predictive of failure and associated pregnancy outcomes. *Am. J. Obstetr. Gynecol.* **195**, 1090–1094 (2006).
60. Yogev, Y. et al. Glyburide in gestational diabetes–prediction of treatment failure. *J. Matern.-Fetal Neonatal Med.* **24**, 842–846 (2011).
61. Gante, I., Melo, L., Dores, J., Ruas, L. & Almeida, M. D. C. Metformin in gestational diabetes mellitus: predictors of poor response. *Eur. J. Endocrinol.* **178**, 129–135 (2018).
62. Khin, M. O., Gates, S. & Saravanan, P. Predictors of metformin failure in gestational diabetes mellitus (GDM). *Diabetes Metab. Syndr.* **12**, 405–410 (2018).
63. McGrath, R. T., Glastras, S. J., Hocking, S. & Fulcher, G. R. Use of metformin earlier in pregnancy predicts supplemental insulin therapy in women with gestational diabetes. *Diabetes Res. Clin. Pract.* **116**, 96–99 (2016).
64. Picón-César, M. J. et al. Metformin for gestational diabetes study: metformin vs insulin in gestational diabetes: glycemic control and obstetrical and perinatal outcomes: randomized prospective trial. *Am. J. Obstetr. Gynecol.* **225**, 517.e511–517.e517 (2021).
65. Rowan, J. A., Hague, W. M., Gao, W., Battin, M. R. & Moore, M. P. Metformin versus insulin for the treatment of gestational diabetes. *N. Engl J. Med.* **358**, 2003–2015 (2008).
66. Tertti, K., Ekblad, U., Koskinen, P., Vahlberg, T. & Rönnemaa, T. Metformin vs. insulin in gestational diabetes. A randomized study characterizing metformin patients needing additional insulin. *Diabetes Obes. Metab.* **15**, 246–251 (2013).
67. Bouchghoul, H. et al. Hypoglycemia and glycemic control with glyburide in women with gestational diabetes and genetic variants of cytochrome P450 2C9 and/or OATP1B3. *Clin. Pharmacol. Ther.* **110**, 141–148 (2021).
68. Huhtala, M. S., Tertti, K. & Rönnemaa, T. Serum lipids and their association with birth weight in metformin and insulin-treated patients with gestational diabetes. *Diabetes Res. Clin. Pract.* **170**, 108456 (2020).
69. Ayman, G. et al. The top 10 research priorities in diabetes and pregnancy according to women, support networks and healthcare professionals. *Diabet. Med.* **38**, e14588 (2021).
70. Cooray, S. D. et al. Development, validation and clinical utility of a risk prediction model for adverse pregnancy outcomes in women with gestational diabetes: the PeRSonal GDM model. *EClinicalMedicine* **52**, 101637 (2022).
71. Liao, L. D. et al. Development and validation of prediction models for gestational diabetes treatment modality using supervised machine learning: a population-based cohort study. *BMC Med.* **20**, 307 (2022).
72. Cassinelli, E. H. et al. Preconception health and care policies and guidelines in the UK and Ireland: a scoping review. *Lancet* **400**, S61 (2022).
73. Hjorth, M. F. et al. Pretreatment Fasting glucose and insulin as determinants of weight loss on diets varying in macronutrients and dietary fibers-the POUNDS LOST study. *Nutrients* **11**, 586 (2019).
74. Hjorth, M. F. et al. Pretreatment fasting plasma glucose and insulin modify dietary weight loss success: results from 3 randomized clinical trials. *Am. J. Clin. Nutr.* **106**, 499–505 (2017).
75. Hjorth, M. F., Due, A., Larsen, T. M. & Astrup, A. Pretreatment fasting plasma glucose modifies dietary weight loss maintenance success: results from a stratified RCT. *Obesity* **25**, 2045–2048 (2017).
76. Bergia, R. E. et al. Differential glycemic effects of low- versus high-glycemic index Mediterranean-style eating patterns in adults at risk for type 2 diabetes: the MEDGI-Carb randomized controlled trial. *Nutrients* **14**, 706 (2022).
77. Aldubayan, M. A. et al. A double-blinded, randomized, parallel intervention to evaluate biomarker-based nutrition plans for weight loss: the PREVENTOMICS study. *Clin. Nutr.* **41**, 1834–1844 (2022).
78. Trouwborst, I. et al. Cardiometabolic health improvements upon dietary intervention are driven by tissue-specific insulin resistance phenotype: a precision nutrition trial. *Cell Metab.* **35**, 71–83.e75 (2023).
79. Cifuentes, L. et al. Phenotype tailored lifestyle intervention on weight loss and cardiometabolic risk factors in adults with obesity: a single-centre, non-randomised, proof-of-concept study. *EClinicalMedicine* **58**, 101923 (2023).

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5.3 Conclusions

This chapter presents the findings of a systematic review examining precision markers associated with the success of GDM treatment (245). The review aimed to identify precision approaches, beyond standard care, that enable the achievement of glucose targets through lifestyle measures alone. It also sought to determine the characteristics predicting successful glucose control in women managed with diet and lifestyle alone and in those requiring oral agents.

Several precision markers, including commonly available clinical indicators, were identified as predictors for the need for pharmacological interventions. A total of 48 studies were included in the review, with 34 contributing to meta-analyses. Precision markers for successful management of GDM using lifestyle interventions without pharmacological therapy (insulin, metformin, and/or glyburide) were identified from 34 studies. These markers included:

1. Younger maternal age
2. Nulliparity
3. Lower BMI
4. No prior history of GDM
5. Lower levels of HbA1c, fasting glucose, and post-challenge glucose concentrations (at 1, 2, and 3 hours)
6. No family history of diabetes
7. Later gestational age at diagnosis of GDM
8. No history of macrosomia

Similarly, for women treated with metformin and/or glyburide without requiring supplemental insulin (12 studies), comparable precision markers were identified, with the additional factor of later gestational age at the initiation of oral therapy. However, there was insufficient data to determine precision markers that could predict responses to specific pharmacological agents.

This study was unable to assess whether tailoring lifestyle-based interventions using a precision approach could facilitate the achievement of glucose targets during pregnancy

or improve outcomes related to glycaemic control, such as macrosomia, large-for-gestational-age infants, or neonatal hypoglycaemia

5.3.1 From study findings into clinical practice

This study has identified several predictors that can help recognise women who are less likely to require treatment. Lower HbA1C levels, alongside reduced fasting and post-challenge glucose concentrations, serve as predictors of diet-controlled gestational diabetes (GDM). These findings suggest that the severity of hyperglycaemia at diagnosis is a strong tool for predicting the need for treatment — a pattern that has been demonstrated across 15 clinical studies in diverse populations (245).

However, while these studies highlight the potential of hyperglycaemia markers to predict treatment needs, they also reveal significant variation — particularly in insulin requirements — between populations. These differences are likely driven by underlying population-specific factors. Therefore, to develop this strategy for clinical practice developing tailored, population-specific tools will be essential to accurately identify women who require treatment based on the degree of hyperglycaemia.

In the UK, the severity of hyperglycaemia at diagnosis is not currently used as a clinical indicator to stratify women or guide decisions about escalating treatment. Chapter 2 outlines the burden of GDM on NHS services, emphasising the urgent need for more effective approaches. From my clinical experience, some NHS trusts have local policies where women are only referred to high-risk, multidisciplinary care settings once medication has been initiated. An alternative approach could involve creating population-specific models based on local data, rather than relying on arbitrary, non-evidence-based thresholds to determine which women receive high-risk care and which are managed by midwifery or obstetric services.

Another area of interest is whether the duration of hyperglycaemia predicts the need for treatment. The recent TOBOGM study found no clear benefit to starting GDM treatment before 20 weeks' gestation in improving pregnancy outcomes (74). Further research is needed to explore whether early identification of women who may go on to develop GDM

requiring treatment could improve outcomes — again, likely through a population-specific modelling approach.

5.3.2 Biomarker precision tools

This review identified only two studies that examined non-routine clinical markers, those included maternal genetics and metabolomics, as potential precision markers for predicting treatment response. This highlights a significant gap in evidence regarding the role of biomarkers in identifying women who require treatment or escalation of treatment. It also underscores the major challenge in conducting this review: the majority of included studies were not designed to specifically address the use of precision tools in GDM treatment and were therefore not adequately powered for such outcomes.

For most included studies, data on treatment or precision markers had to be extracted from supplementary materials. Many studies identified through the search strategy were excluded for this reason. Where authors referenced relevant data on treatment response, attempts were made to contact them for clarification, but this did not yield additional information. As clinical researchers, we strongly believe that data on treatment outcomes may have been available at the time of publication, suggesting the potential for unpublished findings on the role of precision tools, particularly non-routine biomarkers.

This review was conducted as part of a broader consortium effort to identify gaps and opportunities for the clinical translation of precision medicine in diabetes care. A second systematic review and meta-analysis focused on maternal and fetal anthropometry, clinical and sociocultural/environmental risk factors, genetics, omics, and non-glycaemic biomarkers. This review aimed to identify subgroups of individuals with GDM at differential risk of adverse pregnancy outcomes.

The second review included 30 studies evaluating non-glycaemic biomarkers, including lipids and indices of insulin sensitivity and secretion, and an additional five studies investigating genetics, genomics, and other omics approaches. Lipids and insulin

resistance/secretion indices (33 studies) were the most extensively studied non-glycaemic biomarkers, with increased triglycerides and insulin resistance generally associated with a higher risk of macrosomia or large-for-gestational-age (LGA) infants. Findings for other markers were inconsistent, making it unclear whether they could be reliably used as precision markers (246).

The publication of findings from the second PMDI review, along with its broader dissemination in the field of diabetes in pregnancy, is expected to play a key role in identifying knowledge gaps, particularly in biomarker research (247). Recently building on this, White et al. analysed glycaemia patterns identified at OGTT at 28 weeks in obese women, linking these to insulin secretion, sensitivity, and lipid profiles (112). Women with the most severe hyperglycaemia (both fasting and post-load) exhibited the greatest defects in insulin secretion, sensitivity, and lipid disturbances associated with lipogenesis.

Notably, women with isolated fasting hyperglycaemia had lipid profiles similar to those without GDM, while those with isolated post-load hyperglycaemia showed significant lipid alterations akin to women with severe hyperglycaemia, despite having insulin indices comparable to euglycaemic women (112). These findings suggest that neither insulin indices or lipid profiling alone are sufficient for distinguishing degrees of hyperglycaemia from euglycaemia but highlight the ongoing potential of lipid metabolites as potential targets for GDM prevention and intervention.

Future research into biomarker discovery is expected to be both time-intensive and costly, emphasising the importance of strategic planning. When designing future studies, it is crucial to account for the multiple roles that biomarkers can play—not only in detecting GDM but also in predicting treatment responses and evaluating short- and long-term outcomes for both mother and child. While the development of novel biomarkers to predict disease prognosis and clinical outcomes represents a valuable area of research, it is essential to recognise the limitations of such efforts. Complex precision markers, such as genetic or metabolomic biomarkers, may have limited utility in low- and middle-income countries, which account for 90% of the global GDM burden (3, 79). Addressing these disparities should be a key consideration in the pursuit of biomarker research to ensure broader applicability and impact.

5.3.3 Prediction modelling in GDM management

The routine clinical precision markers identified in this review highlight their potential for distinguishing between women with GDM who will respond to lifestyle interventions and those requiring escalation of treatment, including pharmacological interventions. Identifying women likely to need treatment escalation—and thus those with the poorest glycaemic control—enables stratification into "high-risk" and "low-risk" groups. High-risk women could benefit from more intensive monitoring and earlier therapeutic intervention, while low-risk women, who typically exhibit milder phenotypes and are more likely to maintain glycaemic control with diet and lifestyle alone, could be managed outside of high-risk obstetric care pathways. This type of stratification would provide an evidence base to support the enthusiasm reported by health care professionals in chapter 2 of supporting women receiving “low risk” GDM care in a community setting, avoiding unnecessary interventions, thereby improving efficiency and care quality in clinical practice.

5.3.4 Moving from findings to stratification

The transition from identifying precision markers to stratifying women by risk requires robust validation of these markers. Traditional approaches assess discriminative abilities, such as sensitivity and specificity, alongside external validation. However, alternative methods like machine learning offer promising alternatives. Machine learning approaches can integrate diverse datasets, encompassing clinical, biochemical, and demographic variables, to uncover complex patterns and interactions that conventional statistical methods might miss.

These models could incorporate precision markers identified in this review, as well as data from ongoing studies such as the Westlake Precision Birth Cohort (WeBirth) in China (NCT04060056) and the Hoosier Moms Cohort in the USA (NCT03696368).

Variables such as glycaemic profiles, maternal age, BMI, and GDM history could be used to generate personalised risk scores that accurately predict treatment needs or escalation. Predictive models, including decision trees, support vector machines, and neural networks, could be trained to forecast treatment requirements as surrogate markers for poor outcomes.

5.3.5 Challenges in developing predictive models

Despite the potential of predictive modelling, progress in this field faces several challenges. Developing effective models requires large datasets—ideally tens of thousands of high-quality, integrated data points. While many precision markers identified in this review are routinely available, generating sufficiently large datasets remains a significant hurdle. Challenges include limited access to integrated clinical data for both mothers and offspring, and inconsistencies in diagnostic approaches. In chapter 1 I presented the difficulties faced in generating data sets with granular data on glycaemic indices and high-quality data capturing key precision markers of BMI, ethnicity and family history. This represents the major challenge for developing a model for GDM risk prediction in a UK population.

Recent years have seen a surge in the development of prediction models for adverse pregnancy outcomes in women with GDM, including the likelihood of requiring pharmacological treatment (248-252). However, these models suffer from small datasets, limiting their robustness. The largest dataset used in a modelling for predicting treatment response, included 30,474 pregnancies(248). To achieve this size, the authors relied on data spanning back to 2007, introducing challenges such as variations in baseline populations (maternal age, ethnicity, BMI) and evolving screening and diagnostic thresholds. Additionally, integrated versus non-integrated healthcare systems complicate data availability, particularly for glycaemic control via self-monitoring of blood glucose after GDM diagnosis.

5.3.6 The Path Forward

Advancing this field will require significant investment to generate the large, high-quality datasets necessary for training predictive models. International collaboration will be essential to pool data across populations and healthcare systems, enabling the development of tools applicable to diverse populations and ethnic groups. Such efforts could pave the way for personalised, data-driven approaches to GDM management, improving outcomes for both mothers and their offspring while reducing the burden on healthcare systems.

6 Discussion

In this final discussion I will summarise the main findings of each study and highlight key strengths and limitations while identifying important areas for future research to explore.

6.1 Chapter 1 discussion

The COVID-19 pandemic created an opportunity to explore alternative strategies for identifying women with GDM. I presented findings demonstrating that, despite adopting a different approach to GDM diagnostic screening during the SARS-CoV-2 pandemic, once women received a diagnosis and entered a GDM pathway, pregnancy outcomes were comparable. This has been supported by recent multicentre studies evaluating screening approaches and early intervention (50, 61, 73). Additionally, personal correspondence from researchers leading the ongoing national GDM audit in England suggests that women diagnosed with GDM experience similar pregnancy risks to the general population.

Under the COVID-19 GDM emergency care pathways, all women were offered an HbA1c test at booking. I reported that the incidence of overt diabetes in pregnancy in the UK was 3%, based on an HbA1c ≥48mmol/L. This figure may represent an underestimate, as not all women in the dataset had an HbA1c performed. This screening strategy identifies a population of women with significant dysglycaemia who may have previously remained undetected until 24-28 weeks of pregnancy, or possibly throughout the entire pregnancy. Offering early screening, through a simple blood test, presents an opportunity to identify women at risk and provide timely intervention for both mothers and their offspring. This approach is reflected in the recent SIGN guidance update (SIGN 2024) and I believe this is under consideration in the next NICE update.

6.1.1 Strengths and limitations

At the time, my dataset represented the largest contemporary collection of women with GDM in the UK, including data on demographics, glycaemic indices, and pregnancy outcomes. This study remains the largest research on GDM outcomes during the pandemic, while other studies were primarily single-centre or used retrospective data (121, 130, 204, 253).

We were able to draw valuable conclusions from changes in screening approaches, such as the use of HbA1c for early detection of overt diabetes and as a tool for women who do not attend for OGTT. Another key strength of this study was identifying a trend of increasing GDM prevalence across the UK, despite predictions of a decline during the emergency care pathways. This led to a proposal to the BHF Diabetes Data Catalyst for a much larger cohort utilising data from a COVID research network established by Health Data Research UK (HDR UK), with analysis currently underway.

In Chapter 1, I briefly touched on the challenges of using routinely collected healthcare data in research. Here, I will provide a more detailed account of the issues encountered during this study and their impact on other work presented in this PhD. Routinely collected healthcare data—defined as data gathered without specific, predefined research questions—includes sources such as disease registries, primary care databases, and electronic health record repositories (254). These datasets, derived from diverse healthcare settings and geographical locations, offer valuable opportunities for informing clinical management, health service planning, and public health through innovative and cost-effective research (8).

The objective of this study was to evaluate the impact of rapid changes in screening, diagnostic, and management approaches for GDM during the SARS-CoV-2 pandemic. Routinely collected healthcare data was a logical approach for this study. However, national datasets in England (HES and MDDS) and Scotland (SMRO2), while containing information on patient demographics and birth outcomes, lacked the detailed diagnostic data necessary to address the study's aims. To overcome this, the Diabetes in Pregnancy working group identified several NHS trusts capable of providing more granular data.

Ethical approval for the study was granted in April 2021. Because the study utilised unconsented data with access to confidential patient information, additional approvals were sought from relevant bodies. Following these approvals, data acquisition from individual health boards became a significant barrier. The local research and development (R&D) approval process, delayed by COVID-19-related backlogs, took over nine months to complete. Furthermore, local processes-imposed restrictions on data fields, limiting access to key information such as age, BMI, GDM diagnosis dates, and certain outcomes deemed identifiable, including stillbirth, neonatal death, and obstetric haemorrhage.

Initially, 14 hospital sites agreed to participate, but only nine contributed data due to delays and capacity constraints. At five of these sites, manual data collection was required for certain fields, and two sites were unable to provide diagnostic data due to the labour-intensive nature of the task. Even where electronic data collection was possible, linking disparate databases proved challenging, leading to varying levels of missing data.

A critical goal of the study was to assess GDM incidence. Since identifying the screened population was outside the study's remit, GDM cases diagnosed per month relative to live births per month were used as a denominator to estimate incidence. The intensity of data collection limited pre-pandemic data availability at several sites, so conclusions about GDM prevalence were drawn from a time-matched cohort from 2019 and 2020. This constraint impacts the reliability of conclusions regarding GDM incidence, as noted in the published paper.

This research study had the goal of evaluating the impact of pandemic-related changes on the incidence of GDM and associated maternal, obstetric, and neonatal outcomes. Initially it was conceived as a mixed methods approach, where findings from the data study would inform the design of the qualitative study. Delays in approvals and data acquisition disrupted the timeline. Consequently, the qualitative study had to begin before the data study, limiting opportunities to explore key findings further. For instance, findings from the data study, such as the use of HbA1c to improve detection rates among marginalized women, could have been further explored qualitatively. Difficulties in

recruiting healthcare providers made it not feasible to conduct further interviews after completion of the data study, restricting the depth of insights gathered.

6.1.2 Future directions

Future research should prioritize monitoring ongoing trends in GDM incidence to identify if increased GDM diagnosis will return to pre COVID-19 rates; this information will be key in informing health service planning, particularly as the global pandemic continues, albeit in a non-acute state. A secondary research focus should be the exploration of previously unrecognised mediators of GDM risk. Leveraging biobanks established during the pandemic could provide valuable insights into mechanistic pathways driven by pandemic-related stress, systemic inflammation, and their potential role in GDM pathogenesis.

6.2 Chapter 2 discussion

Chapter 2 presents a qualitative study based on interviews with 23 NHS healthcare providers across three distinct NHS sites. The study provides an in-depth analysis of how GDM care was reconfigured and delivered in the early phases of the SARS-CoV-2 pandemic. It highlights pre-existing shortcomings in GDM care and demonstrates how remote antenatal brought greater convenience and accessibility. This research also explores strategies employed by healthcare providers to address language barriers, offer culturally sensitive care, and develop alternative pathways to reduce inequalities in remote care delivery.

6.2.1 Strengths and limitations

This is the first study to qualitatively examine the COVID-19 reconfiguration of GDM services in the NHS from the perspective of HCPs. While other research has investigated the use of the GDm health app among women (233) or explored remote care experiences in other health care systems (226, 234, 238), this study uniquely focuses on NHS

providers. It also sheds light on the specific challenges and adaptations required to deliver remote GDM care, providing insights for future service improvements in the post-pandemic era.

The timing of the data collection, from November 2020 to April 2021, was particularly advantageous. Although delays due to ethical and study approvals postponed the research, this allowed healthcare providers to reflect on their experiences after immediate safety concerns had subsided and new practices had become embedded. This approach enabled the application of the Normalization Process Theory framework to analyse the evolution and sustainability of remote GDM care.

Conducting the study during a period of unprecedented change offered the opportunity to explore the real-world use of remote care technologies, particularly for hard-to-reach groups often excluded from research (195).

Another strength of this study is the inclusion of a diverse range of healthcare providers from various disciplines within multidisciplinary teams, as well as those serving geographically and socio-demographically diverse populations—a significant achievement given the challenges faced by researchers during the pandemic (255). By capturing a broad spectrum of perspectives within individual teams, I was able to thoroughly explore team dynamics and gain valuable insights into whether and how multidisciplinary care could be effectively delivered remotely.

I have reflected on my role as a clinical researcher and how my own experiences and beliefs about GDM care may have influenced the study findings. These influences were evident at various stages, from shaping the research questions to conducting interviews, eliciting responses, and analysing, interpreting, and presenting the data. While this could be seen as a limitation, Braun and Clarke's concept of reflexive thematic analysis frames it differently. This approach views themes as "creative and interpretive stories" that emerge through the interplay between the data and the researcher's knowledge, analytical skills, and theoretical assumptions (256). From this perspective, my role as a clinical researcher can be seen as a strength rather than a bias. During the interviews, I was struck by the participants' honesty. Many healthcare providers appeared to find the interviews cathartic, using them as an opportunity to offload and share their experiences.

I believe their openness stemmed, at least in part, from seeing me as an “insider.” They seemed more comfortable speaking candidly to someone who understood their professional challenges. Had they been speaking to someone outside the healthcare community, their responses might have been more measured and guarded.

The first and perhaps most obvious limitation of this study was the decision to explore remote delivery of care solely from the perspective of HCPs, without including the perspectives of women. This choice was made for sound reasons. Primarily, the time required to include both women and HCPs in a qualitative study would not have been feasible within the constraints of a multi-methods PhD study. Therefore, it was necessary to focus on one group. Given that existing literature on remote care delivery often overlooks the views of HCPs, I saw an opportunity to address this gap. Additionally, practical considerations, such as easier recruitment and a simplified ethics process, made studying HCPs experiences more manageable than including women.

It is undeniable that, without the time constraints of a PhD study, including women's perspectives would have enriched the findings and allowed for a more comprehensive understanding by addressing the perceptions presented by HCPs. One way to have increased women's representation within these time constraints would have been to establish a group of women to provide Patient and Public Involvement (PPI) input. This might have generated additional and different interview questions that held value for women, making the findings more relevant. The absence of this PPI input represents a significant limitation of the study, one I would address if involving PPI had been feasible at the time.

My decision to focus this study on individual multidisciplinary teams (MDTs) to gain a deeper understanding of team dynamics has affected the generalizability of some findings. Although I selected three substantially different sites to mitigate this limitation, these sites are not fully representative of the UK healthcare system as a whole

One methodological consideration I have reflected on was the decision not to use a combination of individual interviews and multi-disciplinary focus groups. Evidence suggests that collecting various sources of qualitative data, alongside individual interviews, can enhance analysis and allow for the triangulation of findings (257). Focus

groups are particularly known for offering deeper insights into team dynamics and the social context of delivering remote clinical care (257). However, in the context of conducting a multi-methods PhD study, focus groups presented several methodological and practical challenges beyond those posed by social restrictions during the SARS-CoV-2 pandemic. These included scheduling difficulties, a lack of experienced focus group facilitators, a higher volume, intensity, and complexity of data collection, and the potential influence of professional hierarchies on group dynamics. These factors could have affected the types of insights and information that participants felt comfortable sharing. Given these considerations, and despite the pandemic's constraints, it is unlikely that using focus groups would have been feasible within the timeframe of my research.

Throughout this study, I relied on the expertise of my PhD supervisor (JL), who played a key role in developing and revising the interview topic guide, the coding framework, and helping to generate the themes presented in the findings. However, according to the COREQ guidelines for reporting qualitative research (215), it is recommended that a second qualitative researcher independently code and analysing the data before reaching a consensus. Since this work is part of a doctoral study, this level of involvement was not required. However, involving a second coder could have enhanced the rigor and robustness of the findings.

6.2.2 Future direction

This study highlights key areas for future research and policy considerations. A logical next step is to examine the use of remote clinical care for GDM over the five years following the pandemic's onset. Such research should include the experiences of service users—women and their support networks—as well as input from stakeholders like managerial and systems-level staff, to capture a comprehensive understanding of remote care's impact.

To explore the factors that have supported remote care delivery since the pandemic, qualitative methodologies such as ethnography and longitudinal case studies could

provide richer, more nuanced data. These approaches would help capture changes over time, offering insights into how remote care has evolved and is sustained.

The study also suggests that HCP fatigue may be affecting obstetric antenatal care. Future research should focus on how provider well-being impacts care delivery, aligning with the UK government's emphasis on staff welfare (258). Addressing burnout is essential for retaining staff and ensuring sustainable, high-quality patient care.

Additionally, there is potential to develop care models tailored to women with uncomplicated GDM. These models, led by allied health professionals and incorporating remote technologies, could offer personalized care, reduce hospital visits, and improve accessibility. A pilot study could assess the experiences of both service users and providers, along with maternal and offspring outcomes and cost implications. Insights from such a study could guide sustainable improvements in NHS maternity care.

6.3 Chapter 3 discussion

Overall, based on findings from moderate-to-good quality studies, key maternal characteristics were identified that may be used to build prediction models for pharmacological GDM treatment. Precision markers for GDM treatment are usually available from routine clinical measures; however, it is unknown whether other precision markers could be identified (for example, genetics or "omics") or whether these can be implemented in clinical practice.

6.3.1 Strengths and limitations

This work was commissioned through the PMDI with the broad concept of synthesizing the evidence for precision markers in the treatment of GDM. The main strength of this study lies in the decision to narrow the focus of this study into two reviews one examining precision approaches that enable the achievement of glucose targets through lifestyle measures alone and a second review examining whether personal characteristics of the mother or offspring predict the need for treatment or escalation of treatments above lifestyle interventions. In designing our research questions this way, the need for treatment or escalation of treatment acts as a surrogate for stratifying women and babies

at greatest risk. Utilising robust methods, we have maximised the opportunity to summarise the available evidence to most helpfully guide future researchers and funders.

The main strengths and limitations of this work are outlined in detail Chapter 3.

6.3.2 Future directions

The findings from the systematic review(s) highlight a significant gap in studies evaluating the role of genomics and small molecules (lipidomics, proteomics, insulin resistance). Inadequate numbers of studies were available to draw even basic conclusions. Another area for consideration is the role of precision markers that could predict responses to specific pharmacological agents. There is a need for well-designed large cohort studies where precision markers assessed at numerous time points throughout pregnancy are reported to outcomes of GDM diagnosis, requirement for treatment and linked through to both maternal and neonatal outcomes and postnatal outcomes. There is a need for such studies to be conducted across multiple populations.

While the identification and quantification of risk are clinically useful to better inform the patient and clinician, there is also a need for evidence-based interventions running in parallel. Traditional interventional studies have targeted whole populations. Moving away from this approach to precision-based treatment will be an important next stage. This review highlights the potential of routine clinical precision markers, such as BMI and lipid profiles, to predict treatment response in GDM. Importantly, many of these markers are modifiable, offering opportunities for targeted interventions. Future research should explore interventions in the preconception or early pregnancy periods aimed at addressing these precision markers

6.4 Overall reflections

A key strength of this thesis is its alignment with the top 3 of the 10 JLA priorities. My early involvement in the JLA GDM Priority Setting Partnership (PSP) allowed me to ensure that each study conducted as part of my PhD was aligned with the priorities outlined in this process, ensuring that my work reflects the views of women, their families, and healthcare providers.

The majority of the work presented in this thesis was conceived and began during the first year of the SARS-CoV-2 pandemic. During this time, developing research skills, gaining study approvals, and recruiting participants for clinical research proved to be an exceptionally challenging process—due not only to the risk of infection but also the immense pressure on acute health services to continue providing care. Despite these challenges and the limitations, they created, I am proud of what these studies have achieved in making a significant contribution to the field of knowledge in delivering GDM care during the pandemic.

This thesis has provided me with a solid foundation in health service evaluation research methodologies. Through this work, I have explored critical issues in GDM care during an unprecedented time for the NHS, shaping my approach to service delivery, equity, and innovation in healthcare.

6.5 Final conclusion

This thesis highlights several strategies for optimising GDM care in the UK. Key findings from the pandemic include the rising incidence of GDM, the potential for adjunct screening tools to better detect overt diabetes and reach marginalised women, and the effectiveness of remote antenatal care. Beyond existing approaches, precision methods may refine treatment pathways by enabling earlier identification of women requiring

escalated care however significant effort will be required to acquire the data needed to generate and validate precision tools in the future.

7 Appendices

7.1 Appendix 1. Diabetes in pregnancy James Lind Alliance priority setting partnership

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RESEARCH: TREATMENT

DIABETIC Medicine

The top 10 research priorities in diabetes and pregnancy according to women, support networks and healthcare professionals

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Abstract

Aims: To undertake a Priority Setting Partnership (PSP) to establish priorities for future research in diabetes and pregnancy, according to women with experience of pregnancy, and planning pregnancy, with any type of diabetes, their support networks and healthcare professionals.

Marian Knight and Katherine Cowan should be considered joint senior authors.

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Methods: The PSP used established James Lind Alliance (JLA) methodology working with women and their support networks and healthcare professionals UK-wide. Unanswered questions about the time before, during or after pregnancy with any type of diabetes were identified using an online survey and broad-level literature search. A second survey identified a shortlist of questions for final prioritisation at an online consensus development workshop.

Results: There were 466 responses (32% healthcare professionals) to the initial survey, with 1161 questions, which were aggregated into 60 unanswered questions. There were 614 responses (20% healthcare professionals) to the second survey and 18 questions shortlisted for ranking at the workshop. The top 10 questions were: diabetes technology, the best test for diabetes during pregnancy, diet and lifestyle interventions for diabetes management during pregnancy, emotional and well-being needs of women with diabetes pre- to post-pregnancy, safe full-term birth, post-natal care and support needs of women, diagnosis and management late in pregnancy, prevention of other types of diabetes in women with gestational diabetes, women's labour and birth experiences and choices and improving planning pregnancy.

Conclusions: These research priorities provide guidance for research funders and researchers to target research in diabetes and pregnancy that will achieve greatest value and impact.

KEYWORDS
diabetes mellitus, health priorities, perinatal care, post-natal care, pregnancy, prenatal care, researchNovelty statement

- Women report a lack of consistent evidence-based information to help them manage their diabetes in the period before to after pregnancy.
- The top 10 questions for research in diabetes and pregnancy according to women, their support networks and healthcare professionals were identified.
- Joint top priorities for research were diabetes technology and identifying the best test for diabetes in pregnancy.
- These questions will inform funders of research and researchers towards addressing areas of great need and impact.

1 | INTRODUCTION

Approximately one in every 10 women will experience a pregnancy complicated by either pre-existing or gestational diabetes.[1] Rates are increasing as a result of increased rates of obesity and pregnancy at a later age.[2] Although most women have healthy pregnancies and healthy babies, diabetes increases the risk of complications during pregnancy and birth, and can have long-term effects. Compared to the maternity population without diabetes, the risks are two to six times greater for adverse outcomes such as congenital anomalies, stillbirth, preterm birth, infant death within the first month of life, together with long-term risks of adverse cardiovascular outcomes in both mothers and children.[3,4]

Many pregnant women with diabetes report a lack or inconsistency of information, leaving many of their questions unanswered. National guidelines and high-quality systematic reviews highlight variable quality, heterogeneity and reliability of research. Consequently, treatment guidelines are insufficiently evidenced in line with current context and available healthcare options.[5,6] However, with limited funding and resources available for research, it is important to ensure that the research that is undertaken is of highest value and impact.

Healthcare research led by industry and researchers often does not address the issues that are most important for people living with the condition, or those who support them.[7] The James Lind Alliance (JLA), a UK-based initiative established in 2004, aims to address this mismatch.

Through Priority Setting Partnerships (PSP), the JLA supports the identification of the research questions that matter most to patients and the healthcare professionals that care for them. Sharing the outputs of PSPs with health research funders helps to align the work they fund towards addressing the areas of need prioritised by those directly affected and involved.

Previous successful PSPs have been conducted in diabetes in the UK. The type 1 diabetes PSP identified two questions in pregnancy, but both fell outside the top 10 priorities: 'What impact do changing hormones, for example, during menstruation, pregnancy and menopause, have on blood glucose levels in women with type 1 diabetes?'; 'Is it safe to continue insulin analogues in preconception and pregnancy in type 1 diabetes?'[8] No priorities specific to pregnancy were identified in the type 2 diabetes PSP top 10.[9] There have also been prioritisation exercises using different but overlapping methodology to PSPs in Canada and the USA but focussing on gestational diabetes.[10,11] However, women's health and pregnancy, particularly in relation to diabetes, are not prioritised, despite being consistently identified as an area of much needed research.[2,12,13]

A PSP was therefore established between the University of Oxford, Diabetes UK, Diabetes Research and Wellness Foundation, JDRF the type 1 diabetes charity, and JLA, on World Diabetes Day 2018. The PSP aimed to find out the priorities for future research in diabetes and pregnancy, according to women and their support networks (families, partners, friends and carers) with experience of pregnancy, or planning pregnancy, with any type of diabetes and healthcare professionals.

2 | PARTICIPANTS AND METHODS

The PSP employed the established JLA methodology.[14]

2.1 | Establishing the PSP

The PSP was overseen by a steering group representing key stakeholders (Supplementary Table S1) and was chaired by a senior JLA advisor to ensure transparency of the process, and fair and equal involvement of all members. The group agreed the scope (Table 1) and was responsible for the completeness and appropriateness of the process, ensuring involvement of key stakeholder groups, approval of categorisation, grouping and phrasing of questions and interpretation of data. The protocol was prospectively published online at www.jla.nihr.ac.uk/priority-setting-partnerships/diabetes-and-pregnancy.

2.2 | Initial survey—identifying questions

Women and their support networks (partners, families, friends and carers) with experience of pregnancy or planning pregnancy with any type of diabetes and healthcare professionals were invited via an open survey (26 June–15 November 2019) to suggest up to three questions they felt were important to answer. These could be any questions about the time before, during or after pregnancy with any type of diabetes. The scope was intentionally broad so that the submissions reflected public need.

The survey was available, in English, online and on paper. Targeted efforts to maximise responses, particularly from underrepresented groups, included direct approaches in diabetes and pregnancy clinics, outreach through relevant support groups, professional networks and conferences, diabetes, pregnancy and birth charities' websites and communication channels and social media platforms. Concerted efforts were made to hear the voices of ethnic minorities working with organisations, support groups and community champions, which aim to address health inequalities. Representation across different ethnic minorities was monitored through broad groupings.

TABLE 1 Scope of the James Lind Alliance priority setting partnership in diabetes and pregnancy

Questions about the following were included:	Women, their partners, babies and families Diabetes, including pre-existing diabetes of any type and subtype, and gestational diabetes Time period in relation to pregnancy (i.e. preconception, antenatal, neonatal, post-natal and short- to long-term health outcomes) Management of diabetes in pregnancy (i.e. screening, causes and prevention, diagnosis and treatment) Physical, social, cultural, economic and psychological aspects Co-morbidities and complications Genetics, fertility and related aspects Information, education and service improvement Relevant to the UK population. This was intended to be a UK exercise with a UK focus.
Questions about the following were excluded:	Pregnancy uncertainties not specific to diabetes Care of the baby on a neonatal unit Questions or priorities without a UK focus or relevance

2.3 | Categorisation and grouping

The submitted questions were organised using NVivo qualitative data analysis software (QSR International Pty Ltd. Version 12, 2018). Initial data cleaning was manually completed with any issues about the clinical aspects or interpretation of the submitted questions resolved with the steering group. The questions were analysed using content analysis with an initial stage of open coding of the question content, followed by the grouping of codes into categories.[15] To retain the integrity of the initial submissions, some questions were mapped to two or more categories. Independent second checks were conducted with members of the steering group to ensure potential impact of individual bias, and missed or misinterpreted categorisation was minimised. The steering group further consolidated the categories into groups and summarised the initial survey submissions under an indicative question. Indicative questions were formulated to capture the issues raised by the submitted questions within each group, whether originating from single or multiple respondents.

2.4 | Evidence checking

A broad level and pragmatic evidence checking strategy was taken (January – May 2020) with the aim of ascertaining whether there was evidence of substantial uncertainty for each indicative question. The search was restricted to the Cochrane Database of Systematic Reviews (www.cochranelibrary.com), systematic reviews published since 2017 using Medline or PubMed and National Institute of Clinical Excellence (NICE) and Scottish Intercollegiate Guidelines Network (SIGN) national diabetes and pregnancy guidelines.[5,6] Expanded evidence searches, including evidence highlighted by the steering group, were applied on a question-by-question basis after finalisation of the list of indicative questions. Research underway or recently completed but not available as published was not included as evidence. Where part of the question had sufficient evidence, the question phrasing was amended to reflect the remaining uncertainty.

2.5 | Interim survey and prioritisation

The interim survey presented the long list of indicative questions in groups by phase. The order of the groups and individual questions within the groups were randomised each time the survey was entered. Participants were invited to pick up to 10 that they felt were most important to answer. Due to the Covid-19 pandemic and social distancing restrictions, the survey was offered online only. Following a pilot mid-May, the survey ran for nine weeks (29 May–31 July 2020).

2.6 | Interim ranking and shortlisting

Every selection made by an individual respondent had equal weighting and no weighting changes were made if fewer than 10 questions were selected. However, to account for the differences in observed voting patterns and the number of respondents from different groups, ranking was tallied separately for: women and support networks, healthcare professionals, ethnic minorities and diabetes type, namely type 1, type 2 and other, and gestational diabetes. Within each of the groups, the total points for each question were put into rank order. The questions ranked in the top 10 for the two main groups (women/support networks and healthcare professionals), and the top three, and at least eight of the top 10, for each of the other subgroups, were shortlisted. In total, 18 questions were shortlisted for the final workshop, the maximum number considered feasible by the steering group for effective discussion online.

2.7 | Final workshop—agreeing the top 10

The final stage involved a 1-day workshop (2 October 2020) using the established JLA approach, which was adapted to be delivered online.[14] Twenty-five participants were identified initially through phased targeted approaches to prioritise representation from ethnic minority groups, the devolved nations and Crown dependencies, support networks and specific health professions, for example, psychologists and GPs as underrepresented groups, followed by open invitation. Contacts collated through the surveys, and special interest groups and partner communication channels were used. Participants were screened for possible conflicts of interest and whether they were highly research active in the area. The participants were split into four breakout groups balanced by representation between women, support networks and healthcare professionals, and by experience of diabetes and healthcare specialist.

In breakout groups, the attendees participated in a series of discussion and ranking exercises to jointly rank the shortlist of indicative questions and agree the top 10 most important for future research to answer. The workshop and discussions were facilitated by trained JLA advisors to ensure equal and open participation. Four steering group members joined as observers only. Technical support was made available, and a contact point for emotional support was provided should any participant be upset by the process or discussions. The participants were invited to provide anonymous feedback on the prioritised questions and the workshop generally.

2.8 | Ethics

The Medical Sciences Interdepartmental Research Ethics Committee, University of Oxford confirmed that the project did not require ethics committee approval.

3 | RESULTS

The top 10 areas of most needed research in diabetes and pregnancy identified were: diabetes technology at any stage pre- to post-pregnancy, the best test for diabetes during pregnancy, diet and lifestyle interventions for diabetes management during pregnancy, emotional and well-being needs of women with diabetes pre- to post-pregnancy, safe birth at full term, post-natal care and support needs of women, diagnosis and management late in pregnancy, prevention of other types of diabetes in women with gestational diabetes, women's labour and birth experiences and choices and improving planning for pregnancy (Table 2).

The responses at each stage of the process are summarised in Figure 1. Participant demographics at each stage of the process are in Table 3. The survey submission counts and rankings for the 60 indicative questions are available in Supplementary Table S2.

3.1 | Initial survey

Four hundred and sixty-six responses were submitted (64% women and support networks, 32% healthcare professionals and 4% other/not answered) suggesting 1161 questions covering the whole perinatal period (Supplementary Table S3).

Initial questions submitted by women and support networks were mainly in relation to post-birth effects on themselves and their child, diabetes management during pregnancy and understanding the risks for diabetes in pregnancy. The long-term effects of diabetes in pregnancy on the child (risks of the child developing diabetes and any wider health effects) being the most frequently asked question (20.1% of women and support networks' submissions). This group more specifically raised questions about breastfeeding (8.9%) and labour and birth (8.6%) in terms of informed choice, continuity/availability of care and emotional support more generally. Healthcare professionals' questions were mainly about pre-pregnancy care, and diagnosis and clinical management of diabetes in pregnancy. How to improve preconception care was most frequently asked (9.7% of healthcare professionals' submissions), closely followed by the value and methods of diagnosis and management of diabetes late in pregnancy, that is, after 34 weeks (8.5%). Modes of delivering care, improving uptake and access to services and motivational interventions were more specifically raised by this group. Common to both groups were questions about individualised and risk-based care, optimal management of diabetes, prevention of diabetes and safety of medications.

One hundred and forty-two categories were extracted and broadly organised by the phase of pregnancy: pre-pregnancy (62 questions, 6.3%), pregnancy (376, 38.2%), labour and birth (87, 8.8%) and post-birth (373, 37.9%). Technology (20, 2.0%), mental health and well-being (20, 2.0%) and health services (46, 4.7%) were identified as cross-cutting categories. A total of 934 questions were within scope, of which 50 mapped to more than one category, and consolidated into 60 indicative questions. Rarely was there a need to specify a type of diabetes within an indicative question, which reflects the significant overlap in priorities regardless of diabetes type. The main distinctions were questions relating to gestational diabetes, due to its transient nature and diagnosis in pregnancy. All 60 indicative questions were considered to have substantial uncertainty following evidence checks. The evidence check summary is provided in Supplementary Table S4.

3.2 | Interim survey

Six hundred and fourteen submissions (80% women and support networks and 20% healthcare professionals) were received in the interim survey. In the interim survey rankings, there were notable differences between women and support networks, and healthcare professionals (Figure 2a). Four of the top 10 ranked questions for healthcare professionals were below the 45th ranking for women and support networks. Women and support networks ranked the long-term effects of diabetes in pregnancy on the child's general health (non-diabetes-related) highest. Varying standards and advice across hospitals and giving birth at full term were also in the top three.

Voting patterns varied for the main groups between surveys (Figure 3) with overall movement towards labour and birth and cross-cutting categories. For example, despite being rarely asked in the initial survey, the use of technology became the highest ranked for healthcare professionals in the interim survey.

For ethnic minorities, representation was below national population figures for Black and Black British groups in both surveys (1.6% and 0.5% respectively; national 3.0%), and for Asian and Asian British groups (4.1%; national 7.0%) in the interim survey. With low numbers, the votes across 60 questions became too dispersed to discern a strong pattern. However, peaks in voting overlapped the top 10 for women and support networks, and healthcare professionals, with the eight highest voted questions already shortlisted for the final workshop.

TABLE 2 Top 10 priorities for research in diabetes and pregnancy according to women, their support networks and healthcare professionals

Final rank	Phase	Indicative question	No. initial questions	Interim survey rank by group					
				HCPs	Women & support	Ethnic minorities	T2D/ Other	T1D	GDM
=1	Cross-cutting	How can **diabetes technology** be used to improve pregnancy, birth and mother and child health outcomes?	10	1	13.5	10.5	1	1	23
=1	During pregnancy	What is the **best test** to diagnose diabetes in pregnant women?	14	7	46	13	8	43	21.5
3	During pregnancy	For women with diabetes, what is the best way to manage blood sugar levels using **diet and lifestyle** during pregnancy?	47	45	8	3	37.5	28.5	10
4	Cross-cutting	What are the **emotional and mental well-being needs** of women with diabetes before, during and after pregnancy, and how can they best be supported?	14	20	4	8.5	18.5	9	5
5	Labour and birth	When is it safe for pregnant women with diabetes to give **birth at full term** compared with early delivery via induction or elective caesarean?	16	3	3	5.5	5.5	4	4
6	After pregnancy and birth	What are the specific **post-natal care and support needs** of women with diabetes and their infants?	9	28	13.5	10.5	33	3	35.5
7	During pregnancy	What is the best way to test for and treat **diabetes in late pregnancy,** that is, after 34 weeks?	29	4	57.5	44.5	3.5	41	43.5
8	After pregnancy and birth	What is best way to reduce the risk or prevent **women with gestational diabetes developing other types of diabetes** any time after pregnancy?	64	5.5	6	2	9	52	3
9	Labour and birth	What are the **labour and birth experiences** of women with diabetes, and how can their choices and shared decision making be enhanced?	6	32	10	21	18.5	8	13
10	Before pregnancy	How can care and services be improved for women with diabetes who are **planning pregnancy**?	37	2	47	33	2	10	45

The indicative questions are presented in final rank order, with phase of pregnancy, the question concerns, the number of initial survey questions grouped within the indicative question and the interim survey ranking results by group; HCPs - Healthcare professionals; T1D – Type 1 diabetes; T2D – Type 2 diabetes; GDM – Gestational diabetes mellitus.

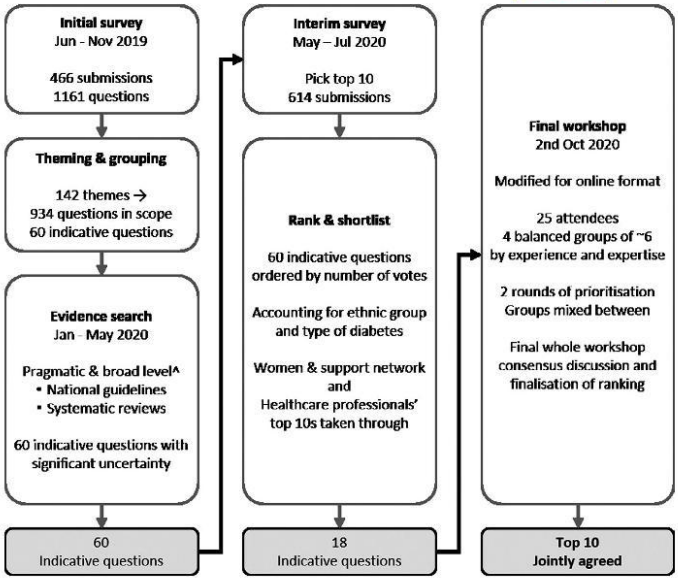

FIGURE 1 Summary of the James Lind Alliance prioritisation process showing how the top 10 questions in diabetes and pregnancy were identified. ^Ongoing studies were not included as evidence as it would not be possible to know if they answer the question

TABLE 3 Participant demographics at each stage of the priority setting process

Participant demographics / Stage n (%)	Initial survey	Interim survey	Workshop[a]
Total	466	614	25
Experience			
Women with lived experience	287 (61.6)	473 (77.0)	9 (36.0)
Support network	11 (2.4)	20 (3.3)	2 (8.0)
Healthcare professionals	149 (32.0)	121 (19.7)	14 (56.0)
Other/not answered	19 (4.0)	-	-
Living in			
England	374 (85.8)	506 (82.4)	19 (76.0)
Scotland	25 (5.7)	29 (4.7)	0 (0.0)
Wales	15 (3.4)	22 (3.6)	5 (20.0)
Northern Ireland	8 (1.8)	24 (3.9)	1 (4.0)
Crown dependency	0 (0.0)	2 (0.3)	0 (0.0)
Not in the UK	7 (1.6)	25 (4.1)	-
Not answered	7 (1.6)	6 (1.0)	-
Age			
19 years old or under	1 (0.2)	0 (0.0)	-
20 to 29 years old	79 (18.1)	92 (15.0)	-
30 to 39 years old	201 (46.1)	350 (57.0)	-
40 years old or over	144 (33.0)	166 (27.0)	-
Not answered	11 (2.5)	6 (1.0)	-
Ethnicity			
White	325 (74.5)	554 (90.2)	17 (68.0)
Asian and Asian British	59 (13.5)	25 (4.1)	5 (20.0)
Mixed and multiple ethnic groups	13 (3.0)	15 (2.4)	3 (12.0)
Black and Black British	7 (1.6)	3 (0.5)	0 (0.0)
Other	10 (2.3)	9 (1.5)	0 (0.0)
Not answered	22 (5.0)	8 (1.3)	-
Education level[b]			
School (up to GCSE or equivalent)	26 (6.0)	11 (1.8)	-
School (A-levels or equivalent)	23 (5.3)	21 (3.4)	-
Higher education (e.g. college)	60 (13.8)	76 (12.4)	-
Degree level or higher	311 (71.3)	343 (55.9)	-

(Continues)

TABLE 3 (Continued)

Participant demographics / Stage n (%)	Initial survey	Interim survey	Workshop[a]
Not answered	16 (3.7)	163 (26.5)	-
Diabetes type[c] (diagnosis/ interest)			
Type 1	-	218 (27.6)	3 (25.0)
Type 2	-	88 (11.2)	3 (25.0)
Gestational	-	406 (51.5)	4 (33.3)
Other, for example, MODY, LADA	-	39 (4.9)	2 (16.7)
None/not indicated	-	38 (4.8)	-
Clinical specialism			
Consultant Nurse in Diabetes	-	-	1 (7.1)
Diabetes Specialist Nurse	-	-	2 (14.3)
Diabetes Specialist Midwife	-	-	3 (21.4)
General Practitioner (GP)	-	-	1 (7.1)
Obstetrician	-	-	3 (21.4)
Diabetes and Pregnancy Specialist Dietician	-	-	1 (7.1)
Diabetologist	-	-	3 (21.4)

[a]Unfortunately, despite purposeful outreach, no expressions of interest were received from people with Black or Black British ethnicity or people living in Crown dependencies, and three people were invited from Scotland but withdrew at a later stage before the workshop. One of the women representatives had experience of pregnancy with Maturity Onset Diabetes of the Young (MODY), and another Latent Autoimmune Diabetes of Adulthood (LADA). The support network representatives, a sister and a husband, brought experience of type 1 diabetes and type 2 diabetes respectively.

[b]Due to a technical error in the interim survey, the first 155 submissions did not have this question completed.

[c]Included in the interim survey to account for differences between priorities in relation to different types of diabetes. Multiple choice was enabled. Workshop data presented only for women and support network representatives. Some women had experience with more than one type of diabetes.

Comparing the interim survey rankings by types of diabetes, there were some clear differences (Figure 2b). Technology was ranked the top priority for type 1 and type 2/other diabetes groups, but ranked low for the gestational diabetes group. Post-birth support came in second for type 1, but ranked low for both type 2/other and gestational diabetes groups, whereas testing for diabetes during pregnancy and prevention of developing diabetes ranked high for type 2/other and gestational diabetes groups but low for the type 1 diabetes group.

3.3 | Final workshop and top 10

The diversity and balance in experiences and expertise of workshop attendees were strong (Table 3). Participants uncovered unexpected overlaps between questions, for example, technology for diabetes care was considered to include telemedicine which was subsequently ranked lower; labour and birth choices was considered to overlap with safety of giving birth at full term and the need for induction. Groups also highlighted recurring themes that linked with multiple questions. For example, technology was considered to improve understanding of diabetes management and reduce burden, linking with mental health and well-being. Therefore, with further such links highlighted, both these questions were more highly ranked as the discussions progressed.

Consistently, top ranking questions through the surveys were regarding the long-term health impact of maternal diabetes on the child. The questions submitted in the initial survey were clearly split into risk of the child developing diabetes or the risk of wider health conditions. Ranking in the top 10 of all groups, both questions were shortlisted for the final workshop. However, neither reached the final top 10 (positions 11 and 12 respectively). Workshop discussions and post-workshop feedback from participants indicated several reasons for this apparent discrepancy. Firstly, the questions were considered to be addressed within the broader research agenda of child health, and not necessarily within pregnancy or women's health. The other questions all affected or contributed to the child outcomes, so it was felt they would help address these questions too. Some participants considered that the answers to the questions about long-term child outcomes would add burden to women already concerned by many factors associated with dealing with the responsibility of a pregnancy and diabetes. For some, 'how can it be prevented' was important wording, as it balanced the concerns of adding burden of information on risks, with learning about what can be done to prevent these being realised. One of the questions did not include the specific wording about prevention and so was ranked less highly. A further possible reason for these questions receiving less priority was because the votes were split; if presented as a single question, this may have meant a higher final ranking. A final possible reason may have been that the workshop consisted of people with recent experience, that is, within the last five years.

Feedback was received from 10 women and support network representatives, and 10 healthcare professionals from the workshop:

> *'It was really good having different perspectives. Moving to a second smaller group was also useful, as it showed how varied priorities can be between 2 groups, despite having a similar mix of people from the different backgrounds'*

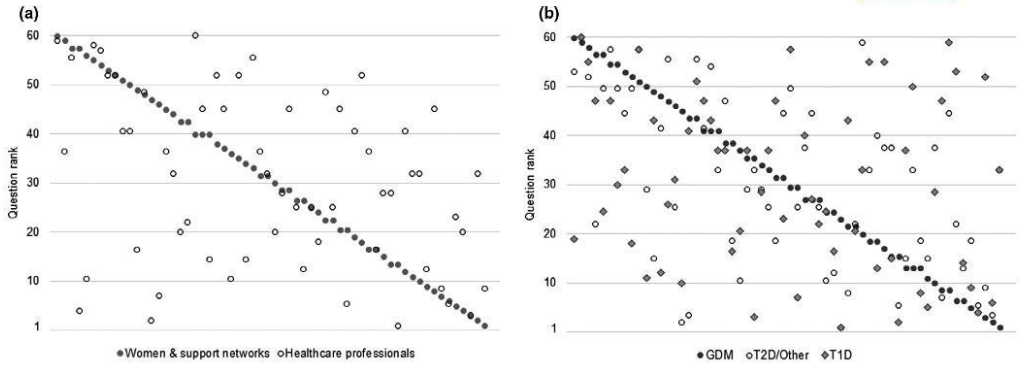

FIGURE 2 Interim survey question ranking comparisons between respondent groups. (a) Main groups: Indicative questions are ordered by rank position for women and support networks (60th to 1st place; left to right). (b) Diabetes type: Indicative questions are ordered by rank position for the group that indicated interest/experience in gestational diabetes (60th to 1st place; left to right). 'Other' types were grouped with type 2 diabetes due to low number and greatest similarity in rankings. T1D – Type 1 diabetes; T2D – Type 2 diabetes; GDM – Gestational diabetes mellitus

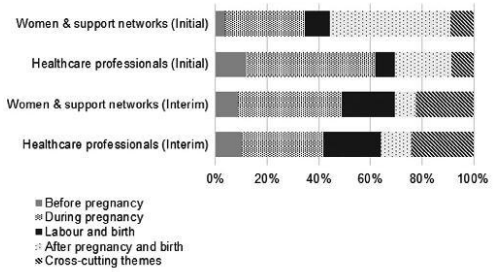

FIGURE 3 Survey submissions by main group. The initial and interim survey submissions for women and support networks, and healthcare professionals proportioned by phase of pregnancy

> *'Although the final top 10 was not the same as my personal top 10 that I had prepared, discussing all of the 18 questions, and reflecting on them as a group, meant I was satisfied with it. It was good to hear the views of women with different forms of diabetes and look at the questions from their perspective'.*

Further excerpts of the feedback and the JLA's review of the online format of the workshop are available at www.jla.nihr.ac.uk/development-of-online-priority-setting-workshop.htm.

4 | DISCUSSION

4.1 | Main findings

We supported women, their support networks and healthcare professionals to jointly identify the top 10 questions for research in diabetes and pregnancy. The final list includes priorities of relevance to all the stakeholders, all types of diabetes and preconception to long-term post-pregnancy. These questions were generated through a robust and inclusive process, which can be trusted and used by funders of research and researchers to inform their research activities towards addressing evidence gaps of great need and impact.

There is consistency across many areas also identified by the modified prioritisation exercises in Canada and the USA focussing on gestational diabetes, such as screening, risk factors, prevention and clinical management of diabetes in the woman.[10,11] For example, whether there is a better test for diabetes during pregnancy than the oral glucose tolerance test was ranked joint first for similar reasons of application, interpretation and practicality, with no apparent consensus on the thresholds, methods and timing to test for diabetes in pregnancy, due to small-sized studies. Our participants raised further questions such as the possible use of testing to predict gestational diabetes, the stratification of testing by risk and testing within special populations, such as those who have undergone gastric bypass surgery, and open up further opportunities for research.

There are also some clear differences in priorities including preconception care, late pregnancy diagnosis, labour and birth experiences and post-natal care needs, particularly breastfeeding. The role of diabetes technology was ranked joint first position, and while explicably not featuring in the gestational diabetes exercises, technology-specific questions formed the top three of the JDRF UK type 1 diabetes PSP final top 10. There have been significant developments in diabetes technology in the last few years with ongoing innovations.[16] In the time since the final workshop, the National Institute of Clinical Excellence has completed their review and approved the

funding of continuous glucose monitoring for pregnant women with type 1 diabetes, in line with *The NHS Long Term Plan*.[17,18] However, our results endorse their recommendations for further large-scale research in different monitoring methods and systems (i.e. insulin pumps) in women with diabetes of different types, through all stages preconception to post-pregnancy, and importantly with wider population diversity. There are also wider facets to consider such as apps, automation, data integration platforms and data sharing in supporting the management of diabetes.

Risks to the child's health was the number one priority identified by women in the Canadian exercise, and ranked highest in the USA exercise, but strikingly fell outside our top 10. However, the possible reasons for this, based on differential prioritisation of two related summary questions, made clear that the impact on the child is still considered highly important for separate study.

Important overarching issues were noted around continuity of care and support (particularly post-birth), consistency in care standards and advice, joint decision making (particularly in labour and birth) and the burden for women of being diagnosed with and managing diabetes. The consequences on women's well-being and mental health were at the core of much of the discussion at the final workshop. The initial survey submissions also raised further unanswered questions about the impact of a 'medicalised' pregnancy, withdrawal of intensive clinical involvement postpartum and support needs of women if adverse outcomes in their child linked to diabetes are realised. There is ongoing lack of evidence on the support pregnant women with diabetes may need as previously echoed by the gestational diabetes prioritisation exercises. However, the Diabetes UK *Too Often Missing* report highlights pregnancy as a time of particular high risk for emotional and psychosocial impact of diabetes requiring increased awareness and support.[19]

5 | STRENGTHS AND LIMITATIONS

This is the first priority setting exercise to focus on all different types of diabetes and at any stage before, during and after pregnancy, including long-term post-pregnancy.

The initial survey was completed in 2019 before the Covid-19 pandemic and lockdowns, but the interim prioritisation survey and final workshop took place during the pandemic over 2020. Due to the restrictions, the interim survey and final workshop could only be completed online. Despite an increased response rate in the interim survey, the online-only nature will have imposed limitations on who could take part. Reliance on online-only means of communication and participation may also have affected outreach, particularly to ethnic minority groups, which was achieved in the initial survey mainly through the support of community champions and face-to-face approaches in hospital clinics. However, despite our best efforts, representation was below what may be expected based on national population statistics, particularly Black and Black British groups.[20] Therefore, the results may not be representative of the priorities of ethnic minority groups.

Although the indicative questions were established before the 2020 Covid-19 pandemic, it is possible that the voting in the interim survey and, consequently, the shortlist of questions for the final workshop have been influenced. The final workshop participants were advised to consider the shortlisted questions thinking longer term beyond the pandemic so that this would not unduly influence the results for the future. More generally, it is not assured that if the exercise was redone that the same priorities would be identified and assigned the same rank.

6 | CONCLUSIONS

Further research is needed to provide evidence-based healthcare for women, with or at risk of diabetes complications, who are planning pregnancy or are pregnant, to ensure the best outcomes for them and their children in the short and long term.

The Covid-19 pandemic has highlighted the importance of inclusive research. Pregnant women, those planning pregnancy or breastfeeding are often actively excluded from clinical trials, perpetuating the population as a vulnerable group.[21] The addition of co-morbidities, such as diabetes, complicates matters further. As well as improved health and well-being for generations of families, interventions which improve outcomes for pregnancy with diabetes provide significant opportunity in terms of cost savings.[13]

The questions identified are areas that still have significant uncertainty and are considered to be of most importance by the beneficiaries of that research. This work presents further opportunity for funders and researchers to focus future research to address the priorities of women, support networks and health professionals.

ACKNOWLEDGEMENTS

The project team thank everyone who contributed through the surveys and took part in the final workshop, our experts by experience steering group members, Rachel Connor, JDRF UK, and Lucy McKillop, University of Oxford, who were advisors to the steering group, our partners and the many people and organisations who supported at various stages throughout the project, sharing their time, expertise, communications and meeting facilities, without whom this project would not have been successful.

CONFLICT OF INTEREST

GA, FA, IB, NB, CB, SC, DC, KC, JG, MK, JLZ, FM, RM, NM, AM, JO, NR, CS, KS, AS and JAS none declared. JEH is a member of the NICE Diabetes Committee and holds a UKRI Future Leaders fellowship. HRM sits on a scientific advisory board for Medtronic (insulin pump and CGM manufacturer) and has received research support from Medtronic, Dexcom and Abbott Diabetes Care Inc. (CGM devices). MWJS has received honoraria from Astellas, AstraZeneca, Eli Lilly, Merck, Sanofi, Eisai and Bristol Myers Squibb, and has contributed to advisory boards for Novo Nordisk, Eisai and Servier.

AUTHOR CONTRIBUTIONS

GA and MK conceived the idea for the project and led the PSP. GA had full access to the data, coordinated the PSP process, drafted the surveys, analysed and led the interpretation of the data and wrote the first draft of the manuscript. GA, FA, IB, NB, CB, SC, DC, KC, MD, JG, JH, MK, AM, HM, JO, CS, KS, AS and MS are members of the Diabetes and Pregnancy Priority Setting Partnership (PSP) steering group and were responsible for the development of the protocol, and conduct, integrity and oversight of this work. All steering group members contributed to the outreach and communication activities to maximise participation and awareness. KC facilitated and chaired the PSP process, steering group and final workshop. GA, JS, NM, NR, RM, JL-Z, FM and MK completed the evidence checks. MK and KC are joint senior authors. All authors reviewed and approved the manuscript and revised it for intellectual content.

DATA AVAILABILITY STATEMENT

The top 10 and the full long-list of indicative questions will be made available on the NPEU project website www.npeu.ox.ac.uk/jla-psp and JLA website www.jla.nihr.ac.uk/priority-setting-partnerships/diabetes-and-pregnancy. For further information, please contact the team at JLAPSP@npeu.ox.ac.uk.

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REFERENCES

1. Feig DS, Hwee J, Shah BR, Booth GL, Bierman AS, Lipscombe LL. Trends in incidence of diabetes in pregnancy and serious perinatal outcomes: a large, population-based study in Ontario, Canada, 1996–2010. *Diabetes Care*. 2014;37(6):1590-1596.
2. Davies SC. *Annual Report of the Chief Medical Officer, 2014, The Health of the 51%: Women*. London: Department of Health; 2015.
3. Lowe WL Jr, Scholtens DM, Lowe LP, et al; HAPO Follow-up Study Cooperative Research Group. Association of gestational diabetes with maternal disorders of glucose metabolism and childhood adiposity. *JAMA*. 2018;320(10):1005-1016.
4. Scholtens DM, Kuang A, Lowe LP, et al; HAPO Follow-up Study Cooperative Research Group; HAPO Follow-Up Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcome follow-up study (HAPO FUS): maternal glycemia and childhood glucose metabolism. *Diabetes Care*. 2019;42(3):381-392.
5. National Institute for Health and Care Excellence. *Diabetes in pregnancy: management from preconception to the postnatal period (NG3)*. London: NICE; 2015 [cited 2020 Nov 27]. (Clinical guideline NG3). Available at: https://www.nice.org.uk/guidance/ng3.
6. Scottish Intercollegiate Guidelines Network. *Management of diabetes: A national clinical guideline (116)*. Edinburgh: SIGN; 2017 [cited 2020 Nov 27]. Clinical guideline 116. Available at: https://www.sign.ac.uk/assets/sign116.pdf.
7. Crowe S, Fenton M, Hall M, Cowan K, Chalmers I. Patient's clinicians' and the research communities' priorities for treatment research: there is an important mismatch [published correction appears. *Res Involv Engagem*. 2015;1:2.
8. Gadsby R, Snow R, Daly AC, et al. Setting research priorities for Type 1 diabetes. *Diabet Med*. 2012;29(10):1321-1326.
9. Finer S, Robb P, Cowan K, Daly A, Shah K, Farmer A. Setting the top 10 research priorities to improve the health of people with Type 2 diabetes: a Diabetes UK-James Lind Alliance Priority Setting Partnership. *Diabet Med*. 2018;35:862-870.
10. Rees SE, Chadha R, Donovan LE, et al. Engaging patients and clinicians in establishing research priorities for gestational diabetes mellitus. *Can J Diabetes*. 2017;41(2):156-163.
11. Bennett WL, Robinson KA, Saldanha IJ, Wilson LM, Nicholson WK. High priority research needs for gestational diabetes mellitus. *J Women's Health*. 2012;925-932.
12. Boddy K, Cowan K, Gibson A, Britten N. Does funded research reflect the priorities of people living with type 1 diabetes? A secondary analysis of research questions. *BMJ Open*. 2017;7:e016540.
13. Susan G, Lichten CA, Leach B, Pollard J, Parkinson S, Altenhofer M. *Pregnancy research review: Policy report*. Santa Monica, CA: RAND Corporation; 2020. [cited 2020 Nov 27]. Available from: https://www.rand.org/pubs/research_reports/RR4340.html.
14. James Lind Alliance. *James Lind Alliance Guidebook*. Southampton: JLA; 2021 [cited 2021 Mar 8]. Guideline version 10. Available from: https://www.jla.nihr.ac.uk/jla-guidebook.
15. Hsieh H-F, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res*. 2005;15(9):1277-1288.
16. Beck RW, Bergenstal RM, Laffel LM, Pickup JC. Advances in technology for management of type 1 diabetes. *The Lancet*. 2019;394(10205):1265-1273.
17. National Institute for Health and Care Excellence. *Evidence review for glucose monitoring in women with type 1 diabetes who are planning to become pregnant or who are already pregnant*. London: NICE; 2020 [cited 2021 Mar 8] (Clinical guideline NG3). Available at: https://www.nice.org.uk/guidance/ng3/evidence/a-evidence-reviews-for-continuous-glucose-monitoring-pdf-8955770797.

18. NHS. *The NHS Long Term Plan*. NHS; 2019 [cited 2021 Mar 8] Available at: https://www.longtermplan.nhs.uk.
19. Diabetes UK. *Too often missing: Making emotional and psychological support routine in diabetes care*. London: Diabetes UK; 2020 [cited 2021 Mar 8] Available at: https://www.diabetes.org.uk/get_involved/campaigning/its-missing-evidence.
20. Office for National Statistics. *Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2019*. . ONS; 2020. [cited 2020 Nov 27]. Available at: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates.
21. van der Zande ISE, van der Graaf R, Oudijk MA, van Dleden JJM. Vulnerability of pregnant women in clinical research. *J Med Ethics*. 2017;43:657-663.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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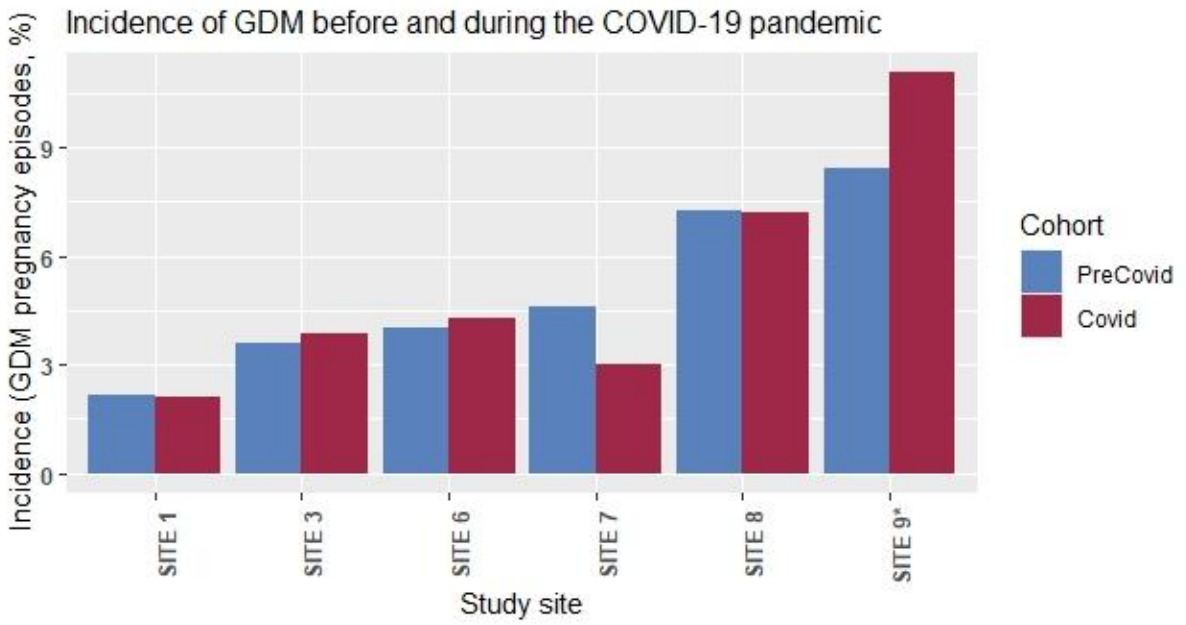
7.2 Appendix 2. Chapter 1 supplementary data

Supplementary Information: IMPACT OF COVID-19 ON GESTATIONAL DIABETES PREGNANCY OUTCOMES IN THE UK: A MULTICENTRE RETROSPECTIVE COHORT STUDY

Figure S1. Regional incidence of GDM before and during COVID 19



Incidence calculated from mean GDM pregnancy episodes/mean monthly pregnancy bookings at six sites with available incidence data (PreCOVID and COVID, April – Dec 2019 and April – Dec 2020, respectively)

Site 9* = Partial adoption of COVID 19 GDM guidance

All other sites = Adoption of COVID 19 GDM guidance

Table S1. GDM practice across the nine study sites before and during COVID

SITE	1	2	3	5	4	6	7	8	9[1]
Study Participants	419 4.9%	57 0.7%	1183 13.9%	1333 15.6%	481 5.64	493 5.8%	844 9.9%	441 5.2%	3131 36.7%
PRE COVID									
Screening for preexisting DM	No	HbA1c	HbA1c	HbA1c	HbA1c	No	No	No	No
Screening for women with previous GDM	OGTT	HBGM	HBGM + HbA1c	HBGM	OGTT	HBGM	OGTT	OGTT	HbA1c + OGTT
Diagnosis at 24-28/40 0hr OGTT value (mmol/L)	5.6	5.1	5.1	5.1	5.6	5.6	5.1	5.6	5.6
Diagnosis at 24-28/40 2Hr OGTT value (mmol/L)	7.8	8.5	8.5	8.5	7.8	7.8	8.5	7.8	7.8
COVID									
Screening for preexisting DM	HbA1c	HbA1c	HbA1c	HbA1c	HbA1c	HbA1c	HbA1c	HbA1c	No
Diagnosis at Booking HBA1c (mmol/mol)	41-47	41-47	41-47	41-47	41-47	41-47	41-47	41-47	NA
Diagnosis at Booking FBG (mmol/L)	NA	NA	NA	NA	9 to 11	9 to 11	9 to 11	9 to 11	NA
Diagnosis at 24-28/40 HBA1c (mmol/mol)	>39	>39	NA	>39	>39	>39	>39	>39	NA
Diagnosis at 24-28/40 FBG (mmol/L)	5.3	5.1	5.1	5.1	NA	NA	5.3	5.3	5.6
Diagnosis at 24-28/40 RBG(mmol/L)	NA	NA	NA	>9	>9	>9	>9	NA	NA

Key

DM - diabetes mellitus

FBG – fasting blood glucose

HbA1C – Glycosylated Haemoglobin

HBGM – Home (capillary) blood glucose monitoring

OGTT – Oral glucose tolerance test

RBG – random blood glucose

ǂ Partial Adoption of RCOG COVID 19 care pathway, all other sites (1-8) were full adopters of RCOG COVID 19 care pathway

Table S2: Maternal outcomes

		Full Adoption RCOG COVID 19 GDM care pathway (*n*=8 sites, 5251 pregnancies)				Partial adoption RCOG COVID 19 GDM care pathway (*n*=1 site, 3131 pregnancies)			
		PRECOVID *n*=2930	COVID *n*=2321	Total *n*= 5251	*P-value*	PRECOVID *n*=1985	COVID *n*=1146	Total *n*=3131	*P-value*
Mode of delivery	SVD	1357 (46.3)	990 (42.7)	2347 (44.7)	<0.001	854 (43.0)	503 (43.9)	1357 (43.3)	0.355
	ELCS	589 (20.1)	548 (23.6)	1137 (21.7)		343 (17.3)	216 (18.8)	559 (17.9)	
	EMCS	626 (21.4)	531 (22.9)	1157 (22.0)		541 (27.3)	281 (24.5)	822 (26.3)	
	OVD	333 (11.4)	204 (8.8)	537 (10.2)		247 (12.4)	146 (12.7)	393 (12.6)	
	missing	25 (0.9)	48 (2.1)	73 (1.4)		0	0	0	
Induction of labour	N	1530 (52.2)	1194 (51.4)	2724 (51.9)	0.79	1437 (72.4)	731 (63.8)	2168 (69.2)	<0.001
	Y	1327 (45.3)	1053 (45.4)	2380 (45.3)		548 (27.6)	415 (36.2)	963 (30.8)	
	missing	73 (2.5)	74 (3.2)	147 (2.8)		0	0	0	
Postpartum haemorrhage	N	2786 (95.1)	2190 (94.4)	4976 (94.8)	0.41	1885 (95.0)	1096 (95.6)	2981 (95.2)	0.444

	Y	123 (4.2)	85 (3.7)	208 (4.0)		100 (5.0)	50 (4.4)	150 (4.8)	
	missing	21 (0.7)	46 (2.0)	67 (1.3)		0	0	0	
Obstetric anal sphincter injury	N	2762 (94.3)	2057 (88.6)	4819 (91.8)	0.638	1944 (97.9)	1127 (98.3)	3071 (98.1)	0.505
	Y	42 (1.4)	27 (1.2)	69 (1.3)		41 (2.1)	19 (1.7)	60 (1.9)	
	missing	126 (4.3)	237 (10.2)	363 (6.9)		0	0	0	
Shoulder dystocia	N	2221 (75.8)	2077 (89.5)	4298 (81.9)	0.49	1964 (98.9)	1128 (98.4)	3092 (98.8)	0.281
	Y	25 (0.9)	18 (0.8)	43 (0.8)		21 (1.1)	18 (1.6)	39 (1.2)	
	missing	684 (23.3)	226 (9.7)	910 (17.3)		0	0	0	
Hypertensive disorder	N	2349 (80.2)	1267 (54.6)	3616 (68.9)	<0.001*	1955 (98.5)	1133 (98.9)	3088 (98.6)	0.475
	Y	131 (4.5)	114 (4.9)	245 (4.7)		30 (1.5)	13 (1.1)	43 (1.4)	
	missing	450 (15.4)	940 (40.5)	1390 (26.5)		0	0	0	
Metformin use	N	1346 (54.6)	809 (57.3)	2155 (55.6)	0.112	NA	NA	NA	
	Y	1119 (45.4)	603 (42.7)	1722 (44.4)		NA	NA	NA	
	missing	465 (15.9)	909 (39.2)	1374 (26.2)		NA	NA	NA	

Insulin use	N	1901 (77.1)	1048 (75.0)	2949 (76.4)	0.151	NA	NA	NA	
	Y	564 (22.9)	349 (25.0)	913 (23.6)		NA	NA	NA	
	missing	465 (15.9)	924 (39.8)	1389 (26.5)		NA	NA	NA	

List of abbreviations

N No
Y Yes
OVD Operative vaginal delivery
SVD Spontaneous vertex delivery
ELCS Elective caesarean section
EMCS Emergency cesarean section

Legend
*p values remain <0.05 in sensitivity analysis (data compared between 2019 and 2020 only)

Table S3: All neonatal outcomes

		Full Adoption RCOG COVID 19 GDM care pathway				Partial adoption RCOG COVID 19 GDM care pathway			
		PRECOVID *n*=2930	COVID *n*=2321	Total *n*= 5251	*P-value*	PRECOVID *n*=1985	COVID *n*=1146	Total *n*=3131	*P-value*
Gestational age at birth (days)	Mean (SD)	269.4 (12.1)	268.9 (11.2)	269.2 (11.7)	0.133	269.0 (15.9)	270.4 (12.5)	269.5 (14.8)	0.011
Birth outcome	Livebirth	2891 (98.7)	2278 (98.1)	5169 (98.4)	0.495	1959 (98.7)	1137 (99.2)	3096 (98.9)	0.381
	Still birth	11 (0.4)	5 (0.2)	16 (0.3)		11 (0.6)	3 (0.3)	14 (0.4)	
	Neonatal death	2 (0.1)	2 (0.1)	4 (0.1)		6 (0.3)	4 (0.3)	10 (0.3)	
	Non-registrable birth	0 (0.0)	1 (0.0)	1 (0.0)		9 (0.5)	2 (0.2)	11 (0.4)	
	missing	26 (0.9)	35 (1.5)	61 (1.2)		0	0	0	
Birthweight (g)	Mean (SD)	3325.4 (563.9)	3332.4 (553.3)	3328.5 (559.2)	0.653	3183.3 (581.5)	3195.3 (551.1)	3187.7 (570.5)	0.571
Birth centile (Intergrow)	AGA	2000 (69.3)	1553 (68.5)	3553 (69.0)	0.521	1530 (77.5)	864 (75.6)	2394 (76.8)	0.079
	LGA	729 (25.3)	602 (26.5)	1331 (25.8)		306 (15.5)	174 (15.2)	480 (15.4)	
	SGA	155 (5.4)	113 (5.0)	268 (5.2)		137 (6.9)	105 (9.2)	242 (7.8)	
	missing	44 (1.5)	52 (2.2)	96 (1.8)		9 (0.5)	2 (0.2)	11 (0.4)	

Apgar at 5 mins	<=7	78 (2.7)	76 (3.3)	154 (2.9)	1	69 (3.5)	48 (4.2)	117 (3.7)	0.369
	>7	2151 (73.4)	2073 (89.3)	4224 (80.4)		1877 (94.6)	1079 (94.2)	2956 (94.4)	
	missing	701 (23.9)	172 (7.4)	873 (16.6)		39 (2.0)	19 (1.7)	58 (1.9)	
Neonatal unit admission	N	2649 (90.4)	2091 (90.1)	4740 (90.3)	0.409	1791 (90.2)	1058 (92.3)	2849 (91.0)	0.056
	Y	256 (8.7)	185 (8.0)	441 (8.4)		194 (9.8)	88 (7.7)	282 (9.0)	
	missing	25 (0.9)	45 (1.9)	70 (1.3)		0	0	0	
Hypoglycaemia	N	2296 (78.4)	1547 (66.7)	3843 (73.2)	0.992	NA	NA	NA	
	Y	89 (3.0)	59 (2.5)	148 (2.8)		NA	NA	NA	
	missing	545 (18.6)	715 (30.8)	1260 (24.0)		NA	NA	NA	
Respiratory distress	N	2386 (81.4)	1312 (56.5)	3698 (70.4)	<0.001	1922 (96.8)	1098 (95.8)	3020 (96.5)	0.168
	Y	71 (2.4)	73 (3.1)	144 (2.7)		63 (3.2)	48 (4.2)	111 (3.5)	
	missing	473 (16.1)	936 (40.3)	1409 (26.8)		0	0	0	

List of abbreviations

AGA Appropriate for gestational age

LGA Large for gestational age

SGA Small for gestational age

N No

Y Yes

Table S4: Primary maternal and neonatal outcomes in the non-white GDM population before and after introduction of the RCOG COVID-19 GDM care pathway

		Full Adoption RCOG COVID 19 GDM care pathway						Partial adoption RCOG COVID 19 GDM care pathway					
		PRECOVID *n*=823	COVID *n*=746	Total *n*= 1569	*P-value*	aOR (95% CI)	*P-value*	PRECOVID *n*=1058	COVID *n*=754	Total *n*=1812	*P-value*	aOR (95% CI)	*P-value*
Operative vaginal delivery, n (%)	N	375 (78.6)	318 (82.8)	693 (80.5)	0.145	0.94 (0.57-1.54)	0.799	460 (77.1)	356 (78.6)	816 (77.7)	0.605	0.77 (0.54-1.11)	0.160
	Y	102 (21.4)	66 (17.2)	168 (19.5)				137 (22.9)	97 (21.4)	234 (22.3)			
Emergency caesarean section, n (%)	N	477 (73.3)	384 (67.7)	861 (70.7)	**0.040**	**1.69 (1.07-2.68)**	**0.024**	597 (65.7)	453 (70.6)	1050 (67.7)	0.052	0.78 (0.61-1.01)	0.240
	Y	174 (26.7)	183 (32.3)	357 (29.3)				311 (34.3)	189 (29.4)	500 (32.3)			
Elective caesarean section, n (%)	N	651 (80.0)	567 (77.6)	1218 (78.8)	0.273	1.15 (0.81-1.64)	0.425	908 (85.8)	642 (85.1)	1550 (85.5)	0.737	1.18 (0.87-1.61)	0.280
	Y	163 (20.0)	164 (22.4)	327 (21.2)				150 (14.2)	112 (14.9)	262 (14.5)			
Perinatal mortality, n (%)	N	809 (99.4)	731 (99.5)	1540 (99.4)	1.000	0.45 (0.02-3.29)	0.643	1048 (99.1)	747 (99.1)	1795 (99.1)	1.000	0.98 (0.36-2.57)	0.971
	Y	5 (0.6)	4 (0.5)	9 (0.6)				10 (0.9)	7 (0.9)	17 (0.9)			
Large for gestational age, n (%)	N	670 (82.9)	618 (84.5)	1288 (83.7)	0.429	0.74 (0.53-1.05)	0.089	923 (87.7)	664 (88.4)	1587 (88.0)	0.677	0.93 (0.68-1.27)	0.658
	Y	138 (17.1)	113 (15.5)	251 (16.3)				130 (12.3)	87 (11.6)	217 (12.0)			
Neonatal unit admission, n (%)	N	760 (93.7)	690 (94.0)	1459 (93.9)	0.893	0.70 (0.41-1.21)	0.206	958 (90.5)	698 (92.6)	1656 (91.4)	0.153	*0.81 (0.52-1.26)*	0.359
	Y	51(6.3)	44 (6.0)	95(6.1)				100 (9.5)	56 (7.40	156 (8.6)			

Table S5: Primary maternal and neonatal outcomes in the most deprived GDM population before and after introduction of the RCOG COVID-19 GDM care pathway

		Full Adoption RCOG COVID 19 GDM care pathway						Partial adoption RCOG COVID 19 GDM care pathway					
		PRECOVID *n*=492	COVID *n*=333	Total *n*= 825	*P-value*	aOR (95% CI)	*P-value*	PRECOVID *n*=145	COVID *n*=114	Total *n*=259	*P-value*	aOR (95% CI)	*P-value*
Operative vaginal delivery, n (%)	N	216 (78.0)	136 (82.4)	352 (79.6)	0.317	0.85 (0.43-1.68)	0.635	47 (67.1)	41 (70.7)	88 (68.8)	0.811	*0.85 (0.26-2.69)*	0.777
	Y	61 (22.0)	29 (17.6)	90 (20.4)				23 (32.9)	17 (29.3)	40 (31.2)			
Emergency caesarean section, n (%)	N	277 (72.7)	165(67.3)	442(70.6)	0.178	**1.61 (1.01-2.57)**	**0.047**	70 (66.7)	58 (67.4)	128 (67.0)	1.000	*0.97 (0.52-1.77)*	0.910
	Y	104 (27.3)	80 (32.7)	184 (29.4)				35 (33.3)	28 (32.6)	63 (33.0)			
Elective caesarean section, n (%)	N	381 (77.4)	245 (75.6)	626 (76.7)	0.605	0.95 (0.58-1.56)	0.845	105 (72.4)	86 (75.4)	191 (73.7)	0.684	*1.36 (0.60-3.08)*	0.458
	Y	111 (22.6)	79 (24.4)	190 (23.3)				40 (27.6)	28 (24.6)	68 (26.3)			
Perinatal mortality, n (%)	N	490 (99.8)	326 (100.0)	816 (99.9)	1.000			143 (98.6)	114 (100.0)	257 (99.2)	0.587		
	Y	1 (0.2)	0 (0.0)	1 (0.1)				2 (1.4)	0 (0.0)	2 (0.8)			
Large for gestational age, n (%)	N	373 (76.9)	225 (72.8)	607 (75.0)	0.154	1.22 (0.83-1.79)	0.318	118 (82.5)	96 (84.2)	214 (83.3)	0.847	*0.88 (0.45-1.71)*	0.718
	Y	112 (23.1)	84 (27.2)	202 (25.0)				25 (17.5)	18 (15.8)	43 (16.7)			
Neonatal unit admission, n (%)	N	443 (90.2)	299 (92.0)	742 (90.9)	0.459	0.69 (0.35-1.35)	0.276	132 (91.0)	103 (90.4)	235 (90.7)	1.000	*0.86 (0.52-3.04)*	0.985
	Y	48 (9.8)	26 (8.0)	74 (9.1)				13 (9.0)	11 (9.6)	24 (9.3)			

aOR – adjusted Odds ratio, CI – Confidence Interval

All models adjusted for maternal characteristics (age, BMI, parity, ethnicity, deprivation, previous GDM, Hypertensive disorder) induction of labour, gestational age at birth.
*Additional adjustment for mode of birth,

** additional adjusted for mode of birth, birth weight centile, Apgar score at 5 mins, neonatal unit admission, respiratory distress.
*** additional adjusted for birth weight centile, mode of birth.

7.3 Appendix 3.1 Participant information sheet

Impact of Covid-19 on gestational diabetes: Health care professional's experience

We are inviting you to take part in an interview study. Before deciding whether you would like to take part, please read the following information carefully. Talk to others about the study if you wish and contact us if there is anything that is not clear, or if you would like more information.

What is the purpose of the research?

The Covid-19 pandemic has led to lots of changes in the way we look after women who have diabetes in pregnancy (gestational diabetes). We want to find out what you think about these changes and whether we can learn anything that will be helpful as we rebuild services after the pandemic.

Why have I been invited to take part?

You have been asked to take part as you are a health care provider who has a current NHS role in providing care women with gestational diabetes.

Do I have to take part?

It is up to you to decide whether you would like to take part. If you do take part, you will be given this information sheet to keep and be asked to provide verbal consent at the time of your interview. The questions you will be asked to give verbal consent are at the end of this information sheet so you can see what you are agreeing to if you take part. You will still be free to withdraw at any time without giving a reason.

What will happen if I take part?

You will be contacted to arrange a convenient date and time for the interview, which will be a one-to-one conversation with a member of the research team by telephone. Your interview will last about 30 minutes, although this will depend on how much you have to say. You have the right not to answer any questions you don't want to, and you are free to stop the interview at any time without giving any reason at all.

The interview will be audio-recorded using an encrypted digital recorder and sent securely to a professional external company to be typed up (transcribed).

What are the possible benefits of taking part?

There are no direct benefits to you taking part in this study, although the interview will present an opportunity to reflect on how Covid-19 has impacted on your clinical practice/clinical care. Unfortunately, we are unable to pay you for your time.

What are the possible disadvantages of taking part?

The main disadvantage is the time required for the interview itself. Every effort will be made to schedule this at your convenience and keep related correspondence to a minimum.

What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time without giving reason. If you choose to withdraw after your interview, any recordings, transcripts and data resulting from your involvement will be destroyed and will not contribute to the findings of the study.

What happens when the study is finished?

The data we collect will be used only for the purposes of this research. Recordings, transcripts and all study documents (paper and electronic), including identifiable information about you, will be kept for 3 years after the study has finished.

Will my taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage. The professional transcription company will be held to the same levels of confidentiality as the researchers. Nothing that could identify you will be kept in the typed-up transcript and you will not be identifiable from any publications or presentations of the findings, including any quotes we use.

For details on what data will be held about you and who will hold and store this information please refer to the Data Protection Information Sheet.

What will happen to the results of the study?

The results of the study may be published in a scientific journal or presented at conferences. You will be asked if you wish to receive information on the overall findings in the form of a short report.

Who is organising and funding the research?

The study is funded by Tommy's and jointly sponsored by the University of Edinburgh and NHS Lothian (ACCORD).

Who has reviewed the study?

The study is sponsored by ACCORD (Academic and Clinical Central Office for Research and Development) and a favourable ethical opinion has been obtained from the Edinburgh medical school research ethics committee.

Researcher Contact Details

If you have any further questions about the study or if you wish to take part, please contact:

Niamh Mclennan

Email:

Telephone: 07932349797

Independent Contact Details

If you would like to discuss this study with someone independent to seek general advice about taking part, please contact:

Dr Sarah Stock

Email:

If you wish to make a complaint about the study please contact:Patient Experience Team

2 – 4 Waterloo Place, Edinburgh, EH1 3EG Email: feedback@nhslothian.scot.nhs.uk

Telephone: 0131 536 3370

Thank you for taking the time to read this information sheet.

Questions asked during verbal consent

- You have read and understood the Participant Information Sheet version 1.0, dated 24th June 2020 and the Data Protection Information Sheet version 1.1, dated 3rd November 2020 for the above study; and you have had the opportunity to ask questions and have had these answered satisfactorily.

- You understand that your participation is voluntary and that you are free to withdraw at any time, without giving reason and without your legal rights or employment being affected.

- You understand that relevant sections of data collected during the study may be looked at by individuals from the Sponsors (University of Edinburgh and NHS Lothian) or other regulatory authorities where it is relevant to your taking part in this research; and you give permission for these individuals to have access to your data.

- You understand that data collected about you during the study may be converted to anonymised data; and you are happy to be quoted anonymously in any publicised materials.

- You agree to your interview being audio-recorded and transcribed securely by a professional external company.

- Would you like to receive a short report summarising the main findings of the study?

- Finally, do you agree to take part in the study?

7.4 Appendix 3.2 Topic guide

Impact of Covid-19 on Gestational Diabetes, the healthcare provider's experience.

Topic Guide

Note – The contents of the topic guide may be revised in light of findings that emerge during data collection and analysis, as is standard procedure in a qualitative study of this design.

Introduction i.e. statement of purpose, interview length approx 60 minutes

Background

- Demographic details – Age, Gender, Geographical location of principal place of work, Job Title, Education (highest qualification), Length of time in current post/position.
- Can you tell me about the kind of population you serve (e.g. age, affluent, high ethnic minority population, rural/urban, hospital based/community based, size of unit you work in)

Looking back to GDM practice before Covid-19

- How and in what ways you were involved in the clinical care for women with GDM before Covid 19?
- Can you describe the different colleagues you worked with, how did your role fit in with your colleagues?
- Were you following any clinical guidelines/protocols and whether and to what extent (and why) they and their colleagues followed these guidelines; reasons for not following guidance
- , did they think there are any aspects of the pathway and care given to women that they felt wasn't working and which could be improved
- What guides your practice

Experiences of GDM practice during Covid 19 ('meaning and sense')

- Can you describe the ways care you give to women with GDM has changed during pandemic? [1]
- Can you describe how your work with different colleagues has changed

- Are you following any specific changes (e.g following a guideline/protocol/care pathway), if yes, why and what do you feel is the purpose of the change?

Attitudes ('commitment and engagement')

- Did you have any worries and concerns when changes were first instigated? What were these and why?
- Did anything excite you about introducing these changes, why?
- Have any aspects surprised you and/or have led to unexpected benefits either for yourself or for women with GDM -also any women in particular

- Do you think the changes in care delivery have affected women's diabetes self-management practices, glycaemic control, feelings/worries about their own pregnancy and pregnancy outcomes?
- Do you think some women are more affected by these changes than others, if so who and why? And Could anything be done to better to support them?

Workability ('collective action')

- Has there been a change (increase or reduction) in your workload as a result of changes in GDM care delivery and why?
- Have you found any aspects of the change in care delivery challenging? [2]
- What changes in GDM care delivery have worked particularly well or badly? [3]

- How do you think the changes have affected the quality of care you and your colleagues are able to give to women with GDM?
- Have these changes affected your satisfaction within your role?

Implementing change and Future directions ('Reflexivity')

- Do you think any of the changes made to GDM care delivery during the pandemic should be retained? Why?
- What resourcing and support would be needed to make these changes more permanent?
- Are there any ways in which service delivery for people with diabetes more generally could be improved considering the lessons you have learned during pandemic? Greater use of 'virtual' clinics (eg telephone versus secure video consultations)
- Do you have any thoughts about how we could improve the care and support given to women with GDM in the event of future, similar, pandemics?
- Probe Question – Telemedicine interventions have been available for a number of years, do you know of any reasons why they not been utilised more in management of GDM in the UK

Wind up

- Reflecting on this interview, how do you think the way we look after women with GDM might change over the next 5 years
- Do you have anything else you would like to add?

[1] probe into changes in screening pathways /diagnostic thresholds for GDM/ use of virtual rather than face-to-face clinics/ transition from group based to one-to-one virtual educational sessions/ if a joint model (i.e. obstetrics/diabetes) is this the same or are women reviewed separately/ If virtual – are BG texted in/web-site/app or just over the phone with verbal report

[2] Invite interviewee to talk about any aspects of care delivery reconfiguration which they have found challenging; encourage them also to talk about any aspects which have surprised them and/or have led to unexpected benefits either for themselves or for women with GDM

[3] For those that have worked badly, encourage interviewee to talk about whether and how any problems and concerns were or could be addressed?

7.5 Appendix 3.3 Consent form

Impact of Covid-19 on gestational diabetes: Health care professional's experiences

Oral consent

Participant ID:

I'm Niamh Mclennan a researchers from the University of Edinburgh and I wanted to talk to you about the gestational diabetes study. To recap, the broad aims of the study are to understand the impact that COVID-19 has had on the antenatal care you give to pregnant women with gestational diabetes

Are you still interested in taking part? [*Await confirmation*].

I need to confirm some of the details of the study to make sure you understand what's involved. As the study is being carried out by telephone, I would like to audio-record this part of our conservation as a record of your consent to take part – is that OK? [*Await confirmation*].

Please listen carefully and respond, with a simple Yes or No, to the following:

You have read and understood the Participant Information Sheet version 1.1, dated 3rd November 2020 and the Data Protection Information Sheet version 1.0, dated 24th June 2020 for the above study; and you have had the opportunity to ask questions and have had these answered satisfactorily.

You understand that your participation is voluntary and that you are free to withdraw at any time, without giving reason and without your legal rights or employment being affected.

You understand that relevant sections of data collected during the study may be looked at by individuals from the Sponsors (University of Edinburgh and NHS Lothian)

or other regulatory authorities where it is relevant to your taking part in this research; and you give permission for these individuals to have access to your data.

You understand that data collected about you during the study may be converted to anonymised data; and you are happy to be quoted anonymously in any publicised materials.

You agree to your interview being audio-recorded and transcribed securely by a professional external company.

Would you like to receive a short report summarising the main findings of the study?

Finally, do you agree to take part in the study?

Dr Niamh Mclennan		16.3.21
Name of Researcher Receiving Consent	Signature	Date

1x original – into Site File as oral consent record form

8 References

1. Standards of medical care in diabetes--2014. Diabetes Care. 2014;37 Suppl 1:S14-80.
2. Wang H, Li N, Chivese T, Werfalli M, Sun H, Yuen L, et al. IDF Diabetes Atlas: Estimation of Global and Regional Gestational Diabetes Mellitus Prevalence for 2021 by International Association of Diabetes in Pregnancy Study Group's Criteria. Diabetes Res Clin Pract. 2022;183:109050.
3. Saravanan P, Diabetes in Pregnancy Working G, Maternal Medicine Clinical Study G, Royal College of O, Gynaecologists UK. Gestational diabetes: opportunities for improving maternal and child health. Lancet Diabetes Endocrinol. 2020;8(9):793-800.
4. Sacks DA, Hadden DR, Maresh M, Deerochanawong C, Dyer AR, Metzger BE, et al. Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. Diabetes Care. 2012;35(3):526-8.
5. Schwartz N, Nachum Z, Green MS. Risk factors of gestational diabetes mellitus recurrence: a meta-analysis. Endocrine. 2016;53(3):662-71.
6. Getahun D, Fassett MJ, Jacobsen SJ. Gestational diabetes: risk of recurrence in subsequent pregnancies. Am J Obstet Gynecol. 2010;203(5).
7. Farrar D, Simmonds M, Bryant M, Lawlor DA, Dunne F, Tuffnell D, Sheldon TA. Risk factor screening to identify women requiring oral glucose tolerance testing to diagnose gestational diabetes: A systematic review and meta-analysis and analysis of two pregnancy cohorts. PLoS One. 2017;12(4):e0175288.
8. Farahvar S, Walfisch A, Sheiner E. Gestational diabetes risk factors and long-term consequences for both mother and offspring: a literature review. Expert Rev Endocrinol Metab. 2019;14(1):63-74.
9. Weiss JL, Malone FD, Emig D, Ball RH, Nyberg DA, Comstock CH, et al. Obesity, obstetric complications and cesarean delivery rate--a population-based screening study. Am J Obstet Gynecol. 2004;190(4):1091-7.
10. Li Y, Ren X, He L, Li J, Zhang S, Chen W. Maternal age and the risk of gestational diabetes mellitus: A systematic review and meta-analysis of over 120 million participants. Diabetes Res Clin Pract. 2020;162:108044.
11. Johns EC, Denison FC, Norman JE, Reynolds RM. Gestational Diabetes Mellitus: Mechanisms, Treatment, and Complications. Trends Endocrinol Metab. 2018;29(11):743-54.
12. Catalano PM, Tyzbir ED, Roman NM, Amini SB, Sims EA. Longitudinal changes in insulin release and insulin resistance in nonobese pregnant women. Am J Obstet Gynecol. 1991;165(6 Pt 1):1667-72.
13. Lain KY, Catalano PM. Metabolic changes in pregnancy. Clin Obstet Gynecol. 2007;50(4):938-48.
14. Catalano PM, Huston L, Amini SB, Kalhan SC. Longitudinal changes in glucose metabolism during pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus. Am J Obstet Gynecol. 1999;180(4):903-16.
15. Catalano PM, Shankar K. Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. Bmj-Brit Med J. 2017;356.
16. Catalano PM. Trying to understand gestational diabetes. Diabet Med. 2014;31(3):273-81.

17. McLennan NM, Hazlehurst J, Thangaratinam S, Reynolds RM. ENDOCRINOLOGY IN PREGNANCY: Targeting metabolic health promotion to optimise maternal and offspring health. Eur J Endocrinol. 2022;186(6):R113-R26.
18. Desoye G, Hauguel-de Mouzon S. The human placenta in gestational diabetes mellitus. The insulin and cytokine network. Diabetes Care. 2007;30 Suppl 2:S120-6.
19. Murray SR, Reynolds RM. Short- and long-term outcomes of gestational diabetes and its treatment on fetal development. Prenat Diagn. 2020;40(9):1085-91.
20. Ye W, Luo C, Huang J, Li C, Liu Z, Liu F. Gestational diabetes mellitus and adverse pregnancy outcomes: systematic review and meta-analysis. Bmj. 2022;377:e067946.
21. Kampmann U, Knorr S, Fuglsang J, Ovesen P. Determinants of Maternal Insulin Resistance during Pregnancy: An Updated Overview. J Diabetes Res. 2019;2019:5320156.
22. Catalano PM, Hauguel-De Mouzon S. Is it time to revisit the Pedersen hypothesis in the face of the obesity epidemic? Am J Obstet Gynecol. 2011;204(6):479-87.
23. Furse S, Koulman A, Ozanne SE, Poston L, White SL, Meek CL. Altered Lipid Metabolism in Obese Women With Gestational Diabetes and Associations With Offspring Adiposity. J Clin Endocrinol Metab. 2022;107(7):e2825-e32.
24. Esakoff TF, Cheng YW, Sparks TN, Caughey AB. The association between birthweight 4000 g or greater and perinatal outcomes in patients with and without gestational diabetes mellitus. Am J Obstet Gynecol. 2009;200(6):672.e1-4.
25. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet. 2009;373(9677):1773-9.
26. Kramer CK, Campbell S, Retnakaran R. Gestational diabetes and the risk of cardiovascular disease in women: a systematic review and meta-analysis. Diabetologia. 2019;62(6):905-14.
27. Lowe WL, Lowe LP, Kuang A, Catalano PM, Nodzenski M, Talbott O, et al. Maternal glucose levels during pregnancy and childhood adiposity in the Hyperglycemia and Adverse Pregnancy Outcome Follow-up Study. Diabetologia. 2019;62(4):598-610.
28. Lowe WL, Jr., Scholtens DM, Kuang A, Linder B, Lawrence JM, Lebenthal Y, et al. Hyperglycemia and Adverse Pregnancy Outcome Follow-up Study (HAPO FUS): Maternal Gestational Diabetes Mellitus and Childhood Glucose Metabolism. Diabetes Care. 2019;42(3):372-80.
29. Chen S, Zhao S, Dalman C, Karlsson H, Gardner R. Association of maternal diabetes with neurodevelopmental disorders: autism spectrum disorders, attention-deficit/hyperactivity disorder and intellectual disability. International Journal of Epidemiology. 2020;50(2):459-74.
30. O'Sullivan JB, Mahan CM. CRITERIA FOR THE ORAL GLUCOSE TOLERANCE TEST IN PREGNANCY. Diabetes. 1964;13:278-85.
31. Diabetes mellitus. Report of a WHO expert committee. World Health Organ Tech Rep Ser. 1965;310:1-44.
32. Coustan DR, Lowe LP, Metzger BE, Dyer AR, International Association of D, Pregnancy Study G. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study: paving the way for new diagnostic criteria for gestational diabetes mellitus. Am J Obstet Gynecol. 2010;202(6):654 e1-6.
33. Bogdanet D, O'Shea P, Lyons C, Shafat A, Dunne F. The Oral Glucose Tolerance Test-Is It Time for a Change?-A Literature Review with an Emphasis on Pregnancy. J Clin Med. 2020;9(11).
34. Sermer M, Naylor CD, Gare DJ, Kenshole AB, Ritchie JW, Farine D, et al. Impact of increasing carbohydrate intolerance on maternal-fetal outcomes in 3637 women without gestational diabetes. The Toronto Tri-Hospital Gestational Diabetes Project. Am J Obstet Gynecol. 1995;173(1):146-56.

35. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358(19):1991-2002.
36. Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33(3):676-82.
37. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy: a World Health Organization Guideline. Diabetes Res Clin Pract. 2014;103(3):341-63.
38. Excellence NIfHaC. Diabetes in pregnancy: management from preconception to the postnatal period London: NICE; 2015 [updated 16 December 2020; cited 2022 23rd July]. Available from: https://www.nice.org.uk/guidance/ng3.
39. Catalano PM, Avallone DA, Drago NM, Amini SB. Reproducibility of the oral glucose tolerance test in pregnant women. Am J Obstet Gynecol. 1993;169(4):874-81.
40. Ko GT, Chan JC, Woo J, Lau E, Yeung VT, Chow CC, Cockram CS. The reproducibility and usefulness of the oral glucose tolerance test in screening for diabetes and other cardiovascular risk factors. Ann Clin Biochem. 1998;35 (Pt 1):62-7.
41. Sacks DB, Arnold M, Bakris GL, Bruns DE, Horvath AR, Kirkman MS, et al. Position statement executive summary: guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Diabetes Care. 2011;34(6):1419-23.
42. Jones DL, Kusinski LC, Barker P, Burling K, Halsall I, Turner E, et al. Enhanced glucose processing in gestational diabetes diagnosis: Effects on health equity and clinical outcomes. Diabet Med. 2024:e15476.
43. Potter JM, Hickman PE, Oakman C, Woods C, Nolan CJ. Strict Preanalytical Oral Glucose Tolerance Test Blood Sample Handling Is Essential for Diagnosing Gestational Diabetes Mellitus. Diabetes Care. 2020;43(7):1438-41.
44. Farrar D, Fairley L, Wright J, Tuffnell D, Whitelaw D, Lawlor DA. Evaluation of the impact of universal testing for gestational diabetes mellitus on maternal and neonatal health outcomes: a retrospective analysis. BMC Pregnancy Childbirth. 2014;14:317.
45. Avalos GE, Owens LA, Dunne F. Applying current screening tools for gestational diabetes mellitus to a European population: is it time for change? Diabetes Care. 2013;36(10):3040-4.
46. Cosson E, Benbara A, Pharisien I, Nguyen MT, Revaux A, Lormeau B, et al. Diagnostic and prognostic performances over 9 years of a selective screening strategy for gestational diabetes mellitus in a cohort of 18,775 subjects. Diabetes Care. 2013;36(3):598-603.
47. American Diabetes A. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care. 2021;44(Suppl 1):S15-S33.
48. Berger H, Gagnon R, Sermer M. Guideline No. 393-Diabetes in Pregnancy. Journal of Obstetrics and Gynaecology Canada. 2019;41(12):1814-25.e1.
49. Gynaecologists TRAaNZCoOa. Diagnosis of Gestational Diabetes

Mellitus (GDM) 2017 [Available from: https://ranzcog.edu.au/wp-content/uploads/Diagnosis-Gestational-Diabetes-Mellitus.pdf.
50. Hillier TA, Pedula KL, Ogasawara KK, Vesco KK, Oshiro CES, Lubarsky SL, Van Marter J. A Pragmatic, Randomized Clinical Trial of Gestational Diabetes Screening. N Engl J Med. 2021;384(10):895-904.
51. Davis EM, Abebe KZ, Simhan HN, Catalano P, Costacou T, Comer D, et al. Perinatal Outcomes of Two Screening Strategies for Gestational Diabetes Mellitus: A Randomized Controlled Trial. Obstet Gynecol. 2021;138(1):6-15.

52. Brady M, Hensel DM, Paul R, Doering MM, Kelly JC, Frolova AI, et al. One-Step Compared With Two-Step Gestational Diabetes Screening and Pregnancy Outcomes: A Systematic Review and Meta-analysis. Obstet Gynecol. 2022;140(5):712-23.
53. Amaefule CE, Sasitharan A, Kalra P, Iliodromoti S, Huda MSB, Rogozinska E, et al. The accuracy of haemoglobin A1c as a screening and diagnostic test for gestational diabetes: a systematic review and meta-analysis of test accuracy studies. Curr Opin Obstet Gynecol. 2020;32(5):322-34.
54. O'Sullivan EP, Avalos G, O'Reilly M, Dennedy MC, Gaffney G, Dunne F. Atlantic Diabetes in Pregnancy (DIP): the prevalence and outcomes of gestational diabetes mellitus using new diagnostic criteria. Diabetologia. 2011;54(7):1670-5.
55. Lapolla A, Dalfrà MG, Ragazzi E, De Cata AP, Fedele D. New International Association of the Diabetes and Pregnancy Study Groups (IADPSG) recommendations for diagnosing gestational diabetes compared with former criteria: a retrospective study on pregnancy outcome. Diabet Med. 2011;28(9):1074-7.
56. Meek CL, Lewis HB, Patient C, Murphy HR, Simmons D. Diagnosis of gestational diabetes mellitus: falling through the net. Diabetologia. 2015;58(9):2003-12.
57. Farrar D, Simmonds M, Bryant M, Sheldon TA, Tuffnell D, Golder S, et al. Hyperglycaemia and risk of adverse perinatal outcomes: systematic review and meta-analysis. Bmj. 2016;354:i4694.
58. Saeedi M, Cao Y, Fadl H, Gustafson H, Simmons D. Increasing prevalence of gestational diabetes mellitus when implementing the IADPSG criteria: A systematic review and meta-analysis. Diabetes Res Clin Pract. 2021;172:108642.
59. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS, Australian Carbohydrate Intolerance Study in Pregnant Women Trial G. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med. 2005;352(24):2477-86.
60. Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, et al. A multicenter, randomized trial of treatment for mild gestational diabetes. N Engl J Med. 2009;361(14):1339-48.
61. Crowther CA, Samuel D, McCowan LME, Edlin R, Tran T, McKinlay CJ. Lower versus Higher Glycemic Criteria for Diagnosis of Gestational Diabetes. N Engl J Med. 2022;387(7):587-98.
62. Duran A, Sáenz S, Torrejón MJ, Bordiú E, Del Valle L, Galindo M, et al. Introduction of IADPSG criteria for the screening and diagnosis of gestational diabetes mellitus results in improved pregnancy outcomes at a lower cost in a large cohort of pregnant women: the St. Carlos Gestational Diabetes Study. Diabetes Care. 2014;37(9):2442-50.
63. Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and Trends in Diabetes Among Adults in the United States, 1988-2012. Jama. 2015;314(10):1021-9.
64. Corrado F, Pintaudi B, D'Anna R, Santamaria A, Giunta L, Di Benedetto A. Perinatal outcome in a Caucasian population with gestational diabetes and preexisting diabetes first diagnosed in pregnancy. Diabetes Metab. 2016;42(2):122-5.
65. Li M, Hinkle SN, Grantz KL, Kim S, Grewal J, Grobman WA, et al. Glycaemic status during pregnancy and longitudinal measures of fetal growth in a multi-racial US population: a prospective cohort study. Lancet Diabetes Endocrinol. 2020;8(4):292-300.
66. Sovio U, Murphy HR, Smith GC. Accelerated Fetal Growth Prior to Diagnosis of Gestational Diabetes Mellitus: A Prospective Cohort Study of Nulliparous Women. Diabetes Care. 2016;39(6):982-7.
67. Riskin-Mashiah S, Younes G, Damti A, Auslender R. First-trimester fasting hyperglycemia and adverse pregnancy outcomes. Diabetes Care. 2009;32(9):1639-43.

68. Corrado F, D'Anna R, Cannata ML, Interdonato ML, Pintaudi B, Di Benedetto A. Correspondence between first-trimester fasting glycaemia, and oral glucose tolerance test in gestational diabetes diagnosis. Diabetes Metab. 2012;38(5):458-61.
69. Zhu WW, Yang HX, Wei YM, Yan J, Wang ZL, Li XL, et al. Evaluation of the value of fasting plasma glucose in the first prenatal visit to diagnose gestational diabetes mellitus in china. Diabetes Care. 2013;36(3):586-90.
70. Raets L, Beunen K, Benhalima K. Screening for Gestational Diabetes Mellitus in Early Pregnancy: What Is the Evidence? J Clin Med. 2021;10(6).
71. McLaren RA, Jr., Ruymann KR, Ramos GA, Osmundson SS, Jauk V, Berghella V. Early screening for gestational diabetes mellitus: a meta-analysis of randomized controlled trials. Am J Obstet Gynecol MFM. 2022;4(6):100737.
72. Rayanagoudar G, Hashi AA, Zamora J, Khan KS, Hitman GA, Thangaratinam S. Quantification of the type 2 diabetes risk in women with gestational diabetes: a systematic review and meta-analysis of 95,750 women. Diabetologia. 2016;59(7):1403-11.
73. Simmons D, Immanuel J, Hague WM, Teede H, Nolan CJ, Peek MJ, et al. Treatment of Gestational Diabetes Mellitus Diagnosed Early in Pregnancy. N Engl J Med. 2023;388(23):2132-44.
74. Haque MM, Tannous WK, Herman WH, Immanuel J, Hague WM, Teede H, et al. Cost-effectiveness of diagnosis and treatment of early gestational diabetes mellitus: economic evaluation of the TOBOGM study, an international multicenter randomized controlled trial. EClinicalMedicine. 2024;71:102610.
75. Sweeting A, MacMillan F, Simmons D, attendees TS. The first International Association of Diabetes and Pregnancy Study Groups summit on the diagnosis of gestational diabetes in early pregnancy: TOBOGM Summit Report. Aust N Z J Obstet Gynaecol. 2024.
76. Nathan DM, Genuth S, Lachin J, Cleary P, Crofford O, Davis M, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993;329(14):977-86.
77. Hughes RC, Rowan J, Florkowski CM. Is There a Role for HbA1c in Pregnancy? Curr Diab Rep. 2016;16(1):5.
78. Venkatesh KK, Fareed N, Kiefer MK, Ware CA, Buschur E, Landon MB, et al. Differences in Hemoglobin A1c during Pregnancy between Non-Hispanic Black versus White Women with Prepregnancy Diabetes. Am J Perinatol. 2022;39(12):1279-87.
79. Saravanan P, Deepa M, Ahmed Z, Ram U, Surapaneni T, Kallur SD, et al. Early pregnancy HbA_{1c} as the first screening test for gestational diabetes: results from three prospective cohorts. The Lancet Diabetes & Endocrinology. 2024;12(8):535-44.
80. Lowe LP, Metzger BE, Dyer AR, Lowe J, McCance DR, Lappin TR, et al. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study: associations of maternal A1C and glucose with pregnancy outcomes. Diabetes Care. 2012;35(3):574-80.
81. Renz PB, Chume FC, Timm JRT, Pimentel AL, Camargo JL. Diagnostic accuracy of glycated hemoglobin for gestational diabetes mellitus: a systematic review and meta-analysis. Clin Chem Lab Med. 2019;57(10):1435-49.
82. Ho YR, Wang P, Lu MC, Tseng ST, Yang CP, Yan YH. Associations of mid-pregnancy HbA1c with gestational diabetes and risk of adverse pregnancy outcomes in high-risk Taiwanese women. PLoS One. 2017;12(5):e0177563.
83. Claire B, Sharon H. Should HbA1C be used to screen pregnant women for undiagnosed diabetes in the first trimester? A review of the evidence. J Public Health (Oxf). 2020;42(1):132-40.
84. Hughes RC, Moore MP, Gullam JE, Mohamed K, Rowan J. An early pregnancy HbA1c >/=5.9% (41 mmol/mol) is optimal for detecting diabetes and identifies women at increased risk of adverse pregnancy outcomes. Diabetes Care. 2014;37(11):2953-9.

85. Rayis DA, Ahmed ABA, Sharif ME, ElSouli A, Adam I. Reliability of glycosylated hemoglobin in the diagnosis of gestational diabetes mellitus. J Clin Lab Anal. 2020;34(10):e23435.
86. Sweeting AN, Ross GP, Hyett J, Molyneaux L, Tan K, Constantino M, et al. Baseline HbA1c to Identify High-Risk Gestational Diabetes: Utility in Early vs Standard Gestational Diabetes. J Clin Endocrinol Metab. 2017;102(1):150-6.
87. Mou SS, Gillies C, Hu J, Danielli M, Al Wattar BH, Khunti K, Tan BK. Association between HbA1c Levels and Fetal Macrosomia and Large for Gestational Age Babies in Women with Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis of 17,711 Women. J Clin Med. 2023;12(11).
88. Kattini R, Hummelen R, Kelly L. Early Gestational Diabetes Mellitus Screening With Glycated Hemoglobin: A Systematic Review. J Obstet Gynaecol Can. 2020;42(11):1379-84.
89. Immanuel J, Simmons D, Desoye G, Corcoy R, Adelantado JM, Devlieger R, et al. Performance of early pregnancy HbA(1c) for predicting gestational diabetes mellitus and adverse pregnancy outcomes in obese European women. Diabetes Res Clin Pract. 2020;168:108378.
90. Valadan M, Bahramnezhad Z, Golshahi F, Feizabad E. The role of first-trimester HbA1c in the early detection of gestational diabetes. BMC Pregnancy Childbirth. 2022;22(1):71.
91. Diabetes Canada Clinical Practice Guidelines Expert C, Feig DS, Berger H, Donovan L, Godbout A, Kader T, et al. Diabetes and Pregnancy. Can J Diabetes. 2018;42 Suppl 1:S255-S82.
92. American Diabetes A. 14. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes-2021. Diabetes Care. 2021;44(Suppl 1):S200-S10.
93. Brown J, Alwan NA, West J, Brown S, McKinlay CJ, Farrar D, Crowther CA. Lifestyle interventions for the treatment of women with gestational diabetes. Cochrane Database Syst Rev. 2017;5(5):Cd011970.
94. Han S, Middleton P, Shepherd E, Van Ryswyk E, Crowther CA. Different types of dietary advice for women with gestational diabetes mellitus. Cochrane Database Syst Rev. 2017;2(2):Cd009275.
95. Brown J, Grzeskowiak L, Williamson K, Downie MR, Crowther CA. Insulin for the treatment of women with gestational diabetes. Cochrane Db Syst Rev. 2017(11).
96. Farrar D, Simmonds M, Bryant M, Sheldon TA, Tuffnell D, Golder S, Lawlor DA. Treatments for gestational diabetes: a systematic review and meta-analysis. BMJ Open. 2017;7(6):e015557.
97. Network SIG. Management of diabetes

A national clinical guideline Edinburgh: SIGN; 2010 [updated November 2017. Available from: https://www.sign.ac.uk/assets/sign116.pdf.
98. Martine-Edith G, Johnson W, Hunsicker E, Hamer M, Petherick ES. Associations between maternal characteristics and pharmaceutical treatment of gestational diabetes: an analysis of the UK Born in Bradford (BiB) cohort study. BMJ Open. 2021;11(11):e053753.
99. Farrar D, Simmonds M, Griffin S, Duarte A, Lawlor DA, Sculpher M, et al. The identification and treatment of women with hyperglycaemia in pregnancy: an analysis of individual participant data, systematic reviews, meta-analyses and an economic evaluation. Health Technol Assess. 2016;20(86):1-348.
100. Stacey T, Tennant PWG, McCowan LME, Mitchell EA, Budd J, Li M, et al. Gestational diabetes and the risk of late stillbirth: a case-control study from England, UK. Bjog-Int J Obstet Gy. 2019;126(8):973-82.

101. Murphy NM, McCarthy FP, Khashan AS, Myers JE, Simpson NA, Kearney PM, et al. Compliance with National Institute of Health and Care Excellence risk-based screening for Gestational Diabetes Mellitus in nulliparous women. Eur J Obstet Gynecol Reprod Biol. 2016;199:60-5.
102. Chung WK, Erion K, Florez JC, Hattersley AT, Hivert MF, Lee CG, et al. Precision Medicine in Diabetes: A Consensus Report From the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2020;43(7):1617-35.
103. Ahmad A, Imran M, Ahsan H. Biomarkers as Biomedical Bioindicators: Approaches and Techniques for the Detection, Analysis, and Validation of Novel Biomarkers of Diseases. Pharmaceutics. 2023;15(6).
104. Rodrigo N, Glastras SJ. The Emerging Role of Biomarkers in the Diagnosis of Gestational Diabetes Mellitus. J Clin Med. 2018;7(6).
105. Coomar D, Hazlehurst JM, Austin F, Foster C, Hitman GA, Heslehurst N, et al. Diet and physical activity in pregnancy to prevent gestational diabetes: a protocol for an individual participant data (IPD) meta-analysis on the differential effects of interventions with economic evaluation. BMJ Open. 2021;11(6):e048119.
106. Kotzaeridi G, Blätter J, Eppel D, Rosicky I, Linder T, Geissler F, et al. Characteristics of gestational diabetes subtypes classified by oral glucose tolerance test values. Eur J Clin Invest. 2021;51(9):e13628.
107. Cooray SD, Wijeyaratne LA, Soldatos G, Allotey J, Boyle JA, Teede HJ. The Unrealised Potential for Predicting Pregnancy Complications in Women with Gestational Diabetes: A Systematic Review and Critical Appraisal. Int J Environ Res Public Health. 2020;17(9).
108. Zhang Z, Yang L, Han W, Wu Y, Zhang L, Gao C, et al. Machine Learning Prediction Models for Gestational Diabetes Mellitus: Meta-analysis. J Med Internet Res. 2022;24(3):e26634.
109. Kokori E, Olatunji G, Aderinto N, Muogbo I, Ogieuhi IJ, Isarinade D, et al. The role of machine learning algorithms in detection of gestational diabetes; a narrative review of current evidence. Clin Diabetes Endocrinol. 2024;10(1):18.
110. Benhalima K, Van Crombrugge P, Moyson C, Verhaeghe J, Vandeginste S, Verlaenen H, et al. Characteristics and pregnancy outcomes across gestational diabetes mellitus subtypes based on insulin resistance. Diabetologia. 2019;62(11):2118-28.
111. Powe CE, Allard C, Battista MC, Doyon M, Bouchard L, Ecker JL, et al. Heterogeneous Contribution of Insulin Sensitivity and Secretion Defects to Gestational Diabetes Mellitus. Diabetes Care. 2016;39(6):1052-5.
112. White SL, Koulman A, Ozanne SE, Furse S, Poston L, Meek CL. Towards Precision Medicine in Gestational Diabetes: Pathophysiology and Glycemic Patterns in Pregnant Women With Obesity. J Clin Endocrinol Metab. 2023;108(10):2643-52.
113. Retnakaran R, Ye C, Hanley AJ, Connelly PW, Sermer M, Zinman B. Subtypes of gestational diabetes and future risk of pre-diabetes or diabetes. EClinicalMedicine. 2021;40:101087.
114. Powe CE, Udler MS, Hsu S, Allard C, Kuang A, Manning AK, et al. Genetic Loci and Physiologic Pathways Involved in Gestational Diabetes Mellitus Implicated Through Clustering. Diabetes. 2021;70(1):268-81.
115. Ayman G, Strachan JA, McLennan N, Malouf R, Lowe-Zinola J, Magdi F, et al. The top 10 research priorities in diabetes and pregnancy according to women, support networks and healthcare professionals. Diabet Med. 2021;38(8):e14588.
116. Parasher A. COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment. Postgraduate Medical Journal. 2020;97(1147):312-20.

117. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. Bmj-Brit Med J. 2020;370.
118. Royal College of OaG. Guidance for maternal medicine

services in the evolving coronavirus

(COVID-19) pandemic London: RCOG; 2020 [updated 9 December 2020. Available from: https://www.rcog.org.uk/media/nkpfvim5/2020-12-09-guidance-for-maternal-medicine-services-in-the-coronavirus-c.pdf.
119. McIntyre HD, Gibbons KS, Ma RCW, Tam WH, Sacks DA, Lowe J, et al. Testing for gestational diabetes during the COVID-19 pandemic. An evaluation of proposed protocols for the United Kingdom, Canada and Australia. Diabetes Res Clin Pract. 2020;167:108353.
120. van-de-l'Isle Y, Steer PJ, Watt Coote I, Cauldwell M. Impact of changes to national UK Guidance on testing for gestational diabetes screening during a pandemic: a single-centre observational study. BJOG. 2021;128(5):917-20.
121. van Gemert TE, Moses RG, Pape AV, Morris GJ. Gestational diabetes mellitus testing in the COVID-19 pandemic: The problems with simplifying the diagnostic process. Aust N Z J Obstet Gynaecol. 2020;60(5):671-4.
122. Meek CL, Lindsay RS, Scott EM, Aiken CE, Myers J, Reynolds RM, et al. Approaches to screening for hyperglycaemia in pregnant women during and after the COVID-19 pandemic. Diabetic Med. 2021;38(1).
123. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M, Medical Research Council G. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ. 2008;337:a1655.
124. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ. 2021;374:n2061.
125. Greenhalgh T, Robert G, Macfarlane F, Bate P, Kyriakidou O. Diffusion of innovations in service organizations: systematic review and recommendations. Milbank Q. 2004;82(4):581-629.
126. Knight M, Bunch, K., Tuffnell,. D, Patel, R., Shakespeare, J., Kotnis, R., Kenyon, S., & Kurinczuk, J. J. (Eds.). Saving lives, improving mothers' care: Lessons learned to inform maternity care from the UK and Ireland confidential enquiries into maternal deaths and morbidity 2017-19. 2021 [Available from: https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/maternal-report-2020/MBRRACE-UK_Maternal_Report_Dec_2020_v10_ONLINE_VERSION_1404.pdf.
127. Jardine J, Walker K, Gurol-Urganci I, Webster K, Muller P, Hawdon J, et al. Adverse pregnancy outcomes attributable to socioeconomic and ethnic inequalities in England: a national cohort study. The Lancet. 2021;398(10314):1905-12.
128. Jardine J, Gurol-Urganci I, Harris T, Hawdon J, Pasupathy D, van der Meulen J, Walker K. Associations between ethnicity and admission to intensive care among women giving birth: a cohort study. Bjog. 2022;129(5):733-42.
129. Venkatesh KK, Lynch CD, Powe CE, Costantine MM, Thung SF, Gabbe SG, et al. Risk of Adverse Pregnancy Outcomes Among Pregnant Individuals With Gestational Diabetes by Race and Ethnicity in the United States, 2014-2020. Jama. 2022;327(14):1356-67.
130. Cooke H, Craig S, Kahal H, Talbot F, Lonnen K. Impact of using fasting plasma glucose and HbA instead of OGTT as a screening tool for gestational diabetes: a retrospective study. Pract Diabetes. 2023;40(1):15-8a.

131. Khurana R, Tong J, Burrows J, Stafford S, Singh A, Jain A, et al. Successful implementation of virtual care to overcome the challenges of managing gestational diabetes during the COVID-19 pandemic: a quality improvement project. BMJ Open Qual. 2023;12(4).
132. Thirugnanasundralingam K, Davies-Tuck M, Rolnik DL, Reddy M, Mol BW, Hodges R, Palmer KR. Effect of telehealth-integrated antenatal care on pregnancy outcomes in Australia: an interrupted time-series analysis. Lancet Digit Health. 2023;5(11):e798-e811.
133. El Moazen G, Pfeifer B, Loid A, Kastner P, Ciardi C. The Effectiveness of Telemedical Monitoring Program DiabCare Tirol for Patients with Gestational Diabetes Mellitus. Stud Health Technol Inform. 2021;285:205-10.
134. Xie W, Dai P, Qin Y, Wu M, Yang B, Yu X. Effectiveness of telemedicine for pregnant women with gestational diabetes mellitus: an updated meta-analysis of 32 randomized controlled trials with trial sequential analysis. BMC Pregnancy Childbirth. 2020;20(1):198.
135. Leblalta B, Kebaili H, Sim R, Lee SWH. Digital health interventions for gestational diabetes mellitus: A systematic review and meta-analysis of randomised controlled trials. PLOS Digit Health. 2022;1(2):e0000015.
136. Eberle C, Stichling S. Telemedical Approaches to Managing Gestational Diabetes Mellitus During COVID-19: Systematic Review. JMIR Pediatr Parent. 2021;4(3):e28630.
137. Munda A, Indihar B, Okanovič G, Zorko K, Steblovnik L, Barlovič DP. Maternal and Perinatal Outcomes During the COVID-19 Epidemic in Pregnancies Complicated by Gestational Diabetes. Zdr Varst. 2023;62(1):22-9.
138. Cauldwell M, van-de-L'Isle Y, Watt Coote I, Steer PJ. Seasonal and SARS-CoV-2 pandemic changes in the incidence of gestational diabetes. Bjog. 2021;128(11):1881-7.
139. Zanardo V, Tortora D, Sandri A, Severino L, Mesirca P, Straface G. COVID-19 pandemic: Impact on gestational diabetes mellitus prevalence. Diabetes Res Clin Pract. 2022;183:109149.
140. Chelu S, Bernad E, Craina M, Neamtu R, Mocanu AG, Vernic C, et al. Prevalence of Gestational Diabetes in preCOVID-19 and COVID-19 Years and Its Impact on Pregnancy: A 5-Year Retrospective Study. Diagnostics (Basel). 2022;12(5).
141. La Verde M, Torella M, Riemma G, Narciso G, Iavarone I, Gliubizzi L, et al. Incidence of gestational diabetes mellitus before and after the Covid-19 lockdown: A retrospective cohort study. J Obstet Gynaecol Res. 2022;48(5):1126-31.
142. He Z, Lv Y, Zheng S, Pu Y, Lin Q, Zhou H, et al. Association of COVID-19 Lockdown With Gestational Diabetes Mellitus. Front Endocrinol (Lausanne). 2022;13:824245.
143. Rhou YJJ, Elhindi J, Melov SJ, Cheung NW, Pasupathy D. Indirect effects of the COVID-19 pandemic on risk of gestational diabetes and factors contributing to increased risk in a multiethnic population: a retrospective cohort study. BMC Pregnancy Childbirth. 2023;23(1):341.
144. Mendez Y, Alpuing Radilla LA, Delgadillo Chabolla LE, Castillo Cruz A, Luna J, Surani S. Gestational diabetes mellitus and COVID-19: The epidemic during the pandemic. World J Diabetes. 2023;14(8):1178-93.
145. Auger N, Wei SQ, Dayan N, Ukah UV, Quach C, Lewin A, et al. Impact of Covid-19 on rates of gestational diabetes in a North American pandemic epicenter. Acta Diabetol. 2023;60(2):257-64.
146. Park AH, Zhong S, Yang H, Jeong J, Lee C. Impact of COVID-19 on physical activity: A rapid review. J Glob Health. 2022;12:05003.
147. Kołomańska-Bogucka D, Pławiak N, Mazur-Bialy AI. The Impact of the COVID-19 Pandemic on the Level of Physical Activity, Emotional State, and Health Habits of Women in Late Pregnancy and Early Puerperium. Int J Environ Res Public Health. 2023;20(3).
148. Cao W, Sun S, Danilack VA. Analysis of Gestational Weight Gain During the COVID-19 Pandemic in the US. JAMA Netw Open. 2022;5(9):e2230954.

149. Hillyard M, Sinclair M, Murphy M, Casson K, Mulligan C. The impact of COVID-19 on the physical activity and sedentary behaviour levels of pregnant women with gestational diabetes. PLoS One. 2021;16(8):e0254364.
150. Mirsky EL, Mastronardi AM, Paudel A, Young ML, Zite NB, Maples JM. The COVID-19 pandemic and prevalence of gestational diabetes: Does gestational weight gain matter? Am J Obstet Gynecol MFM. 2023;5(5):100899.
151. Heeralall C, Ibrahim UH, Lazarus L, Gathiram P, Mackraj I. The effects of COVID-19 on placental morphology. Placenta. 2023;138:88-96.
152. Tosto V, Meyyazhagan A, Alqasem M, Tsibizova V, Di Renzo GC. SARS-CoV-2 Footprints in the Placenta: What We Know after Three Years of the Pandemic. J Pers Med. 2023;13(4).
153. Alecrim MdJ, Mattar R, Torloni MR. Pregnant women's experience of undergoing an oral glucose tolerance test: A cross-sectional study. Diabetes Res Clin Pr. 2022;189:109941.
154. Lachmann EH, Fox RA, Dennison RA, Usher-Smith JA, Meek CL, Aiken CE. Barriers to completing oral glucose tolerance testing in women at risk of gestational diabetes. Diabet Med. 2020;37(9):1482-9.
155. Di Filippo D, Henry A, Bell C, Haynes S, Chang MHY, Darling J, Welsh A. A new continuous glucose monitor for the diagnosis of gestational diabetes mellitus: a pilot study. BMC Pregnancy Childbirth. 2023;23(1):186.
156. Yu Q, Aris IM, Tan KH, Li L-J. Application and Utility of Continuous Glucose Monitoring in Pregnancy: A Systematic Review. Frontiers in Endocrinology. 2019;10.
157. Tartaglione L, di Stasio E, Sirico A, Di Leo M, Caputo S, Rizzi A, et al. Continuous Glucose Monitoring in Women with Normal OGTT in Pregnancy. J Diabetes Res. 2021;2021:9987646.
158. Durnwald C, Beck RW, Li Z, Norton E, Bergenstal RM, Johnson M, et al. Continuous Glucose Monitoring Profiles in Pregnancies With and Without Gestational Diabetes Mellitus. Diabetes Care. 2024;47(8):1333-41.
159. Kusinski LC, Brown J, Hughes DJ, Meek CL. Feasibility and acceptability of continuous glucose monitoring in pregnancy for the diagnosis of gestational diabetes: A single-centre prospective mixed methods study. PLoS One. 2023;18(9):e0292094.
160. DIrectorate NET. Supporting care with remote monitoring Online: NHS England 2022 [Available from: https://transform.england.nhs.uk/covid-19-response/technology-nhs/supporting-the-innovation-collaboratives-to-expand-their-remote-monitoring-plans/.
161. Fatehi F, Samadbeik M, Kazemi A. What is Digital Health? Review of Definitions. Stud Health Technol Inform. 2020;275:67-71.
162. Wootton R. Recent advances: Telemedicine. BMJ. 2001;323(7312):557-60.
163. Kruger DF, White K, Galpern A, Mann K, Massirio A, McLellan M, Stevenson J. Effect of modem transmission of blood glucose data on telephone consultation time, clinic work flow, and patient satisfaction for patients with gestational diabetes mellitus. J Am Acad Nurse Pract. 2003;15(8):371-5.
164. di Biase N, Napoli A, Sabbatini A, Borrello E, Buongiorno AM, Fallucca F. Telemedicine in the treatment of diabetic pregnancy. Ann Ist Super Sanita. 1997;33(3):347-51.
165. Dalfra MG, Nicolucci A, Lapolla A, Tisg. The effect of telemedicine on outcome and quality of life in pregnant women with diabetes. J Telemed Telecare. 2009;15(5):238-42.
166. Shaver J. The State of Telehealth Before and After the COVID-19 Pandemic. Prim Care. 2022;49(4):517-30.
167. Bartholomew ML, Soules K, Church K, Shaha S, Burlingame J, Graham G, et al. Managing Diabetes in Pregnancy Using Cell Phone/Internet Technology. Clin Diabetes. 2015;33(4):169-74.

168. Given JE, Bunting BP, O'Kane MJ, Dunne F, Coates VE. Tele-Mum: A Feasibility Study for a Randomized Controlled Trial Exploring the Potential for Telemedicine in the Diabetes Care of Those with Gestational Diabetes. Diabetes Technol Ther. 2015;17(12):880-8.
169. Carral F, Ayala MD, Fernández JJ, González C, Piñero A, García G, et al. Web-Based Telemedicine System Is Useful for Monitoring Glucose Control in Pregnant Women with Diabetes. Diabetes Technol The. 2015;17(5):349-54.
170. Caballero-Ruiz E, Garcia-Saez G, Rigla M, Villaplana M, Pons B, Hernando ME. A web-based clinical decision support system for gestational diabetes: Automatic diet prescription and detection of insulin needs. Int J Med Inform. 2017;102:35-49.
171. Homko CJ, Deeb LC, Rohrbacher K, Mulla W, Mastrogiannis D, Gaughan J, et al. Impact of a telemedicine system with automated reminders on outcomes in women with gestational diabetes mellitus. Diabetes Technol Ther. 2012;14(7):624-9.
172. Mackillop L, Hirst JE, Bartlett KJ, Birks JS, Clifton L, Farmer AJ, et al. Comparing the Efficacy of a Mobile Phone-Based Blood Glucose Management System With Standard Clinic Care in Women With Gestational Diabetes: Randomized Controlled Trial. JMIR Mhealth Uhealth. 2018;6(3):e71.
173. Miremberg H, Ben-Ari T, Betzer T, Raphaeli H, Gasnier R, Barda G, et al. The impact of a daily smartphone-based feedback system among women with gestational diabetes on compliance, glycemic control, satisfaction, and pregnancy outcome: a randomized controlled trial. Am J Obstet Gynecol. 2018;218(4):453 e1- e7.
174. Guo H, Zhang Y, Li P, Zhou P, Chen LM, Li SY. Evaluating the effects of mobile health intervention on weight management, glycemic control and pregnancy outcomes in patients with gestational diabetes mellitus. J Endocrinol Invest. 2019;42(6):709-14.
175. Rigla M, Martinez-Sarriegui I, Garcia-Saez G, Pons B, Hernando ME. Gestational Diabetes Management Using Smart Mobile Telemedicine. J Diabetes Sci Technol. 2018;12(2):260-4.
176. Chen L, Zhang W, Fu A, Zhou L, Zhang S. Effects of WeChat platform-based nursing intervention on disease severity and maternal and infant outcomes of patients with gestational diabetes mellitus. Am J Transl Res. 2022;14(5):3143-53.
177. Yang P, Lo W, He ZL, Xiao XM. Medical nutrition treatment of women with gestational diabetes mellitus by a telemedicine system based on smartphones. J Obstet Gynaecol Res. 2018;44(7):1228-34.
178. Borgen I, Smastuen MC, Jacobsen AF, Garnweidner-Holme LM, Fayyad S, Noll J, Lukasse M. Effect of the Pregnant+ smartphone application in women with gestational diabetes mellitus: a randomised controlled trial in Norway. BMJ Open. 2019;9(11):e030884.
179. Rasekaba TM, Furler J, Young D, Liew D, Gray K, Blackberry I, Lim WK. Using technology to support care in gestational diabetes mellitus: Quantitative outcomes of an exploratory randomised control trial of adjunct telemedicine for gestational diabetes mellitus (TeleGDM). Diabetes Res Clin Pract. 2018;142:276-85.
180. Yew TW, Chi C, Chan SY, van Dam RM, Whitton C, Lim CS, et al. A Randomized Controlled Trial to Evaluate the Effects of a Smartphone Application-Based Lifestyle Coaching Program on Gestational Weight Gain, Glycemic Control, and Maternal and Neonatal Outcomes in Women With Gestational Diabetes Mellitus: The SMART-GDM Study. Diabetes Care. 2021;44(2):456-63.
181. Wickramasinghe N, Gururajan R. Innovation Practice Using Pervasive Mobile Technology Solutions to Improve Population Health Management: A Pilot Study of Gestational Diabetes Patient Care in Australia. J Healthc Qual. 2016;38(2):93-105.

182. Bromuri S, Puricel S, Schumann R, Krampf J, Ruiz J, Schumacher M. An expert Personal Health System to monitor patients affected by Gestational Diabetes Mellitus: A feasibility study. J Amb Intel Smart En. 2016;8(2):219-37.
183. Singh H, Sendejas M, Pallivathucal LB, Gonzalez M, Decker S, Pimentel AR, et al. Using Telehealth to Enhance Engagement and Reduce Patient Burden in the Management of Gestational Diabetes: A Randomized Trial in a Diverse Community Setting. Diabetes. 2019;68.
184. Peleg M, Shahar Y, Quaglini S, Broens T, Budasu R, Fung N, et al. Assessment of a personalized and distributed patient guidance system. Int J Med Inform. 2017;101:108-30.
185. Hirst JE, Mackillop L, Loerup L, Kevat DA, Bartlett K, Gibson O, et al. Acceptability and user satisfaction of a smartphone-based, interactive blood glucose management system in women with gestational diabetes mellitus. J Diabetes Sci Technol. 2015;9(1):111-5.
186. Jo S, Park HA. Development and Evaluation of a Smartphone Application for Managing Gestational Diabetes Mellitus. Healthc Inform Res. 2016;22(1):11-21.
187. Harrison TN, Sacks DA, Parry C, Macias M, Ling Grant DS, Lawrence JM. Acceptability of Virtual Prenatal Visits for Women with Gestational Diabetes. Womens Health Issues. 2017;27(3):351-5.
188. Alqudah A, McMullan P, Todd A, O'Doherty C, McVey A, McConnell M, et al. Service evaluation of diabetes management during pregnancy in a regional maternity hospital: potential scope for increased self-management and remote patient monitoring through mHealth solutions. BMC Health Serv Res. 2019;19(1):662.
189. Khalil C. Understanding the Adoption and Diffusion of a Telemonitoring Solution in Gestational Diabetes Mellitus: Qualitative Study. JMIR Diabetes. 2019;4(4):e13661.
190. Edwards KJ, Bradwell HL, Jones RB, Andrade J, Shawe JA. How do women with a history of gestational diabetes mellitus use mHealth during and after pregnancy? Qualitative exploration of women's views and experiences. Midwifery. 2021;98:102995.
191. Pais S, Parry D, Petrova K, Rowan J. Acceptance of Using an Ecosystem of Mobile Apps for Use in Diabetes Clinic for Self-Management of Gestational Diabetes Mellitus. Stud Health Technol Inform. 2017;245:188-92.
192. Skar JB, Garnweidner-Holme LM, Lukasse M, Terragni L. Women's experiences with using a smartphone app (the Pregnant+ app) to manage gestational diabetes mellitus in a randomised controlled trial. Midwifery. 2018;58:102-8.
193. Garnweidner-Holme L, Hoel Andersen T, Sando MW, Noll J, Lukasse M. Health Care Professionals' Attitudes Toward, and Experiences of Using, a Culture-Sensitive Smartphone App for Women with Gestational Diabetes Mellitus: Qualitative Study. JMIR Mhealth Uhealth. 2018;6(5):e123.
194. Rasekaba T, Nightingale H, Furler J, Lim WK, Triay J, Blackberry I. Women, clinician and IT staff perspectives on telehealth for enhanced gestational diabetes mellitus management in an Australian rural/regional setting. Rural Remote Health. 2021;21(1).
195. Homko CJ, Santamore WP, Whiteman V, Bower M, Berger P, Geifman-Holtzman O, Bove AA. Use of an internet-based telemedicine system to manage underserved women with gestational diabetes mellitus. Diabetes Technol Ther. 2007;9(3):297-306.
196. Graffigna G, Barello S, Riva G, Savarese M, Menichetti J, Castelnuovo G, et al. Fertilizing a Patient Engagement Ecosystem to Innovate Healthcare: Toward the First Italian Consensus Conference on Patient Engagement. Frontiers in Psychology. 2017;8.
197. Graffigna G, Barello S, Bonanomi A, Riva G. Factors affecting patients' online health information-seeking behaviours: The role of the Patient Health Engagement (PHE) Model. Patient Educ Couns. 2017;100(10):1918-27.
198. Jardine J, Relph S, Magee LA, von Dadelszen P, Morris E, Ross-Davie M, et al. Maternity services in the UK during the coronavirus disease 2019 pandemic: a national survey of modifications to standard care. BJOG. 2021;128(5):880-9.

199. Sarre G, Hyer S, Chauhan-Whittingham P, Johnson A. Patients' experience of antenatal diabetic care during the current COVID-19 pandemic: an exploratory study. Pract Diabetes. 2021;38(6):23-30.
200. McLennan NM, Lindsay R, Saravanan P, Sukumar N, White SL, von Dadelszen P, et al. Impact of COVID-19 on gestational diabetes pregnancy outcomes in the UK: A multicentre retrospective cohort study. BJOG. 2024;131(6):858-68.
201. Palmer KR, Tanner M, Davies-Tuck M, Rindt A, Papacostas K, Giles ML, et al. Widespread implementation of a low-cost telehealth service in the delivery of antenatal care during the COVID-19 pandemic: an interrupted time-series analysis. Lancet. 2021;398(10294):41-52.
202. Albert L, Capel I, García-Sáez G, Martín-Redondo P, Hernando ME, Rigla M. Managing gestational diabetes mellitus using a smartphone application with artificial intelligence (SineDie) during the COVID-19 pandemic: Much more than just telemedicine. Diabetes Res Clin Pr. 2020;169.
203. Gianfrancesco C, Darwin Z, McGowan L, Smith DM, Haddrill R, Carter M, et al. Exploring the Feasibility of Use of An Online Dietary Assessment Tool (myfood24) in Women with Gestational Diabetes. Nutrients. 2018;10(9).
204. Wilk M, Surowiec P, Matejko B, Wrobel A, Zieba-Parkitny J, Cyganek K, et al. Diabetes Management Delivery and Pregnancy Outcomes in Women with Gestational Diabetes Mellitus during the First Wave of the 2020 COVID-19 Pandemic: A Single-Reference Center Report. J Diabetes Res. 2021;2021:5515902.
205. Quinn LM, Olajide O, Green M, Sayed H, Ansar H. Patient and Professional Experiences With Virtual Antenatal Clinics During the COVID-19 Pandemic in a UK Tertiary Obstetric Hospital: Questionnaire Study. J Med Internet Res. 2021;23(8):e25549.
206. Mizrak Sahin B, Kabakci EN. The experiences of pregnant women during the COVID-19 pandemic in Turkey: A qualitative study. Women Birth. 2021;34(2):162-9.
207. Karavadra B, Stockl A, Prosser-Snelling E, Simpson P, Morris E. Women's perceptions of COVID-19 and their healthcare experiences: a qualitative thematic analysis of a national survey of pregnant women in the United Kingdom. BMC Pregnancy Childbirth. 2020;20(1):600.
208. Shipton E, Meloncelli N, D'Emden M, McIntyre HD, Callaway L, Barnett A, de Jersey S. Gestational diabetes screening from the perspective of consumers: Insights from early in the COVID-19 pandemic and opportunities to optimise experiences. Aust N Z J Obstet Gynaecol. 2023;63(2):154-62.
209. Jeganathan S, Prasannan L, Blitz MJ, Vohra N, Rochelson B, Meirowitz N. Adherence and acceptability of telehealth appointments for high-risk obstetrical patients during the coronavirus disease 2019 pandemic. Am J Obstet Gynecol MFM. 2020;2(4):100233.
210. Madden N, Emeruwa UN, Friedman AM, Aubey JJ, Aziz A, Baptiste CD, et al. Telehealth Uptake into Prenatal Care and Provider Attitudes during the COVID-19 Pandemic in New York City: A Quantitative and Qualitative Analysis. Am J Perinatol. 2020;37(10):1005-14.
211. Teti M, Schatz E, Liebenberg L. Methods in the Time of COVID-19: The Vital Role of Qualitative Inquiries. Int J Qual Meth. 2020;19.
212. Murray E, Treweek S, Pope C, MacFarlane A, Ballini L, Dowrick C, et al. Normalisation process theory: a framework for developing, evaluating and implementing complex interventions. BMC Med. 2010;8:63.
213. May CR, Cummings A, Girling M, Bracher M, Mair FS, May CM, et al. Using Normalization Process Theory in feasibility studies and process evaluations of complex healthcare interventions: a systematic review. Implement Sci. 2018;13(1):80.

214. Huddlestone L, Turner J, Eborall H, Hudson N, Davies M, Martin G. Application of normalisation process theory in understanding implementation processes in primary care settings in the UK: a systematic review. BMC Fam Pract. 2020;21(1):52.
215. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care. 2007;19(6):349-57.
216. Pope C, Mays N. Reaching the parts other methods cannot reach: an introduction to qualitative methods in health and health services research. BMJ. 1995;311(6996):42-5.
217. Knott E, Rao AH, Summers K, Teeger C. Interviews in the social sciences. Nat Rev Method Prime. 2022;2(1).
218. Britten N, Jones R, Murphy E, Stacy R. Qualitative research methods in general practice and primary care. Family practice. 1995;12(1):104-14.
219. Savin-Baden M, Major CH. Qualitative research : the essential guide to theory and practice / Maggi Savin-Baden, Claire Howell Major. Milton Park, Abingdon, Oxon ;: Routledge; 2012.
220. Drabble L, Trocki KF, Salcedo B, Walker PC, Korcha RA. Conducting qualitative interviews by telephone: Lessons learned from a study of alcohol use among sexual minority and heterosexual women. Qual Soc Work. 2016;15(1):118-33.
221. Novick G. Is there a bias against telephone interviews in qualitative research? Res Nurs Health. 2008;31(4):391-8.
222. Sah LK, Singh DR, Sah RK. Conducting Qualitative Interviews using Virtual Communication Tools amid COVID-19 Pandemic: A Learning Opportunity for Future Research. JNMA J Nepal Med Assoc. 2020;58(232):1103-6.
223. Thunberg S, Arnell L. Pioneering the use of technologies in qualitative research - A research review of the use of digital interviews. Int J Soc Res Method. 2022;25(6):757-68.
224. Khalil K, Das P, Kammowanee R, Saluja D, Mitra P, Das S, et al. Ethical considerations of phone-based interviews from three studies of COVID-19 impact in Bihar, India. Bmj Glob Health. 2021;6(Suppl_5).
225. Braun V, Clarke V. Is thematic analysis used well in health psychology? A critical review of published research, with recommendations for quality practice and reporting. Health Psychol Rev. 2023;17(4):695-718.
226. Kozica-Olenski SL, Soldatos G, Marlow L, Cooray SD, Boyle JA. Exploring the acceptability and experience of receiving diabetes and pregnancy care via telehealth during the COVID-19 pandemic: a qualitative study. BMC Pregnancy Childbirth. 2022;22(1):932.
227. Care DoHaS. Independent report

Ockenden review: summary of findings, conclusions and essential actions 2022 [updated 30th March 2022. Available from: https://www.gov.uk/government/publications/final-report-of-the-ockenden-review/ockenden-review-summary-of-findings-conclusions-and-essential-actions.
228. Commision CQ. 2019 survey of

women's experiences

of maternity care 2019 [Available from: https://www.cqc.org.uk/sites/default/files/20200128_mat19_statisticalrelease.pdf.
229. Bourne T, Shah H, Falconieri N, Timmerman D, Lees C, Wright A, et al. Burnout, well-being and defensive medical practice among obstetricians and gynaecologists in the UK: cross-sectional survey study. BMJ Open. 2019;9(11):e030968.

230. Midwives Rco. RCM warns of midwife exodus as maternity staffing crisis grows 2020 [Available from: https://pre.rcm.org.uk/media-releases/2021/september/rcm-warns-of-midwife-exodus-as-maternity-staffing-crisis-grows/.
231. Townsend R, Chmielewska B, Barratt I, Kalafat E, van der Meulen J, Gurol-Urganci I, et al. Global changes in maternity care provision during the COVID-19 pandemic: A systematic review and meta-analysis. EClinicalMedicine. 2021;37:100947.
232. Almuslim H, AlDossary S. Models of Incorporating Telehealth into Obstetric Care During the COVID-19 Pandemic, Its Benefits And Barriers: A Scoping Review. Telemed J E Health. 2022;28(1):24-38.
233. Safiee L, Rough D, George P, Mudenha R. Baseline Perceptions of Women With Gestational Diabetes Mellitus and Health Care Professionals About Digital Gestational Diabetes Mellitus Self-Management Health Care Technologies: Interview Study Among Patients and Health Care Professionals. JMIR Hum Factors. 2023;10:e51691.
234. Clark A, Jung E, Prusky C, Shah BR, Halperin IJ. An Evaluation of Virtual Care for Gestational Diabetes Using the Quadruple Aim Framework: Assessment of Patient and Provider Experience, Cost, and Clinical Outcomes. Can J Diabetes. 2023;47(3):236-42 e3.
235. Cordey S, Moncrieff G, Cull J, Sarian A, Group A-CC. 'There's only so much you can be pushed': Magnification of the maternity staffing crisis by the 2020/21 COVID-19 pandemic. BJOG. 2022;129(8):1408-9.
236. Alayoub H, Curran S, Coffey M, Hatunic M, Higgins M. Assessment of the effectiveness of group education on knowledge for women with newly diagnosed gestational diabetes. Ir J Med Sci. 2018;187(1):65-8.
237. Minschart C, Amuli K, Delameillieure A, Calewaert P, Mathieu C, Benhalima K. Multidisciplinary Group Education for Gestational Diabetes Mellitus: A Prospective Observational Cohort Study. J Clin Med. 2020;9(2).
238. Szabo RA, Wilson AN, Homer C, Vasilevski V, Sweet L, Wynter K, et al. Covid-19 changes to maternity care: Experiences of Australian doctors. Aust N Z J Obstet Gynaecol. 2021;61(3):408-15.
239. Flaherty SJ, Delaney H, Matvienko-Sikar K, Smith V. Maternity care during COVID-19: a qualitative evidence synthesis of women's and maternity care providers' views and experiences. BMC Pregnancy Childbirth. 2022;22(1):438.
240. Hinton L, Dakin FH, Kuberska K, Boydell N, Willars J, Draycott T, et al. Quality framework for remote antenatal care: qualitative study with women, healthcare professionals and system-level stakeholders. BMJ Qual Saf. 2024;33(5):301-13.
241. Chaloner J, Qureshi I, Gogoi M, Ekezie WC, Al-Oraibi A, Wobi F, et al. A qualitative study exploring healthcare workers' lived experiences of the impacts of COVID-19 policies and guidelines on maternal and reproductive healthcare services in the United Kingdom. Eur J Midwifery. 2023;7:30.
242. Tassone C, Keshavjee K, Paglialonga A, Moreira N, Pinto J, Quintana Y. Evaluation of mobile apps for treatment of patients at risk of developing gestational diabetes. Health Informatics J. 2020;26(3):1983-94.
243. Collins E, Keedle H, Jackson M, Lequertier B, Schmied V, Boyle J, et al. Telehealth use in maternity care during a pandemic: A lot of bad, some good and possibility. Women Birth. 2024;37(2):419-27.
244. Benhalima K, Van Crombrugge P, Moyson C, Verhaeghe J, Vandeginste S, Verlaenen H, et al. Women with Mild Fasting Hyperglycemia in Early Pregnancy Have More Neonatal Intensive Care Admissions. J Clin Endocrinol Metab. 2021;106(2):e836-e54.
245. Benham JL, Gingras V, McLennan NM, Most J, Yamamoto JM, Aiken CE, et al. Precision gestational diabetes treatment: a systematic review and meta-analyses. Commun Med (Lond). 2023;3(1):135.

246. Francis EC, Powe CE, Lowe WL, Jr., White SL, Scholtens DM, Yang J, et al. Refining the diagnosis of gestational diabetes mellitus: a systematic review and meta-analysis. Commun Med (Lond). 2023;3(1):185.
247. Tobias DK, Merino J, Ahmad A, Aiken C, Benham JL, Bodhini D, et al. Second international consensus report on gaps and opportunities for the clinical translation of precision diabetes medicine. Nat Med. 2023;29(10):2438-57.
248. Liao LD, Ferrara A, Greenberg MB, Ngo AL, Feng J, Zhang Z, et al. Development and validation of prediction models for gestational diabetes treatment modality using supervised machine learning: a population-based cohort study. BMC Med. 2022;20(1):307.
249. Barnes RA, Wong T, Ross GP, Jalaludin BB, Wong VW, Smart CE, et al. A novel validated model for the prediction of insulin therapy initiation and adverse perinatal outcomes in women with gestational diabetes mellitus. Diabetologia. 2016;59(11):2331-8.
250. Souza A, Costa RA, Paganoti CF, Rodrigues AS, Zugaib M, Hadar E, et al. Can we stratify the risk for insulin need in women diagnosed early with gestational diabetes by fasting blood glucose? J Matern Fetal Neonatal Med. 2019;32(12):2036-41.
251. Eleftheriades M, Chatzakis C, Papachatzopoulou E, Papadopoulos V, Lambrinoudaki I, Dinas K, et al. Prediction of insulin treatment in women with gestational diabetes mellitus. Nutrition & Diabetes. 2021;11(1):30.
252. Cooray SD, Boyle JA, Soldatos G, Allotey J, Wang H, Fernandez-Felix BM, et al. Development, validation and clinical utility of a risk prediction model for adverse pregnancy outcomes in women with gestational diabetes: The PeRSonal GDM model. eClinicalMedicine. 2022;52.
253. Molina-Vega M, Gutierrez-Repiso C, Lima-Rubio F, Suarez-Arana M, Linares-Pineda TM, Cobos Diaz A, et al. Impact of the Gestational Diabetes Diagnostic Criteria during the Pandemic: An Observational Study. J Clin Med. 2021;10(21).
254. Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med. 2015;12(10):e1001885.
255. Aziz A, Zork N, Aubey JJ, Baptiste CD, D'Alton ME, Emeruwa UN, et al. Telehealth for High-Risk Pregnancies in the Setting of the COVID-19 Pandemic. Am J Perinatol. 2020;37(8):800-8.
256. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3(2):77-101.
257. Gill P, Baillie J. Interviews and focus groups in qualitative research: an update for the digital age. British Dental Journal. 2018;225(7):668-72.
258. care DohaS. Mental health and wellbeing support for NHS staff: government pledges overhaul 2020 [