PREVENTING GESTATIONAL DIABETES MELLITUS USING IPD-META ANALYSIS AND COST EFFECTIVENESS ANALYSIS IN PREDICTING FETAL GROWTH RESTRICTION

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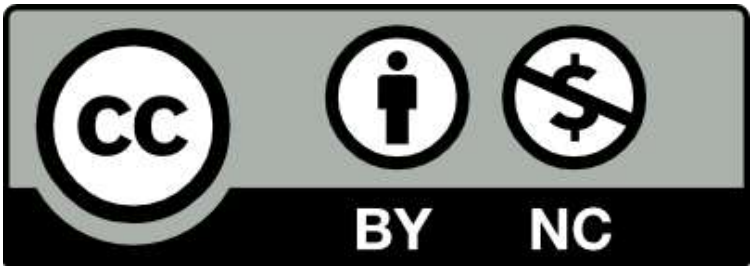
DYUTI COOMAR

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Institute of Metabolism and Systems Research
College of Medical and Dental Sciences
University of Birmingham
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Abstract

Introduction: This thesis looked at two aspects of evidence-based medicine (EBM): evidence synthesis and assessing the cost-effectiveness of new evidence, by focusing on two high risk pregnancy conditions: gestational diabetes mellitus (GDM) and fetal growth restriction (FGR). Evidence was synthesised to study the effect of lifestyle interventions in preventing GDM in women, using different definitions of GDM. Further, a cost-effectiveness analysis was conducted for three different approaches used in detecting fetal growth restriction (FGR) during pregnancy , namely, (1) no routine testing of FGR; (2) using symphysis fundal height (SFH) and ultrasound scans and (3) using the International Prediction of Pregnancy Complications (IPPIC) prediction model.

Methods: A systematic review was used to identify randomised controlled trials which assessed the effect of lifestyle interventions on preventing GDM from inception up to January 2024, and the individual participant data (IPD) were collected via the International Weight Management in Pregnancy (i-WIP) Collaborative Network. The analysis was repeated for all lifestyle interventions combined, and separately for diet, physical activity and mixed interventions. Both one stage and two-stage random-effects IPD meta-analysis models were applied, to obtain summary estimates (odds ratio OR) with 95% confidence intervals (CI) and 95% prediction interval (PI). Heterogeneity was summarised using tau^2 and I^2. Aggregate data from non-IPD trials were also added to the IPD meta-analysis, where possible. The interventions were categorised according to their core components using the TIDieR framework and were ranked based on their effectiveness using network meta-analysis. Covariate-intervention interaction was assessed for age, baseline BMI, ethnicity, parity, and mother's education.

The cost-effectiveness analysis was conducted using decision tree modelling. I only considered nulliparous women in the UK with singleton pregnancies, and the endpoint was considered as whether the baby was delivered via caesarean section or non-caesarean section methods. Costs were presented in 2019-20 prices and the outcome was the number of the perinatal deaths avoided. The results were presented in terms of an incremental cost-effectiveness ratio (ICER) which is the cost per perinatal death avoided. A sensitivity analysis was also conducted by varying the performance (sensitivity and specificity) of the prediction model.

Results: 54 trials (24,391 women) were included in the IPD meta-analysis, along with aggregate data from an additional 46 trials (10,993 women) for which IPD was either not shared upon request or not collected. On average, there was a 10% reduction in the odds of developing GDM according to trial author's definition (OR= 0.90; 95% CI= 0.8, 1.02), which increased to a 20% reduction when aggregate data were added from the non-IPD trials (OR= 0.80; 95% CI= 0.73, 0.88). These results were mostly consistent, regardless of what definition of GDM was used: 2% reduction based on the NICE definition (OR=0.98; 95% CI= 0.84, 1.13), 14% reduction based on the IADPSG definition (OR=0.86; 95% CI= 0.75, 0.97), and 8% reduction based on the modified IADPSG definition (OR=0.92; 95% CI= 0.78, 1.1). Physical activity reduced the odds of developing GDM by 36%, diet-based interventions reduced the odds of developing GDM by 19%, while mixed interventions increased the odds of developing GDM by 5% on average. Women with middle and high educational level benefited more than those with low educational status, and no differences in outcomes were seen for any other maternal group. According to the network meta-analysis, physical activity was ranked with the highest probability of being the most effective intervention. For the cost-effectiveness

analysis of the different strategies used to predict FGR it was found that the IPPIC prediction model was the most cost-effective approach. For every additional death prevented, it cost an additional £1,062.80 compared to not testing for FGR. Detecting FGR using ultrasound and SFH was not supported by the analysis, as its additional benefits were not justified by the increase in costs.

Conclusions: Lifestyle interventions lowered the odds of developing GDM, irrespective of the definitions used, with varying statistical significance. The results suggest that these interventions, particularly physical activity, should be incorporated into standard care due to their demonstrated efficacy. Further, using the IPPIC prediction model to predict FGR was the most cost-effective method, compared to traditional diagnostic tools used in practice.

Dedication

To Ma and Baba, who taught me that with hard work, dreams do come true.

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List of abbreviations (in alphabetical order)

BMI	Body Mass Index
CDSR	Cochrane Database of Systematic Reviews
CEA	Cost-Effectiveness Analysis
CENTRAL	Cochrane Central Register of Controlled Trials
CI	Confidence Interval
CREP	Centro Rosarino de Estudios Perinatales
CS	Caesarean Section
DADS	Direct Access Diagnostic Services
DARE	Database of Abstracts of Reviews of Effects
DM	Diabetes Mellitus
DPP	Diabetes Prevention Programme
EBM	Evidence Based Medicine
EMBASE	Excerpta Medica dataBASE
FGR	Fetal Growth Restriction
FN	False Negative
FP	False Positive
GA	Gestational Age
GDM	Gestation Diabetes Mellitus
GLMM	Generalised Linear Mixed Model
HDU	High Dependency Unit
HKSJ	Hartung-Knapp-Sidik-Jonkman
HR	Hazard Ratio
HRG	Health Resource Groups
HRQoL	Health-Related Quality of Life
HTA	Health Technology Assessment
IADPSG	International Association of Diabetes and Pregnancy Study Group
ICER	Incremental Cost-Effectiveness Ratio
IPD	Individual Participant Data
IPPIC	International Prediction of Pregnancy Complications
IQR	Interquartile Range
ITU	Intensive Treatment/Therapy Unit
IUGR	Intra-Uterine Growth Restriction
i-WIP	International Weight Management in Pregnancy
LGA	Large for Gestational Age
LILACS	Latin American and Caribbean Health Sciences Literature
LR	Low Risk
MD	Mean Difference
ML	Maximum Likelihood Estimation
NA	Not Applicable
NHS	National Health Services
NHSCII	NHS Cost Inflation Index
NICE	National Institute of Health and Care Excellence

NICU	Neonatal Intensive Care Unit
NIHR	National Institute for Health Research
NK	Not Known
NMA	Network Meta-Analysis
NR	Not Reported
OGTT	Oral Glucose Tolerance Test
OR	Odds Ratio
PI	Prediction Interval
PICO	Population, Intervention, Comparison, and Outcomes
PIH	Pregnancy Induced Hypertension
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
PSSRU	Personal Social Services Research Unit
QALY	Quality-Adjusted Life Year
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	Randomized Controlled Trial
REML	Restricted Maximum Likelihood
RIA	Resource Impact Assessment
ROB	Risk-of-Bias
SAS	Statistical Analysis System
SD	Standard Deviation
SE	Standard Error
SFH	Symphysis Fundal Height
SGA	Small for Gestational Age
SPSS	Statistical Product and Service Solutions
SUCRA	Surface Under the Cumulative Ranking Curve
TIDieR	Template for Intervention Description and Replication
TN	True Negative
TP	True Positive
UAE	United Arab Emirates
UK	United Kingdom
USA	United States of America
USAC	Ultrasound Abdominal Circumference
USS	Ultra-Sound Scan
WHO	World Health Organisation

List of initials of names (in alphabetical order)

AD	Anushka Dixit
BS	Buddhika Sudasinge
JA	John Allotey
SFG	Silvia Fernandez-Garcia

Chapter 1

1. Introduction

1.1. Evidence synthesis and its role in the modern healthcare

Evidence based medicine (EBM) aims to integrate the best available evidence from all available sources to guide healthcare decisions.[1] It helps healthcare professionals, policymakers, and researchers to make informed choices about treatments, interventions, and healthcare policies. A pivotal part of this process is 'evidence synthesis', which is a formal method of systematically collecting, reviewing, and synthesising relevant information.[2] This helps to identify the gaps in the current state-of-the art and prioritise areas and methods for future research [2,3].

There are different epidemiological study designs to generate evidence in EBM, as shown in Figure 1.1. These methods are of varying strengths of evidence, with the top of the pyramid (systematic review with meta-analysis of randomised controlled trials (RCTs)) being the strongest. A systematic review is a comprehensive and structured synthesis of all the empirical evidence related to a specific research question.[4] They provide a lot of benefits over traditional reviews – a few of which are: minimising bias, improving transparency and

reproducibility, and including a critical appraisal of study quality of each study included in the review.

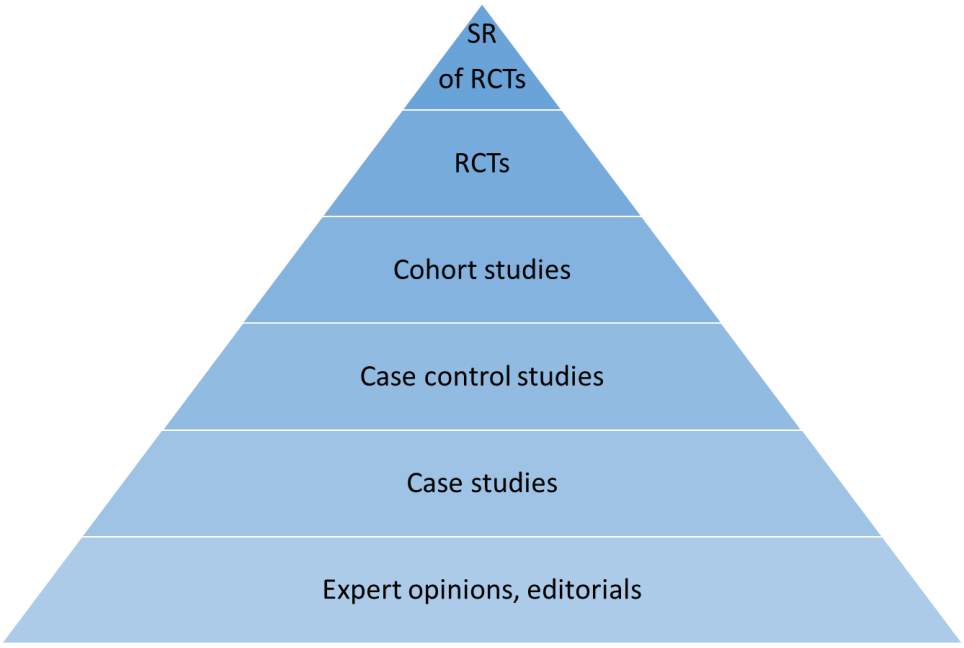


Figure 1.1: Hierarchy of evidence in medical research

Methods to improve evidence synthesis

In recent years, there has been a rapid growth in the amount of existing evidence, be it in the form of RCTs or systematic reviews.[5] However, if systematic reviews are not well conducted, or if they do not provide any additional information (for example, including any additional outcomes) they tend to become redundant or irrelevant.[6] One solution for this issue is to combine effect estimates across studies using meta-analysis techniques.[7] Meta analysis does improve the robustness of the effect estimates when compared to individual RCTs , but as they are completely dependent on the data extracted from publications, they do have some drawbacks.[8] Individual Participant Data (IPD) meta-analysis is a statistical technique to synthesise data from multiple studies by collecting and analysing individual-level data from

each participant from each study. It minimises the drawbacks of traditional meta-analysis techniques. [8,9] As this approach does not solely depend on aggregate data from published studies, it results in a more precise and flexible analysis. [10] Further, it helps to impute missing values, standardise outcomes across studies, adjust for covariates and investigate specific subgroups. It also reduces the chances of publication bias. At present, it is considered as the 'gold standard' in evidence synthesis of RCTs.[10] However, it should be noted that conducting IPDs is a very time and resource intensive process, specially the 'data acquisition' stage.[10–12]

1.2. Economic evaluation

Apart from synthesising reliable evidence regarding a specific intervention, it is important to ensure that it is economically viable to implement the intervention. Thus, the next logical step after evidence synthesis is economic evaluation[13], namely, cost-effectiveness analysis of healthcare interventions. This allows healthcare systems to allocate resources efficiently and prioritise interventions that provide the greatest benefit.[14]

Methods to improve the generalisability of economic evaluation

Cost-effectiveness analysis (CEA) is a technique used to assess the relative efficiency of various interventions or programs, especially within the realms of healthcare and public policy.[15] When resources are limited, it helps to compare costs and outcomes attached to different interventions to find out which option provides the most value for money.

While running the cost-effectiveness analysis, we need to obtain effect-estimates regarding the performance of the different interventions. If these estimates are obtained from the results of a meta-analysis, instead of using single studies, it increases the accuracy of the predicted outcomes.[16] It also enhances the generalisability of the findings to broader populations or contexts. By using the results of the subgroup analysis from a meta-analysis in the decision analytical model, it also allows for the exploration of cost-effectiveness in specific subgroups. These benefits are further increased when using the results of an IPD-meta-analysis, as it further increases the robustness of the effect estimate. By synthesising data from multiple sources directly, IPD meta-analysis strengthens the foundation upon which cost-effectiveness decisions are made, providing policymakers and researchers with more reliable and comprehensive information for resource allocation.[17]

1.3. High risk pregnancies

A 'high-risk pregnancy' refers to situations during pregnancy, childbirth, or the postpartum period where there is an increased risk of developing pregnancy related complications. These complications can be adverse events and/or poor outcomes in both the mother and the baby. There are many factors which can lead to a high-risk pregnancy, such as: advanced maternal age (pregnancy after age 35), preexisting chronic conditions (e.g. hypertension or obesity)[18,19], mental health conditions[20], lifestyle factors, [21] and conditions that develop during pregnancy such as gestational diabetes [22] and gestational hypertension.[23] There are many complications in the baby due to high-risk pregnancy too, such as being large or small for gestational age[21,24], fetal growth restriction[25], and neonatal hypoglycaemia [26], etc. These conditions require special

medical attention and intervention, without which the lives and wellbeing of both the mother and the baby are potentially at stake.[27] Acknowledging the significance of these challenges is crucial, and it aligns with the current global trend advocating for evidence-based decision-making in policy and in practice.[28]. Of the different high-risk pregnancy factors, I chose to explore the following two conditions in this thesis: Gestational Diabetes mellitus (GDM) and Fetal Growth Restriction (FGR). In the following sections these conditions have been briefly described, with reasons on how evidence synthesis and economic evaluation can be beneficial in their prevention.

1.3.1. Gestational diabetes mellitus

When glucose intolerance is diagnosed for the first-time during pregnancy it is referred to as gestational diabetes mellitus. [29] Globally it affects between 7% and 38% of pregnancies, the variation in estimates being introduced due to differences in population, and criteria used for diagnosis. [30] GDM puts pregnant women at a higher risk of pre-eclampsia, caesarean section, and preterm delivery; and the babies at an increased risk of shoulder dystocia, hyperbilirubinaemia, neonatal hypoglycaemia and of being admitted to neonatal intensive care. [31] It is estimated that GDM alone increases the cost of maternity care by 34-95% when compared to pregnant women without GDM.[32,33] There is a 10-fold increased risk for women with GDM to develop type 2 diabetes mellitus in the future, with a cumulative incidence of around 16%. [34] There is a huge effect on the life expectancy [35] and quality of life [36] in the mother and baby due to long term complications of GDM. Further, babies born to mothers with GDM are at risk of developing type 2 diabetes [37] and obesity [38] later in life. In 2024, Hex

et al projected that the UK's National Health Service (NHS) expenditure on diabetes will increase from £10.6 billion to over £17.9billion per year in the next 15 years. [39] There is a possibility that this is further being exacerbated by sedentary behaviour, poor diet, and obesity, all of which lead to the increasing rates of GDM. [40] Thus, lifestyle interventions targeted towards reducing these issues is a possible solution towards preventing GDM.

Till date over 70 trials have been published on the effect of lifestyle interventions on preventing GDM, and fundings of over £10 million has been secured. Despite these trials, their findings have not been translated into real-world use for clinical guidelines or official recommendations. [41–43] Meta-analysis have been conducted to combine the results of these trials, which suggests that implementing these interventions reduces the development of GDM when compared to standard care. However, the drawback of aggregate meta-analysis is that the included studies differed in the definitions for population, intervention and outcome.[43]

Another aspect which is vital to any intervention-based research is to understand the effects of interventions on specific patient subgroups. Currently, it is not clear whether the effects of lifestyle interventions are beneficial to subgroups of women who may have risk factors such as high maternal age, possessing a high body mass index (BMI), having a high parity, belonging to ethnic minorities, or coming from low socioeconomic backgrounds. Thus, having this knowledge of how the intervention performs in interacting with important baseline covariates will provide invaluable information on how policy makers should target them to reach the intended populations. Also, even if the interventions prove to be beneficial, different trials

use different definitions of 'lifestyle interventions', which prevents us from replicating the interventions and implementing them in practice. It will be helpful to understand the comparative effectiveness of diet, physical activity, and mixed interventions separately. The intervention can also be broken down to its core components (details about the intervention duration, intensity, provider, setting, tailoring, materials used in training etc), which will help identify what aspects make the maximum difference in effectiveness.

In this thesis I have addressed the issues discussed above, by performing an IPD meta-analysis on lifestyle interventions and exploring its role in preventing GDM and related complications in mothers and offsprings, and then performing a network meta-analysis to rank the interventions based on their effectiveness. I have not looked at the effect of the interventions on women who already presented with GDM at baseline.

1.3.2. Fetal Growth Restriction

Fetal growth restriction (also known as Intrauterine Growth Restriction (IUGR)) is an associated complication of GDM,[44–46] and often co-occur. It happens when a fetus does not reach its expected genetic growth potential while in the uterus.[47] Studying GDM and FGR together provides valuable insights into their complex relationship, as these two pregnancy complications can have overlapping, yet sometimes contrasting effects on both maternal and fetal health. Exploring their interaction can lead to better understanding, diagnosis, and management of both conditions. Firstly, Both GDM and FGR can affect fetal metabolic programming, altering the risk of metabolic diseases later in life, such as obesity, insulin resistance, and type 2 diabetes. [37,38,48] Secondly, understanding how to balance the treatment

of GDM (which typically involves glucose control) without exacerbating the risk of FGR (which could worsen with excessive glucose restriction) is key for managing high-risk pregnancies.[49] Studying these two conditions together is also important for understanding future pregnancy risks and maternal health. Women who experience either GDM or FGR in a pregnancy are at higher risk of complications in subsequent pregnancies, including a recurrence of GDM, FGR, or preeclampsia. [50–52] Also, both GDM and FGR have long-term implications for population health, as children born from these pregnancies are at greater risk for metabolic and cardiovascular diseases in adulthood.[53,54] Further, both conditions disproportionately affect women from ethnic minorities and disadvantaged socioeconomic backgrounds. [55,56] Studying them together can help identify populations at higher risk for both conditions and tailor interventions to reduce disparities in maternal and fetal outcomes.

The terms FGR and small for gestational age (SGA) are sometimes used interchangeably, but they have distinct meanings. SGA refers to any fetus with an estimated fetal weight less than the 10th percentile for its gestational age, while FGR specifically indicates pathological growth restriction with higher risks for fetal compromise. Not all SGA babies suffer from FGR – around 1/3rd of SGA babies are also FGR. [57]

Undiagnosed FGR has many short-term and long-term complications, including fetal death as well as increased perinatal mortality and morbidity,[58–60] which can be avoided with early identification of women in risk of developing FGR. Then their pregnancies can be closely

monitored, and the setting and timing of their delivery can be strategically planned to minimise adverse perinatal outcomes.

However, there is a lot of variation between international guidelines on how to identify these women – it spans from employing routine ultrasounds for fetal growth in women identified through combinations of arbitrarily designated 'major' or 'minor' clinical risk factors,[61,62] to screening for maternal clinical, biochemical, or Doppler ultrasound risk factors.[63] Further, none of these guidelines makes any distinction between early and late onset FGR, or SGA fetus. A Cochrane review of randomized trials comparing universal ultrasound screening for fetal growth restriction (FGR) in pregnant women with selective screening of high-risk women revealed no reduction in perinatal mortality or morbidity.[64] The selective screening method detects only 20% of small infants, while the universal strategy identifies two normally small babies for each small-for-gestational-age (SGA) fetus with complications.[65] The National Institute for Health and Care Excellence (NICE) antenatal care guideline noted that methods for identifying SGA fetuses during pregnancy are poorly developed or lack rigorous testing.[66] Universal ultrasound screening for FGR places considerable demands on healthcare resources, and its application in low-risk French women did not reduce complications but led to iatrogenic prematurity in screen-positive pregnancies. [67]

Multiple primary studies and meta-analyses have assessed the accuracy of clinical, biochemical, and ultrasound markers, as well as multivariable models, for predicting FGR or SGA fetuses. More than 20 predictive models have been developed, but none are recommended for routine clinical use.[68–72] This is due to challenges in the study design,

population, tests, and outcomes in current research. Firstly, the terms "prediction" and "screening" are often used interchangeably despite their distinct purposes.[73] Prediction aims to foresee FGR when it has not yet occurred, while screening seeks to detect existing FGR. Some prediction models use tests as late as 36 weeks gestation, which are more diagnostic than predictive.[72] Secondly, studies often focus on limited subgroups, such as nulliparous women.[65] Thirdly, predictors are often dichotomized, reducing their power. Fourthly, before recommending models for clinical practice, their predictive performance should be evaluated in intended and external populations. Fifthly, studies frequently predict SGA rather than FGR infants.

IPD meta-analyses can help overcome these limitations, including allowing the standardisation of the FGR definition. To this end, a prediction model was developed by Allotey et al., using the IPD from the previously established International Prediction of Pregnancy Complications (IPPIC) Network [74], which has access to IPD from over three million pregnancies. This model has been explained in detail in the HTA report which has been submitted for publication (Health Technology Assessment programme 17/148/07 of the National Institute for Health Research, PROSPERO CRD42019135045) and has been described in brief below. A random intercept regression model with backward elimination for variable selection was used to predict FGR with complications (a binary outcome) from multiple cohorts. The following variables were included in the final model: gestational age at delivery (weeks), mother's age (years), mother's height (cm), parity, smoking status, ethnicity, history of hypertension, previous pre-eclampsia, previous still-birth, and previous SGA baby. Following the development of the prediction model, the model performance was evaluated

by calculating a pooled C-statistic across datasets, indicating excellent discrimination at 0.962 (95% CI: 0.508 to 0.998). Additionally, the calibration slope, reflecting apparent performance across datasets, was promising at 0.945 (95% CI: 0.665 to 1.230).

After creating the prediction model, the next logical question was to know whether applying the prediction model in practice could be economically viable. Healthcare resources are often limited, and assessing the cost-effectiveness of the prediction model against other methods of detection provides a clearer picture. It shows whether the prediction model provides the greatest health benefits relative to their costs, helps decision makers manage resource allocation burdens more easily, and also justifies their implementation costs. However, the published literature on economic evaluations of FGR detection is sparse[75].

I have addressed this gap in the research by conducting a cost-effectiveness analysis of the IPPIC prediction model against other clinical methods of FGR detection (ultrasound scans and symphysis fundal height (SFH) measurements). I have used a decision analytical framework, building on the economic model provided in the NICE guidelines[75], which is more than a decade old. The aim of this part of my thesis is to help decision makers determine which strategy provides the greatest effectiveness at the most reduced cost in detecting FGR, by looking at the incremental cost-effectiveness ratios (ICERs) of the different strategies.

1.4. Aims and objectives of the thesis.

The overarching aim of this thesis is to synthesise evidence for lifestyle interventions in preventing GDM in women and reducing its related complications in both mothers and babies. Additionally, I have explored the early prediction of FGR and conducted a cost-effectiveness analysis of predicting the risk of FGR. This way, the thesis incorporates not only two different methodological aspects of EBM (evidence synthesis and economic evaluation) but also attempts to study two common pregnancy complications – GDM and FGR, which often occur together, and have similar risk factors, prevention and management techniques.

The specific objectives of this thesis are as follows:

1. To evaluate the effects of diet and physical activity-based lifestyle interventions in pregnancy, across all interventions, and for each type of intervention (diet-based, physical activity-based, mixed) on GDM as defined by the trial authors among all pregnant women.
2. To assess the effects of interventions by different GDM definitions, such as NICE 2015[76], IADPSG[77], (International Association of Diabetes and Pregnancy Study Group), and the modified IADPSG ,[78] definition, and on continuous glucose measurements (fasting and 2-hour post-prandial glucose levels).
3. To assess the differential effects of interventions according to maternal characteristics (age, baseline BMI, parity, ethnicity and socioeconomic status) on GDM.
4. Among women with GDM, evaluate the effects of the interventions on critically important outcomes, such as:

- maternal complications: such as hypertensive diseases, caesarean section and preterm birth
- offspring complications: such as stillbirth, Large for Gestational Age (LGA) , Small for Gestational Age (SGA) and admission to the Neonatal Intensive Care Unit (NICU),

5. To categorise the lifestyle interventions for the prevention of GDM by core components using the Template for Intervention Description and Replication (TIDieR) framework and rank them by effectiveness using network meta-analysis.
6. To determine the cost-effectiveness of the IPPIC prediction model to predict FGR compared to SFH and ultrasound measurements.

1.5. Outputs from this thesis

Various efforts have been made to disseminate the findings of this thesis both to the scientific community as well as to the public, as listed below:

Publications:

Study Protocol	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	Published
NIHR HTA report	Effects of physical activity and diet in pregnancy to prevent gestational diabetes: An individual participant data (IPD) meta-analysis on the differential effects of interventions with economic evaluation.	Submitted

NIHR HTA report	Prediction of fetal growth restriction and complications: Individual Participant Data (IPD) meta-analysis with Decision Curve Analysis and Economic Evaluation International Prediction of Complications in Pregnancy: Fetal Growth restriction (IPPIC-FGR)	Submitted
Article	Effect of Diet and Physical Activity on Gestational Diabetes Mellitus - Individual participant meta-analysis	Being prepared
Article	Economic Evaluation of IPPIC Fetal Growth Restriction (FGR) risk prediction model	Being prepared

Conferences:

RCOG Jan 2023	Poster presentation - RCOG Blair Bell Research Annual Academic Meeting, Feb 2023
RCOG Mar 2023	Oral presentation - RCOG World Congress, June 2023, Awarded 1st prize

Talks and other dissemination activity:

Talks	Public Engagement for Diabetes Day at University of Birmingham, Sept 2021 Global Health Masterclass, Birmingham Women's and Children's Hospital, June 2022 IMSR away day research presentation, June 2022
i-WIP Website	Created, launched, and maintained i-WIP website for public engagement (https://www.i-wip.com)
Animation	Worked on two animations with Science Animated Ltd, which were disseminated on YouTube - https://www.youtube.com/watch?v=4UIGcvLTa58&t=11s&ab_channel=ScienceAnimated And the i-WIP website (https://i-wip.com)

Chapter 2

2. Overview of methods used in the thesis.

In this chapter, I have given an overview of all the methods and statistical techniques which I used in this thesis. Specifications on how each method was adapted to address the objectives of this thesis has been described in the 'Methods' section of each subsequent chapter.

The methodologies for evidence synthesis include systematic reviews (which I employed to select the relevant randomised controlled trials), IPD meta-analysis (statistical technique used to calculate the effect estimates), network meta-analysis using IPD (to rank the effectiveness of the different interventions) and the TIDieR framework (to understand the core components of the intervention). I have also discussed the different sources of bias, impact of effect estimates from small trials ('small-study effects'), and the steps taken to mitigate these effects. In the final section, I have explained the methodology I used for the economic evaluation, namely cost-effectiveness analysis. lists the methodologies I employed to answer the different objectives and the corresponding chapters where they were used.

Table 2.1: Objectives of the thesis and methods used to address them

No.	Objective	Method	Chapter
1	Effect of interventions on GDM (trial authors' definition)	Systematic Review & IPD Meta Analysis	3 and 4

2	Effect of interventions on GDM (NICE, IADPSG, modified IADPSG, fasting, 2 hour post-prandial glucose level)	IPD Meta Analysis	4
3	Differential effects of interventions according to the maternal characteristics	IPD Meta Analysis	5
4	Effect of interventions on maternal & neonatal complications for women with GDM	IPD Meta Analysis	6
5	Categorise interventions and rank them by effectiveness	Network Meta Analysis using IPD, & Meta Regression using TIDieR	7
6	Cost-effectiveness of different approaches to predict FGR	Decision analytical modelling	8

2.1. Evidence Synthesis

2.1.1. Systematic review of RCTs

A systematic review is a comprehensive and structured synthesis of all the empirical evidence related to a specific research question. [4] They are commonly used in healthcare, to summarise and critically appraise all available evidence while minimising bias, providing a reliable basis for informed decision-making.[79] When conducting a systematic review of RCTs, the process typically involves several key steps:

1. Setting up a research question which is specific, answerable, and clearly articulated. It should ideally be defined before starting the systematic review and should not change during the process. [80] It is also advisable to register the protocol before beginning the study to avoid duplication, minimise bias and increase transparency.[81]

2. Setting up an inclusion and exclusion criteria which are clearly defined and described by characteristics such as Population, Intervention, Comparison, and Outcomes (PICO). The type of study design to be included should also be specified.[82]
3. Creating a comprehensive and reproducible search strategy which should include multiple databases (including grey literature sources and manual searching of previous reviews and articles), to identify as many relevant studies as possible.[83] At least two reviewers should independently screen the studies found in the databases based on the inclusion and exclusion criteria to increase reliability. Reasons for excluding studies should also be noted for research reproducibility.
4. Assessing each of the included studies for their risk of bias based on their methodologies. Various tools and checklists are available for this purpose. For RCTs, it is recommended to use the Cochrane risk-of-bias 2 tool (RoB 2).[84] It considers six domains of potential bias: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other potential sources of bias. This step is crucial for evaluating the reliability of the evidence.[85]
5. Creating a data extraction form to collect relevant information from each included study, which may include details about the study design, population characteristics, intervention specifics, outcomes, and results.
6. If possible, performing a meta-analysis to synthesise the findings from individual studies.[7]
7. Summarising the main findings of the review and interpreting the results with consideration given to the overall quality of the evidence, consistency of results, and

any limitations of the included studies.[86] The implications for practice, policy, or future research should also be discussed.

8. It also involves writing up the entire systematic review process in a transparent report following established guidelines, such as the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[87]

2.1.2. Individual Participant Data Meta-analysis

Meta-analysis is a method of synthesising the study-level summary data ('aggregate data') across all relevant studies.[88] In contrast, if a meta-analysis is conducted by synthesising the raw data recorded for each participant ('individual participant data') across all relevant studies, it is known as an Individual Participant Data meta-analysis.[10]

Data acquisition and harmonisation

The first step in an IPD meta-analysis is collecting anonymised, raw, individual-level data from the identified studies. This involves setting up collaborations with trial authors and investigators who contribute the IPD. Formal requests to share data encompasses crucial aspects such as data confidentiality, ethical considerations, and authorship contributions. Obtaining all the IPDs takes considerable time and effort. [9] Once the data are collected, it is checked thoroughly to identify errors, outliers, and inconsistencies. [9,11,89,90] Then the IPDs are harmonised, where all variable definitions and units of measurement are standardised across trials.[11,89] Lastly, all the IPDs are merged into a final analysable dataset. An IPD meta-analysis

can be performed using either a one-stage or a two-stage method which both yield nearly identical results.[91,92]

Two Stage IPD meta-analysis

The two-stage approach is as follows: in the first stage a regression analysis is conducted for each trial included in the study, to generate the study effect estimate. When analysing RCTs, this effect estimate can be mean differences (MD) for continuous outcomes; odds ratios (OR) or risk ratios (RR) for binary (or ordinal) outcomes; incidence rate ratios for count outcomes; or hazard ratios (HR) for time-to-event outcomes.[93] At this stage, it is recommended to adjust for a few key prognostic factors[94,95] , and account for cluster randomisation[96] or repeated measurements [93] , if applicable. If there are any partially missing data in the prognostic factors it can be imputed using mean imputation or the missing indicator method. [91,97]

In the second stage, the individual effect estimates are aggregated to get the summary results and forest plots. The interpretation of forest plots has been provided at the end of this section. The effect estimates are combined assuming either a common-effect or a random-effects model. A common-effect model assumes that the true treatment effect is uniform across all trials. In contrast, a random effects model accommodates heterogeneity in the true treatment effect across trials, which is often more realistic as included trials frequently vary in their characteristics.[98] The random-effects model is solved using restricted maximum likelihood (REML) estimation[99] and the confidence intervals are calculated using the Hartung-Knapp-Sidik-Jonkman (HKSJ) approach. [100–102] Heterogeneity is assessed using the I^2 statistic (proportion of total variability attributed to between-study heterogeneity)[103] along with the

τ^2 statistic (between-study variance). To show the effect of the intervention in a new clinical setting a 95% prediction interval (PI) [104] is also provided.

The difference in treatment effects between subgroups defined by trial characteristics (trial level covariates) is calculated using meta regression.[105] It extends the random-effects model by adding trial level covariates and estimating the parameters using REML estimation and estimating the confidence interval using the HKSJ approach. However, care should be taken to interpret the results as meta-regression usually does not have adequate power.[106]

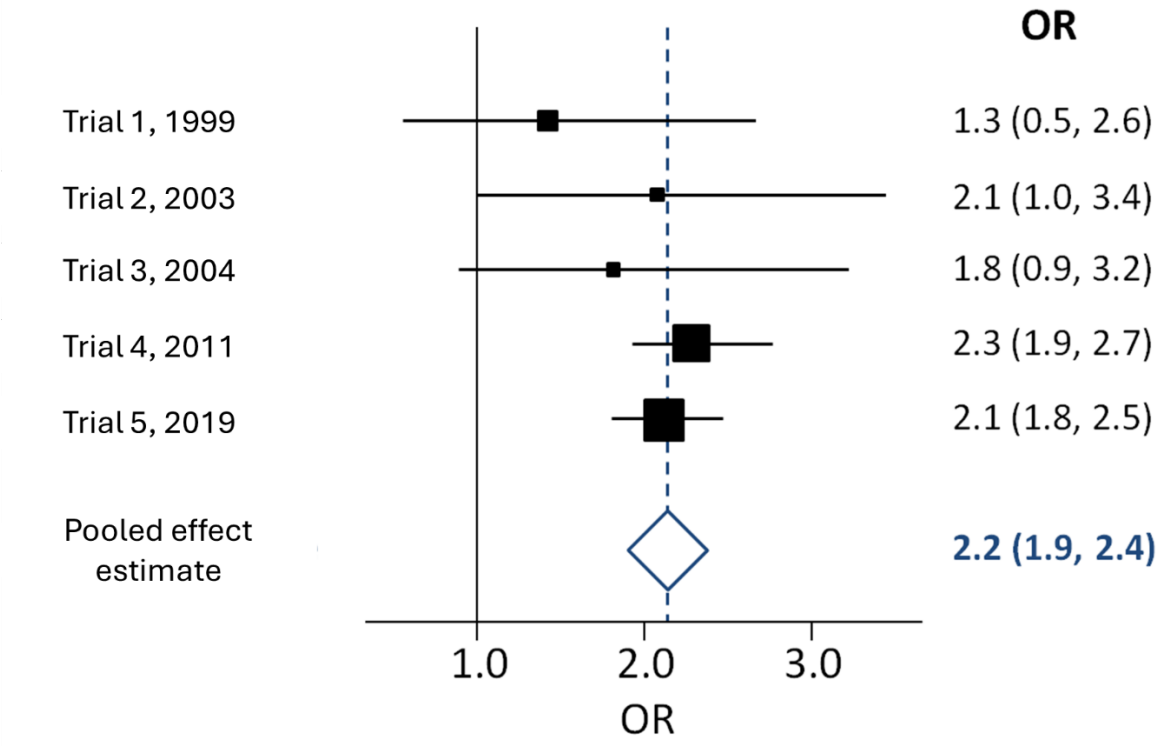


Figure 2.1: Sample forest plot for ease of explanation

The results of an IPD meta-analysis are usually represented using a forest plot. Figure 2.1 explains the various elements of a forest plot using an example forest plot with five trials. The

effect estimates from each study are represented by black squares, where the sizes of the boxes are proportional to the weight of the trial. Each box has a horizontal line, which is the associated confidence interval. The solid vertical line indicates the line of no effect. If the confidence interval crosses this line for a specific trial, the result is not statistically significant. The pooled effect estimate from all the studies is represented by a diamond, with its width representing the confidence interval for the pooled estimate. If the diamond crosses the "line of no effect," the overall result is not significant. On the right, the effect estimate, confidence interval and the weight of each study is also usually provided again.

One Stage IPD meta-analysis

In a one-stage approach, the IPD from all the trials are analysed together to generate a summary effect estimate, usually using a generalised linear mixed model (GLMM). When the number of participants or outcome events are small, the one-stage IPD meta-analysis method is preferable[107,108], as it uses a more exact statistical likelihood than the two-stage method. [108] In this method, the intercept, treatment effect and residual variances are estimated simultaneously. Each of these parameters can be common (the same in each trial), stratified (different in each trial) or random (different in each trial and assumed drawn from a particular distribution), [93] which must be pre-specified.

It is essential to address the clustering of participants within trials, for instance, by incorporating a stratified trial intercept for GLMMs. Failure to do so could lead to biased or excessively precise summary results.[96] For continuous outcomes, it is recommended to use the REML estimation, while for binary outcomes, unless most trials are small, it is

recommended to use REML estimation of a pseudo-likelihood approximation of the exact likelihood [109]. In both cases the Kenward-Roger [110] or Satterthwaite [111] approach can be used to calculate the confidence intervals. However, if the data are sparse, the pseudo likelihood and in turn the REML approach is not applicable. [112] Instead, the maximum likelihood (ML) estimation of the exact likelihood is preferred.[93]

Using IPD meta-analysis to examine interactions between treatment effect and participant level covariates

At times, it is important to identify individual-level factors (covariates) that modify treatment response.[113] This is also known as subgroup effects or effect modifiers and is quantified by treatment-covariate interactions. This is an important advantage of using IPD[8] as individual studies usually have low power to detect them.[114]

It is inappropriate to meta-analyse and compare subgroups separately.[115] Instead, the interaction should be tested to conclude that one subgroup is better than the other.[116] Both two-stage & one-stage approaches are available for identifying interactions with treatment effect and provide similar results.

In the two-stage approach, the covariate -treatment interaction and its variance is analysed separately for each trial, using a chosen meta-analysis model.[117] The interaction estimates are then combined using a common effect or random meta-analysis. Continuous covariates should be handled appropriately – i.e., they should not be categorised,[118] and the possibility

that the interaction is non-linear should be explored.[119,120] In that case, multivariate IPD meta-analysis can be used to synthesise splines. [121]

Examining the potential for bias in IPD meta-analysis

In any IPD meta-analysis project, it is important to examine the robustness of the results for any potential biases.[17] Some of these potential biases are explained below, along with the techniques which can help to mitigate them.

Publication bias occurs when published literature on a particular intervention is not representative of all the studies that have been conducted in that field. It arises when studies demonstrating statistically significant or positive results are more likely to be published than studies with non-significant or negative results.[122–124] This leads to an inaccurate estimation of the true effect of an intervention and the rise of a phenomenon called "small study effects". [125] This occurs when smaller trials tend to report larger treatment effects compared to larger trials. It can be graphically represented using contour enhanced funnel plots, with the study effect estimates on the x-axis and a measure of their precision on the y-axis. Asymmetry in the plot can indicate the presence of small study effects.[126] Statistical tests like Egger's test (for continuous outcomes)[127] and Peter's test (for binary outcomes) [128] can also quantitatively indicate the presence of small study effects. It should however be noted that small study effects can be due to genuine between trial heterogeneity, where the study populations, settings and methodologies of the smaller trials are different from the larger trials.[129,130]

Data availability bias occurs when IPD is sourced from only some of the contacted trials and the availability of the data is associated with the outcomes of those trials. For example, trials with non-significant or negative results are more likely to have destroyed their IPD, leading to a positively biased effect estimate. On the other hand, it can also occur when trials with favourable findings are not keen to share their data as they want to either generate more publications using subgroups or want to follow up with the participants for longer. This leads to a negatively biased effect estimate. Both situations can be addressed by adding aggregate data from trials which did not share their IPD. This is to see if it changes the results of the main IPD meta-analysis.[131] However, it might be difficult to obtain aggregate data for all outcomes, or for interaction effects.

Selection bias occurs if IPD is sought from only some of the identified trials.[9] This can be countered by performing a systematic review without language restrictions and contacting all the trials for data.

The quality of the included trials may also vary depending on what measures the trial authors employed to reduce bias while designing, conducting and analysing their trials. Bias in the individual studies can lead to bias in the IPD meta-analysis. Thus, the quality of each study must be assessed using the ROB 2 tool (see section 2.1.1) and a sensitivity analysis can be conducted by restricting the IPD meta-analysis to only trials with a low risk of bias. [93]

2.1.3. Network Meta Analysis using IPD

A meta-analysis that assesses a specific treatment comparison, (e.g. treatment A vs. B), exclusively based on direct evidence is termed a "pairwise meta-analysis."[93] If there are no trials comparing treatments A and B head-to-head, indirect comparisons can be made through a common comparator treatment C. This is known as Network meta-analysis (NMA) or “multiple treatments meta-analysis”. It allows us to assess the relative treatment effects even when direct evidence is limited, using both direct and indirect evidence.[132–134] It is a powerful tool for synthesising evidence when comparing multiple treatments and can provide valuable insights for decision-makers. However, there are two assumptions which must hold true:

1. Consistency: This states that the treatment contrast of A versus B = (treatment contrast of A versus C) – (treatment contrast of B versus C) holds true on average across all trials.
2. Transitivity: This states that that if we observe any relation between two treatments in a specific trial, it will hold true even in trials where they are unobserved.

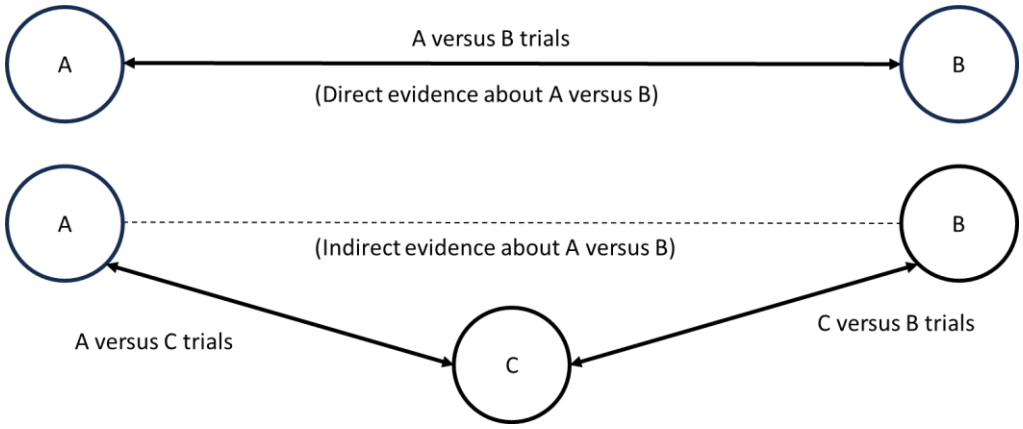


Figure 2.2: Direct and indirect evidence comparing two treatments.

A network meta-analysis using IPD can be conducted using a two-stage method, where the IPD is first analysed for each trial to find treatment effect estimates and their corresponding within-trial variances and correlations. All the effect estimates are then combined in the second stage while taking into consideration both the correlations within individual trials and those across trials, using a multivariate meta-regression model. One of the treatments is considered as the reference treatment, and a design matrix is created to show all the treatment contrasts relative to this reference.

It is not necessary for the reference treatment to be present in every trial. The meta-regression model utilizes indicator variables (-1 or 0 or 1), which represents each treatment effect estimate with respect to the reference treatment. Thus, both the direct and indirect evidence are considered in the overall treatment effect.

After conducting a network meta-analysis, it is useful to arrange treatments in order of their effectiveness.[134–136] Typically, this involves employing simulation or resampling techniques, which draw numerous samples from the estimated distribution of summary treatment effects. These samples are then used to determine the percentage (probability) of samples in which each treatment exhibits the most (or least) advantageous effect.

However, it can be misleading to give undue emphasis to the probability of being ranked first. The probability of being ranked both first and last might be high for the same treatment and its clinical benefit over other treatments may be negligible. To avoid this issue, the mean rank and the surface under the cumulative ranking curve (SUCRA) statistics can be used. The mean

rank offers the average ranking position for each treatment. SUCRA represents the area under a line plot of the cumulative probability across ranks (ranging from most effective to least effective).

2.1.4. Template for Intervention Description and Replication (TIDieR) framework

Without a comprehensive published description of interventions, it is difficult for clinicians and patients to successfully implement proven interventions. It is also difficult for researchers to replicate previous research findings. Unfortunately, the quality of reporting on interventions is poor in trial publications.[137–139] To address this, the Template for Intervention Description and Replication framework [140] makes it easier for others to understand and replicate the intervention in different settings. The checklist consists of twelve items that guide researchers in providing clear and comprehensive information about their interventions.

2.2. Economic Evaluation

2.2.1. Cost effectiveness analysis

Cost-effectiveness analysis (CEA) helps to assess the relative efficiency of two or more options by comparing their associated costs and outcomes. It thereby identifies the option that offers the highest value for the resources invested. [141] It is widely used to assess the value of treatments, diagnostic tests, and public health programs. A systematic quantitative approach

of conducting a cost-effectiveness analysis is to use a decision analytical model. [142] There are different types of decision models which can be used such as decision trees, Markov models, and individual sampling models.

Decision trees are used when there is a short timeframe and there are no recurring events. Each branch of the decision tree denotes a potential future event, with probabilities assigned to each branch reflecting the likelihood of its occurrence. Traditionally, a decision tree follows a unidirectional flow, commencing with the initial decision to provide the intervention. Although the unidirectional nature of the decision trees, could be a limitation in certain scenarios, it can be advantageous for modelling acute disease conditions with a defined course of action. The steps involved in constructing, analysing, and evaluating a decision tree for economic evaluation have been given below:

1. **Tree Structure**: The decision tree starts with a square box representing the main question or choice (decision node). It then reads from left to right, like a flowchart. Each box splits into branches based on possible outcomes, with circles representing random events (chance nodes). Each branch originating from a chance node must be mutually exclusive. It is labelled and is represented by a branch probability. The branch probabilities from a single chance node must add up to 1. The final outcome of the decision tree is represented by a terminal node (triangle).

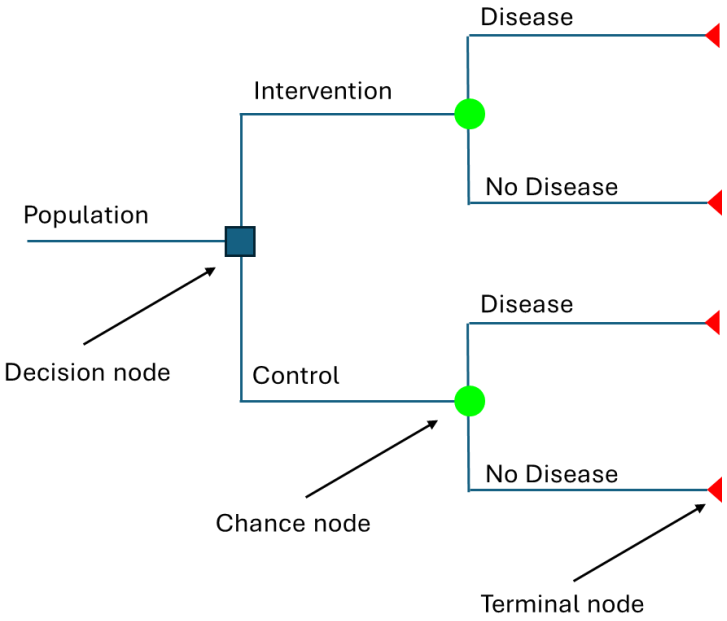


Figure 2.3: Diagramatic representation of a descision tree with descision node, chance nodes, terminal nodes and branches.

2. **Order of events in the decision tree:** While the order of decisions in a decision tree doesn't affect the final outcome, it can make the analysis process easier or harder. Ideally, the order should follow the actual sequence of events over time, making the decision pathway clear. However, sometimes the available probability information might require adjusting this order for better analysis.

3. **Estimating probabilities:** After building the decision tree structure, the branch probabilities needs to be filled. These probabilities typically come from published research. Researchers should do a thorough literature search to find relevant studies; evaluate the quality of the studies they find; combine information from multiple sources if needed (either existing meta-analyses or summarising data themselves). If

no published data exists, they can use data from routine databases or consult with experts.

The most likely value for each probability is called the "base case" estimate. However, since there is always some uncertainty, researchers should also document a range of reasonable alternative values. These can be used later to test how sensitive the overall results are to changes in these probabilities.

4. **Payoffs:** The next step involves adding the payoffs. These represent the final outcomes, like costs and benefits (e.g., life expectancy or quality of life). Payoffs are placed at the very end points (terminal nodes) of the decision tree. In cost-effectiveness analysis, the payoffs are usually both costs and utility values. Utility reflects the value or satisfaction people get from different health outcomes.

5. **Analysing the decision tree: expected values and cost-effectiveness:** After populating the decision tree with the probabilities and payoffs, the analysis involves a process known as "folding back" or "rollback," which calculates the expected value for each available strategy. Starting from the far right of the tree the rollback method iteratively calculates expected values while moving leftward. Mathematically, the expected value is calculated by multiplying the probability of each outcome along a branch by its associated payoff (cost or effect value). Subsequently, these products are summed at each chance node (circular node) to arrive at a single expected value for that specific branch. This process is repeated for all branches emanating from a chance

node. The calculation is performed separately for both costs and effects within the decision tree framework.

The incremental cost-effectiveness ratio (ICER) is calculated by dividing the difference in costs between two alternatives by the difference in their outcomes. It represents the cost incurred to achieve an additional unit of outcome.

$$ICER = \frac{Cost_a - Cost_b}{Effect_a - Effect_b} = \frac{\Delta Cost}{\Delta Effect}$$

6. **Model evaluation:** The next step is to assess the validity and internal consistency of the decision tree model. It helps in ensuring the robustness of the model and should focus on careful examination of the underlying assumptions and the model structure, the input parameters, and the model's output and conclusions. While various published articles address model evaluation, the specific terminology and scope can vary.

7. **Explore uncertainty:** Even when a single strategy emerges as the option, uncertainty surrounding the decision tree structure and parameter values can limit the strength of the conclusion. Sensitivity analysis can be performed to address these concerns: either the model or the input values can be modified, to observe its impact on the base case results. While these methods remain valuable, probabilistic sensitivity analysis (PSA) may offer additional benefits.

Chapter 3

3. Systematic Review of RCTs with lifestyle interventions to prevent GDM and collection of Individual Participant Data (IPD)

In this chapter, I have presented the i-WIP collaboration, the work leading up to this thesis, the systematic review which I conducted to identify trials for the IPD meta-analysis and the collection of the IPD. Before I embarked on starting the data collection, I registered the protocol for the systematic review and IPD meta-analysis on the International prospective register of systematic reviews (PROSPERO) with registration ID CRD42020212884. It was also published[143] to increase transparency and reduce duplication of efforts.

3.1. Methods

3.1.1. Establishment of the i-WIP (International Weight Management in Pregnancy) Group

The IPD meta-analysis was conducted through the International Weight Management in Pregnancy (i-WIP) Group. This group was set up in 2013 and has previously published results of an IPD meta-analysis on the effect of lifestyle interventions on gestational weight gain [43]. The group is supported by the World Health Organization (WHO) and is the largest living global database on diet and physical activity interventions in pregnancy. For this thesis, I used the

studies which were already present in the i-WIP database and contained data on GDM. Further, I expanded the database by updating the systematic review and collecting IPD from the newly identified studies. This work was funded by the National Institute for Health and Care Research (NIHR) (Award ID: NIHR129715) and is going to be concluded with the publication of a Health Technology Assessment (HTA) report.

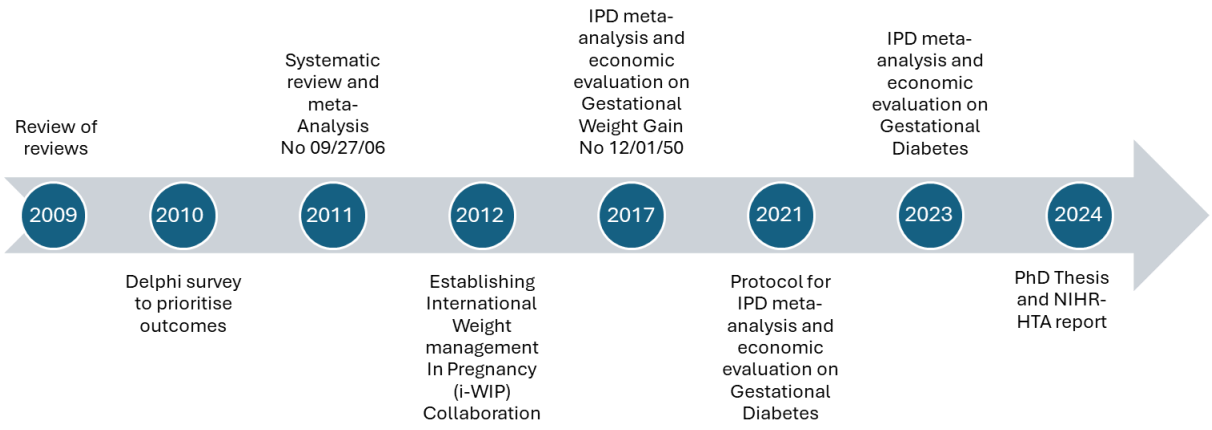


Figure 3.1: Work leading to IPD meta-analysis on effects of diet and physical activity based intervention on GDM

3.1.2. Systematic review update

I updated the literature search by employing the same search strategy as previously documented (Appendix 1) to pinpoint any recent trials published after the conclusion of the earlier review [144]. I searched the following databases: MEDLINE, EMBASE, LILACS, Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment Database (HTA) up until 20th January 2024, without any language limitations.

Additionally, studies were also included if they were identified through other sources (e.g., references of other reviews, authors' recommendation when contacted for IPD).

3.1.3. Study selection

The studies were evaluated in a two-step process: in the first step, the titles and abstracts were assessed for their eligibility using the inclusion and exclusion criteria described in the next section. In the second step, I read the full text articles to complete the screening process, again following the same inclusion and exclusion criteria. This process was independently repeated by another reviewer (AB/BS/SFG) to ensure accuracy and consistency. All conflicts were resolved via meetings. If there was a disagreement, the perspective of a third reviewer (JA) was sought.

3.1.4. Inclusion and exclusion criteria

I included RCTs which assessed the effect of diet and physical activity-based interventions in pregnancy as compared to standard antenatal care. A wide variety of publications were included: pilot and full-scale trials, conference abstracts and posters. I included trials regardless of whether they reported GDM in the paper, as there was a likelihood that they might have collected that information irrespective of whether they reported their findings. Conference abstracts and posters were used as an aid in identifying relevant RCTs, from which IPD was requested (described in Chapter 4), even if they did not publish all the outcome data in the abstract.

The unit of randomization could be either the individuals or clusters (e.g., different hospitals or trial centres). I excluded studies where women had GDM at baseline. Underweight pregnant women with BMI < 18.5 kg/m^2 in early pregnancy were also excluded. This is because it might not be ethical to subject underweight women to lifestyle interventions involving physical exertion, dietary changes, or medications that could exacerbate their condition or increase their potential risks when a benefit is unclear.

I categorized the lifestyle interventions into three categories: diet- based; physical activity-based; and mixed approach interventions, which included both diet and physical activity components, along with a behavioural approach.

Diet-based interventions consisted of diet advice that was offered by clinicians, dietitians, physiotherapists, or commercial companies in both primary care as well as secondary care settings. They included various dietary patterns like the Mediterranean-style diet, low calorie diet, and low glycaemic index diet. These interventions could have been introduced via print or digital media, phone, face-to-face meetings in either one-to-one or group sessions, and could have started at different time points in pregnancy. They could have been delivered and followed up in either an intensely regimented or a more realistic manner.

Physical activity-based interventions consisted of moderate or heavy exercise (water-based physical activity, dance-based exercise programs, stationery cycling, light intensity resistance training) or enhanced routine daily activity (walking). If an intervention contained components

from both diet and physical activity, I referred to it as 'Mixed approach'. I did not include studies which assessed other weight loss interventions such as pharmacotherapy or surgery.

Table 3.1: Components of structured question for IPD meta-analysis

Question components	**Details**
Population	Pregnant women with a BMI of ≥18.5 kg/m2 in early pregnancy
Interventions	Diet-based
	Physical activity-based
	Mixed approach: diet and physical activity with behavioural component
Comparison	Routine antenatal care
Outcomes	Gestational diabetes defined as per trial authors' definition (defined within the study by established criteria)
	Gestational diabetes as defined specifically using the NICE 2015, IADPSG, and modified IADPSG criteria, and 0-hour and 2-hours post prandial continuous glucose outcomes.
	Differential effects of interventions across subgroups based on maternal BMI, age, parity, ethnicity, and socioeconomic status
	Gestational diabetes with maternal and offspring complications
	Categorisation of the interventions by core components and undertake network meta-analysis to rank them by effectiveness
Study design of included studies	RCTs (both pilot and feasibility studies and full-scale studies)
Publication type	Publications from full scale trials, conference abstracts and posters

3.1.5. Data Collection

Collection of IPD

I initiated contact with the lead author and corresponding authors of each trial identified in the systematic review and requested them to join the i-WIP collaboration and provide the IPD from their trial. The contact details of the trial authors were sourced from PubMed or the internet. In cases where there was no response from the primary contact, I reached out to

other investigators involved in the study. I contacted the relevant author(s) from each study at least three times.

If I received a reply and the authors agreed to participate, I provided them with additional information about my research project and instructions on how to share their IPD. Methods for receiving raw data from investigators varied depending on the data governance policies of their individual institutions. Some authors preferred to share their data via email, and others via a secure transfer system hosted by the Centro Rosarino de Estudios Perinatales (CREP), in Rosario, Argentina. CREP is a WHO Collaborative Centre in Child and Maternal Health. In a few cases, I directly downloaded the data from trial data repositories. Some institutions wanted to sign data sharing agreements, which was done with help from University of Birmingham's legal team. After data transfer, it was stored on the web-based server at CREP. I preferred if the authors shared the entire dataset from their trial to reduce chances of selective outcome reporting. However, some authors wanted to send data on only the variables required for the IPD, in which case I provided them with the variable list (Appendix 2).

If I did not receive a reply, it was noted and followed up for at least three times. In cases where authors declined to provide IPD, the reasons were also noted. Reasons for not sharing IPD has been presented in the flowchart provided in Figure 3.2.

Extraction of Aggregate Data

All the studies identified in the systematic review were included in the analysis irrespective of whether they shared their IPD or not. Due to time limitations, I only sought IPD for studies

identified up to March 2021. For all studies that did not share IPD and studies identified between March 2021 to January 2024, I extracted the aggregate data from their publications. I also extracted study characteristics for all the included studies to obtain the year of publication, language, country, methods of randomisation, population, intervention(s), comparisons, and outcome specifics. Additionally, information on diagnostic criteria and oral glucose tolerance test values used to diagnose gestational diabetes was also extracted from each study. The data extraction template has been provided in Appendix 3. This step was independently repeated by another reviewer (AB/BS) to ensure accuracy and consistency. All conflicts were resolved via meetings.

3.1.6. Risk of bias assessment in individual studies

I assessed the quality of each study as described in Chapter 2. However, as per the recommendation from the Cochrane group, [145] I used the 2011 version of the RoB tool [146] as this systematic review was an update of a previous one. I ignored "Blinding – staff participants" as due to the nature of the interventions blinding was difficult, with only one trial[147] achieving blinding of participants. I also ignored "Selective reporting" as all data were requested from authors regardless of whether it were reported in the publications. A study was categorized as having an overall high risk of bias if it received a high-risk assessment in any of the following domains: randomization, allocation concealment, blinding of outcome assessment, or incomplete outcome data.

3.2. Results

3.2.1. Study selection

The search update up to January 2024 yielded 11,848 unique citations, of which 161 trials were eligible for inclusion in the systematic review (100 reported GDM and 61 did not report GDM in the study publication). I sought IPD from 123 trials, of which authors from 62 trials shared their data. 38 trials were identified after the data acquisition date, and thus, IPD was not sought from them. 49.5% of the invited trials did not share their data (61/123; 11,608 women). However, because I prioritised collecting IPD from the larger studies, the number of women in the trials which shared IPD was far greater than the number of women in the trials which did not share their IPD (28,871 or 71.3% vs 11,608 or 28.6%). The most common reason for not obtaining the IPD was absence of any response to the invitation (n=52/61). Of the studies which shared their IPD, GDM data were included in 54 trials (24,391 women) which was our final number of trials included in the IPD meta-analysis. [147–201] Among the trials which did not share their IPD or trials from which IPD was not sought, 46 trials (10,993 women) reported GDM outcomes in their publication and thus were also included in the sensitivity analysis. [202–224], [225–232], [233–247] The entire study selection process has been presented in Figure 3.2 according to PRISMA guidelines.

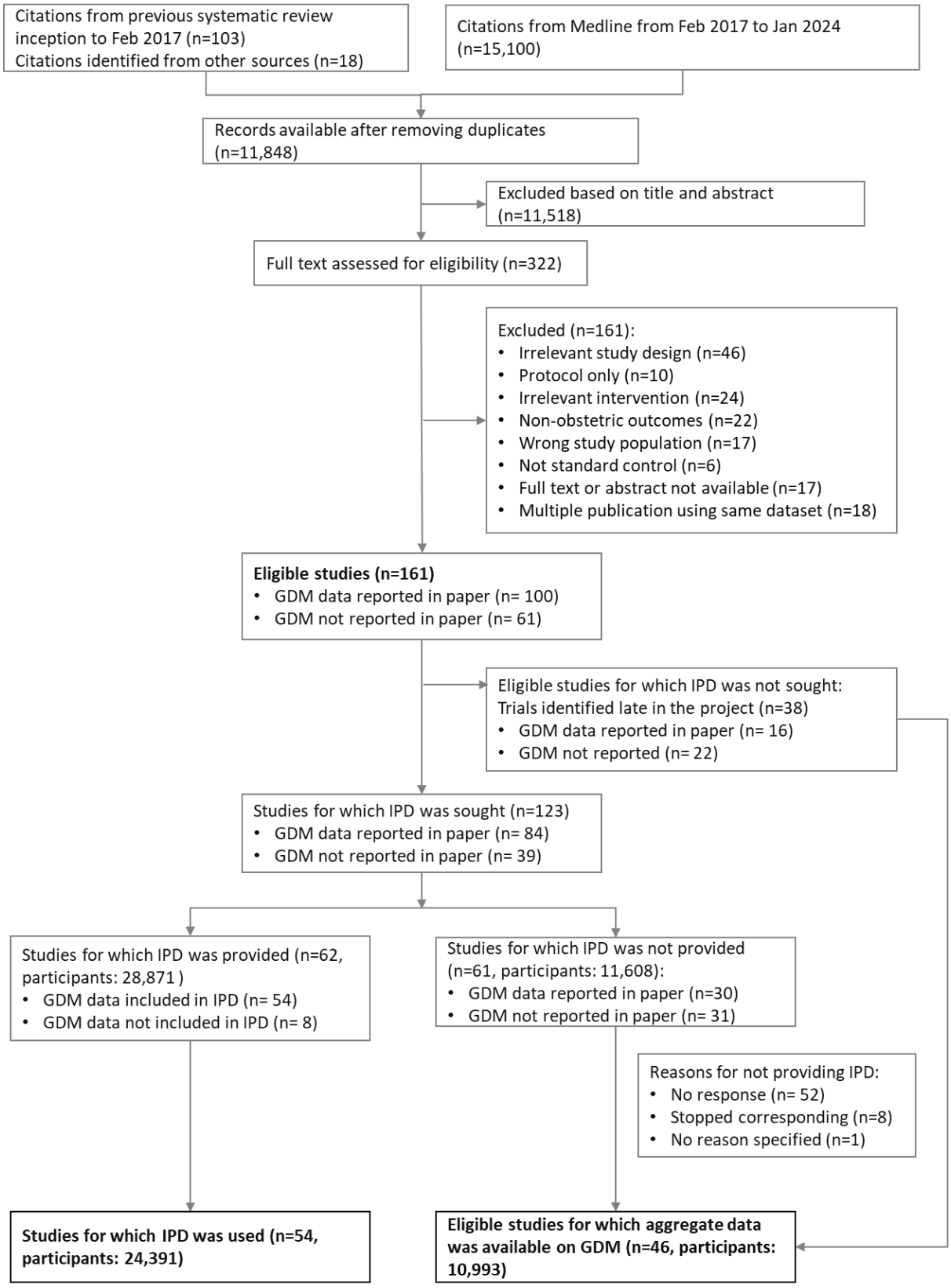


Figure 3.2: PRISMA Flowchart for the selection of included trials

3.2.2. Characteristics of the included trials

54 trials were included in the IPD meta-analysis. Among these, in 51 trials the individual participants were randomised, while 3 were cluster randomised controlled trials. [176,177,189] The sample sizes in the trials ranged from 12 to 4,631 women. There were 3 trials which had more than one intervention arm, and 2 had two arms of the same type of intervention with minor differences– either different types of counselling/diet or different exercise routines, [157,167] while 1 had two intervention arms (mixed and physical activity).[190] Trials were conducted all over the world: 33 trials were in Europe, 9 trials in North America, 8 trials in Australia, and 4 trials in South America. The inclusion criteria of the trials were also varied: 11 trials included women with BMI obese and above, 14 trials included women with a BMI overweight and above, 6 trials included women with BMI normal and above, 1 trial included women with BMI normal only, 22 trials included women of any BMI category. Among the type of interventions, 18 trials evaluated physical activity-based interventions, 7 trials assessed diet-based interventions and 29 trials adopted a mixed approach (Appendix 4).

46 trials without any IPD were also included in the analysis. Among these, in 45 trials the individual participants were randomised, while 1 was a cluster randomised controlled trial. [215]. The sample sizes in the trials ranged from 31 to 1,196 women. 13 trials were from North America, 14 from Europe, 12 from Asia, 2 each from South America, Australia and New Zealand and 1 from Africa. 16 trials evaluated physical activity-based interventions, 8 trials assessed diet-based interventions, 22 trials adopted a mixed approach. 9 trials included women with BMI obese and above, 17 trials included women with BMI overweight and above,

1 trial included women with overweight BMI, 4 trials included women with BMI normal and above, and 15 included women with any BMI (Appendix 4).

Some of the trial characteristics have been presented in . The median year of publication for IPD studies was 2010, while for non-IPD studies it was 2020. This suggested that the non-IPD studies were more recent, which was expected, as collection of IPD was discontinued in the latter years as described earlier. Among both IPD and non-IPD trials, 'Mixed' interventions were the most common. Overall, a vast majority of the trials (84%) were conducted in high income countries. In lower middle-income countries, the number of trials were low and when contacted, the authors were least likely to share their IPD. The clinical study characteristics of all the 100 trials (both IPD and non-IPD) have been presented in Appendix 5 and Appendix 6.

Table 3.2: Study level characteristics of included trials

Characteristics	**Total**	**IPD Studies**	**Non-IPD Studies**		
			Overall non-IPD studies	**Before data acquisition**	**After data acquisition**
Number of Studies	100	54	46	34	12
Number of women	37,599	26,772*	10,827	8,281	2,546
Year of publication Median (IQR)	2020 (7)	2010 (5.75)	2020 (7)	2020 (4.5)	2020 (1)
Type of Intervention					
Diet	15 (15%)	8 (14.8%)	7 (15.2%)	3 (8.8%)	4 (33.3%)
Mixed	51 (51%)	28 (51.9%)	23 (50%)	18 (54.9%)	5 (41.7%)
Physical Activity	35 (34%)	18 (33.3%)	17 (34.8%)	13 (38.2%)	3 (25.0%)
Country of trial**					
High income	84 (84%)	50 (92.6%)	35 (73.9%)	27 (79.4%)	7 (58.3%)
Lower middle income	5 (5.0%)	1 (1.9%)	4 (8.7%)	4 (11.8%)	0 (0%)

Upper middle income	11 (11%)	3 (5.6%)	8 (17.4%)	3 (8.8%)	5 (41.7%)

*As published in trial publications
**According to World Bank[248]

Figure 3.3 shows the frequency and cumulative frequency of the trials published each year, which were included in this thesis. There was a clear upward trend in the cumulative number of trials over time, indicating an increasing interest and investment in researching diet and physical activity-based interventions. The number of trials published each year varied, with some years showing a greater number of published trials than others. For instance, there was a noticeable peak in 2016 with 11 trials published, after which there was another peak in 2018. From 2020 onwards, the number of published trials appeared to stabilise, with approximately 4 to 5 trials published each year, which suggests a steady state of research output in the most recent years.

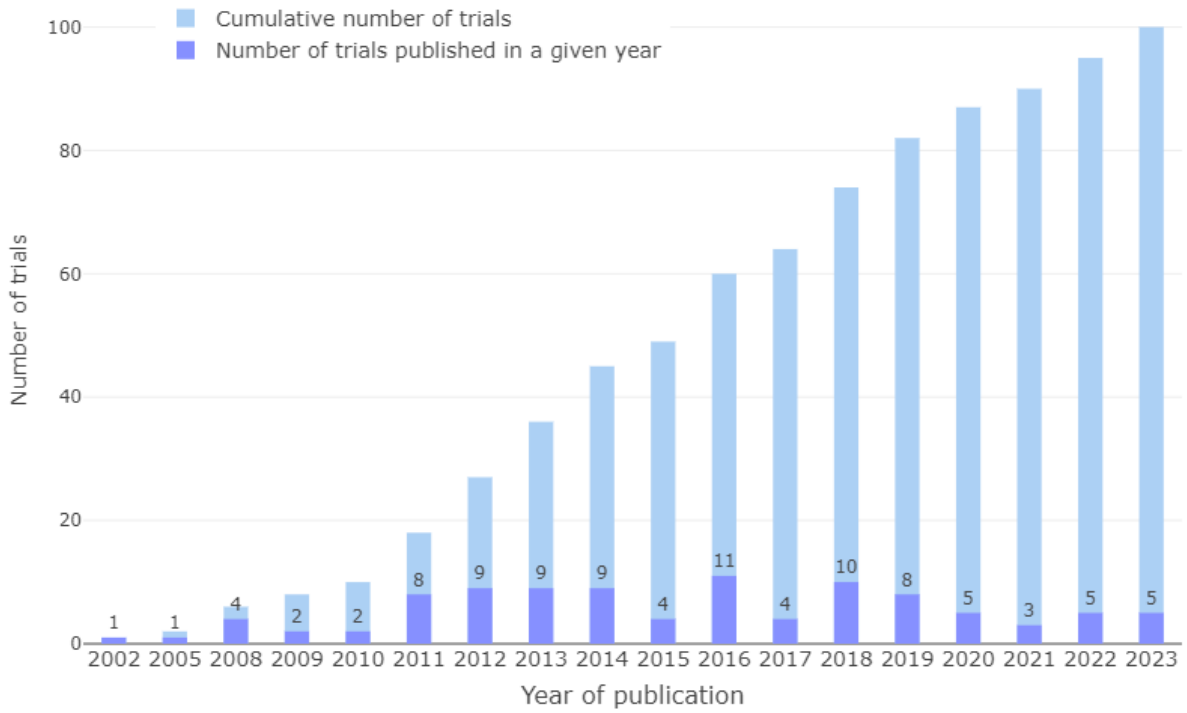


Figure 3.3:Frequency and cumulative frequency of trials included from the systematic review (inception to January 2024)

3.2.3. Quality Assessment

The risk of bias assessment for all the trials has been depicted in Figure 3.4. 64% (64/100) of the total trials were assessed as being low risk of bias. 84% (84/100) of the trials had a low risk of bias in 'Randomisation', indicating that the randomisation process was well described and implemented. The allocation was successfully concealed in 58% (58/100) of the trials. Blinding of outcome assessment was mostly considered as either unclear or high risk (99/100). Incomplete outcome data was low, with only 13% (13/100) of the studies being considered as unclear or high risk.

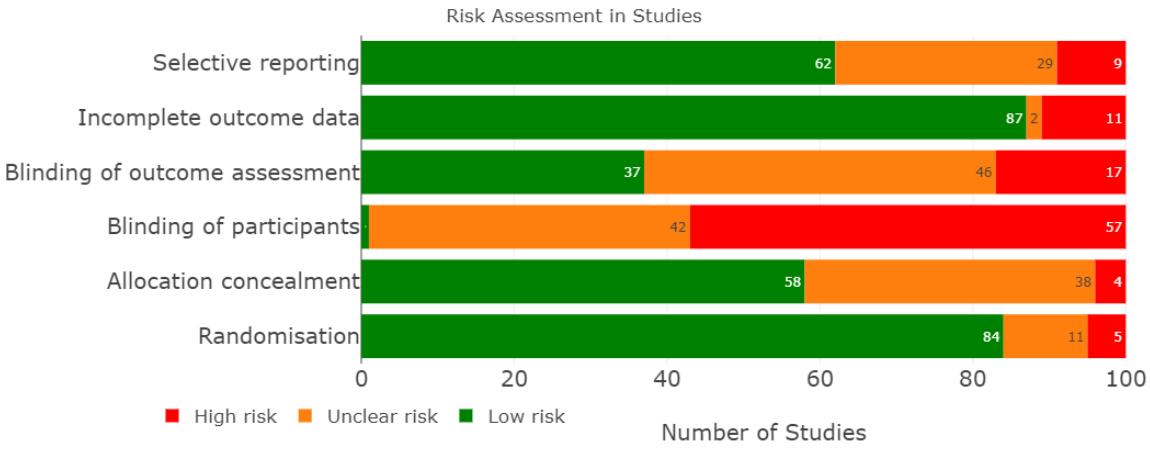


Figure 3.4: Quality Assessment of all included studies according to Risk of Bias 2 tool

Table 3.3 compares the risk of bias assessment for IPD and non-IPD trials separately. It was found that the trials which contributed their IPD were similar to trials which did not contribute their IPD: 61.1% vs 67.4% low risk of overall bias. The risk of bias assessment has been provided for each individual study in Appendix 7 (IPD studies) and Appendix 8 (non-IPD studies).

Table 3.3: Quality assessment for IPD and non-IPD studies based on the Risk of Bias 2011 tool

	IPD	**Non-IPD**
	(N=54)	(N=46)
Randomisation		
Low	49 (90.7%)	35 (76.1%)
Unclear	5 (9.3%)	6 (13%)
High	0 (0%)	5 (10.9%)
Allocation concealment		
High	3 (5.6%)	1 (2.2%)
Low	33 (61.1%)	25 (54.3%)
Unclear	18 (33.3%)	20 (43.5%)
Blinding of participants		

High	34 (63.0%)	23 (50%)
Low	1 (1.9%)	0 (0%)
Unclear	19 (35.2%)	23 (50%)
Blinding of outcome assessment		
High	14 (25.9%)	3 (6.5%)
Low	22 (40.7%)	15 (32.6%)
Unclear	18 (33.3%)	28 (60.9%)
Incomplete outcome data		
High	6 (11.1%)	5 (10.9%)
Low	48 (88.9%)	39 (84.8%)
Unclear	0 (0%)	2 (4.3%)
Selective reporting		
High	8 (14.8%)	1 (2.2%)
Low	33 (61.1%)	29 (63%)
Unclear	13 (24.1%)	16 (34.8%)
Overall risk of bias		
High	21 (38.9%)	15 (32.6%)
Low/Medium	33 (61.1%)	31 (67.4%)

3.3. Summary

Conducting a comprehensive systematic review has shown that despite the year-on-year fluctuations, there is an increasing trend of research in this field. This reflects that there is an increased recognition of the importance of diet and physical activity in health promotion among pregnant women, specifically in preventing GDM. However, hardly any of this research has translated into policy change. This further reinforces the need for an IPD meta-analysis, to create a collective body of evidence.

Collecting the IPD proved to be a massive undertaking and the most time-consuming part of the PhD. Many times, up to date information for authors were not found online, or authors did not reply to multiple requests. This is a well-known issue with most IPD meta-analyses –

only a quarter of IPD meta-analysis succeed in obtaining IPD from all identified trials. [249] Considering the vast number of trials available, and the time constraints present in a PhD, I too could not collect IPD from all the eligible trials. To counter this, it is recommended to assess the proportion of trials from which IPD was obtained, [250] and combine the results of the non-IPD studies to the IPD meta-analysis as part of a sensitivity analysis, [251] both of which I have done in the subsequent chapters. However, it must be acknowledged that if time and resources are not a constraint, the best evidence can be generated by collecting the IPD from 100% of the eligible trials.

It should also be noted that the trials which contribute IPDs also vary in their intervention and their country of origin, which in turn reasonably shows that there is a possibility of heterogeneity in their definitions, populations, methods, and results. This needs to be investigated further by undertaking subgroup analysis to understand whether the effectiveness of the interventions vary according to the women's characteristics. The interventions should also be broken down to their core components and then assessed for their effectiveness. Differences can also be observed in terms of the study quality, which necessitates the need to exclude the trials with higher risk of bias from the evidence synthesis.

All these issues have been addressed in the next two chapters where I have described the IPD meta-analysis.

Chapter 4

4. Effect of lifestyle interventions on developing GDM

In this chapter, I have presented my work on the IPD meta-analysis to study the effect of lifestyle interventions (diet, physical activity, mixed) on gestational diabetes. I have described how the data were harmonised and merged from the IPDs obtained from the different trials. I have analysed the effects of each of the interventions individually, as well as combined together. The analysis was repeated for different definitions of GDM: trial authors' definition, GDM according to the NICE definition, IADPSG definition and modified IADPSG definition, as well as two continuous glucose outcomes: fasting glucose and 2-hour post-prandial glucose.

The reason behind using different outcome definitions is that different countries and international communities have developed their own diagnostic guidelines and thresholds. This is due to a lack of scientific consensus and uniformity in the methods used to diagnose GDM.[252,253] I wanted to explore whether the effect of the interventions varied according to the definitions used. Further, using different outcomes increases the accessibility of the results of the IPD meta-analysis: different countries can see how it affects GDM according to how they define it.

The GDM definitions have been provided below:

- Trial authors' definition: GDM as defined within the trial by established criteria.
- NICE definition: fasting glucose 5.6 mmol/L or above, or 2- hour glucose 7.8 mmol/L or above after a 75 g oral glucose tolerance test.
- IADPSG definition: fasting glucose 5.1 mmol/L or above, or 1- hour glucose 10.0 mmol/L or above, or 2- hour glucose 8.5 mmol/L or above after a 75 g oral glucose tolerance test.
- Modified IADPSG definition: fasting glucose 5.1 mmol/L or above, or 2- hour glucose 8.5 mmol/L or above after a 75 g oral glucose tolerance test.

The NICE definition was adopted in 2015 in the UK and uses a simpler criterion of two thresholds (fasting and 2-hour) and excludes the 1-hour glucose measurement. This makes it easier to implement in clinical practice, with lower costs and good application in resource limited settings. However, it might also cause it to miss mild cases of GDM due to the absence of the 1-hour measurement.

The IADPSG definition was adopted in 2010 and was based on the Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO) study.[254,255] It has been endorsed by many expert groups, including the WHO, in 2013,[256] making it a standard in many countries. It measures fasting, 1-hour, and 2-hour glucose levels, allowing more precise detection of glucose abnormalities. However, the low fasting threshold (≥ 5.1 mmol/L) may lead to more women being diagnosed with GDM. This in turn, along with the time and cost involved in the 3-point OGTT, increases in the costs and medicalisation of pregnancy, which are both causes for concern for healthcare managers and caregivers.[257,258] As evidence in support of this

definition in improving pregnancy outcomes is limited, further studies on clinical outcomes and cost-effectiveness analysis needs to be conducted.

The modified IADPSG definition was adopted by countries or organisations which found the IADPSG thresholds too sensitive or resource intensive. The modifications are not universal and vary depending on the local population and resource constraints. This makes this definition difficult to compare across populations. However, relaxing the strict guidelines reduces overdiagnosis while maintaining acceptable sensitivity and specificity. The modifications include adjusting the fasting plasma glucose threshold upward (e.g., from 5.1 mmol/L to 5.3 mmol/L) [259] or excluding the 1-hour glucose measurement.[78]

Towards the later sections of this chapter, I have described the results of the IPD meta-analyses and the additional sensitivity analyses.

4.1. Methods

The general methods used in this chapter have been explained in section 2.1.2. Some additional points of interest related to the analysis has been given below.

4.1.1. iWIP Database

Anonymised IPD from individual trials, along with any available data dictionaries, were accepted in any format (to minimise the amount of work for trial authors). The data formats

included Stata, SAS, SPSS, Microsoft Excel or any other text formats. All original datasets for the iWIP project were uploaded and stored using the CREP web server. CREP had hosted the database for the previous i-WIP project.[260] This existing i-WIP database was expanded to include new variables like OGTT values, maternal and neonatal complications, which were not in the scope of the previous study. All variable definitions were kept same as previously described [261] and the definitions for the new variables has been provided in Appendix 9.

4.1.2. Data Quality

On receiving the data from each trial, I performed an initial check to ensure sufficient data quality. I assessed whether metrics such as the number of patients, and the descriptive statistics of numeric and categorical variables reported in the publication matched those in the dataset. I also performed additional data checks, such as, numerical range, logical and consistency checks. Any discrepancies were resolved by contacting the authors. Each raw dataset was saved in its original format and then converted to a common format (two-dimensional spreadsheet format with one subject per row and variables listed in columns).

I did not re-analyse the individual datasets, as shared by the trial authors, to compare with their published results, at this stage. This was because even if all the trials had collected data on the outcome variables which I was interested in, some of them did not publish their analysis, or had not adjusted for the same covariates. However, each study was reanalysed as part of the two stage IPD meta-analysis and the effect estimates have been provided in Appendix 10, Appendix 11, Appendix 12, and Appendix 13.

4.1.3. Data harmonisation and database freeze

Datasets were included in the IPD meta-analysis, only if the trials shared their data before end of August 2021. I mapped and merged all the IPDs into to a single dataset, ready for analysis. All data manipulations and harmonisation were completed by August 2022, after which the database was frozen for analysis. If during the analysis any unforeseen queries were generated, they were dealt with on a case-by-case basis.

4.1.4. Statistical Analysis

Analysis population

I analysed all participants based on the group they were allocated to. For trials with two intervention arms, the average effect of these two interventions was used in subsequent meta-analyses for the more complex intervention type.

Methods for missing data

I started with summarising the participant-level variables and outcome data to check the extent of missingness. Participants with missing outcome data were excluded from that specific analysis. It was found that there was no systematic difference in the number of missing outcomes per group. Missing variables were filled using mean imputation for continuous variables. For categorical variables, the missing indicator method was employed. If a specific outcome variable did not occur in both arms of the trial (double zero trials), those trials were

dropped entirely from the study.[93] For all other trials, Firth's continuity correction [262] was added to the logistic regression. This was done to account for trials with small number of outcomes, which can sometimes lead to unreliable parameter estimates and inflated standard errors.

Method for handling clustering of participants within trials in the meta-analysis

In the two-stage meta-analysis, the clustering of participants within trials was automatically addressed by analysing each trial separately in the first stage. For these cluster randomised trials, I included a random effect for the unit of randomization to adjust for clustering. In the one-stage meta-analysis, clustering of participants within trials was accounted for by including a separate intercept term per trial.

Analysis Software:

All analysis was carried out using Stata 18 and R 4.0.2. All the libraries and their versions have been listed in Appendix 14.

Descriptive Statistics

I compared the baseline characteristics of the women in the control and the intervention arm in the merged dataset to see whether they were well-balanced in all measurable aspects. I also presented the number of women and trials contributing to each of the several maternal and neonatal complications.

Primary Analysis

I used both one and two stage IPD meta-analysis to get the summary estimate of each intervention (all interventions combined, diet-based, physical activity-based, and mixed approach) on each GDM definition of interest. I adjusted for two prognostic factors: age and baseline BMI.

Sensitivity analyses

I carried out some additional sensitivity analyses to see whether they altered the main IPD results. They have been listed below:

1. Combined IPD with the aggregate data extracted from trials which did not share their IPD.
2. Restricted IPD to only the trials with a low risk of bias.
3. Examined the presence of small study effects by creating contour enhanced funnel plots for different subgroups of the IPD, such as:
    - IPD only
    - IPD and aggregate data from non-IPD trials
    - IPD with low risk of bias

4.2. Results

4.2.1. Characteristics of participants in IPD trials

Table 4.1 shows a detailed comparison of the baseline characteristics of the control and intervention arms of the IPD. The characteristics of the women in both the arms were very similar, indicating a balanced population. The average age of the women was approximately 29.5 years in both the arms, and most women (>80%) were Caucasian White. Most of the women had a high level of education and were not current smokers. They were mostly nulliparous and around 10% had had a previous diagnosis of GDM, 2.25% had hypertension at baseline and 1.65% had pregnancy induced hypertension. The number of trials and women contributing to each variable has also been listed. 1 trial (Willcox 2017)[263] did not report age, and therefore it was analysed separately by only adjusting for baseline BMI.

Table 4.1: Baseline characteristics of participants in trials that contributed to the IPD meta-analysis.

Baseline characteristics	Number of trials	Number of women	Study arm, number of women, mean (SD) or %	
			Control	Intervention
Age	53	23,602	11,112	12,490
			29.6 (6.02)	29.4 (5.99)
BMI	54	23,693	11,158	12,535
			28.0 (6.21)	27.9 (6.17)
Race Ethnicity	35	12,645	6185	6460
Caucasian			4,993 (80.7%)	5,292 (81.9%)
Asian			497 (8.0%)	488 (7.6%)
Black			407 (6.6%)	398 (6.2%)
Central/South American			87 (1.4%)	77 (1.2%)
Middle East			79 (1.3%)	75 (1.2%)
Other			122 (2.0%)	130 (2.0%)
Educational status of the mother	35	11,715	5,669	6,046
Low			1,108 (19.5%)	997 (16.5%)
Middle			1,880 (33.2%)	1,971 (32.7%)
High			2,681 (47.3%)	3,071 (50.8%)
Current smoker	44	18,325	8,763	9,562
Yes			842 (9.6%)	851 (8.9%)
Ex-smoker (pre-pregnancy)	24	9,969	4,622	5,347

Yes			1494 (32.3%)	1,624 (30.4%)
Parity	45	21,556	10,033	11,523
0			4,929 (49.1%)	5,834 (50.6%)
1			3,317 (33.1%)	3,703 (32.1%)
2			1,180 (11.8%)	1,328 (11.5%)
3			376 (3.7%)	429 (3.7%)
4			231 (2.3%)	229 (2.0%)
Previous GDM	19	5798	2,925	2,873
Yes			289 (9.9%)	287 (10.0%)
Baseline Hypertension	21	5,650	2,432	3,218
Yes			50 (2.1%)	76 (2.4%)
Pregnancy Induced Hypertension	18	4,549	2,215	2,334
Yes			34 (1.5%)	43 (1.8%)

Table 4.2 gives the details of all the outcome variables for all pregnant women and for women with GDM. All 54 trials (23,361 women) contributed to GDM as defined by any established criteria (trial authors' definition). 22 trials contributed to GDM as defined by NICE (11,990 women), IADPSG (6,174 women) and modified IADPSG (13,186 women). The number of trials sharing their continuous glucose measurements differed according to the timepoint: 16 trials shared their fasting and 2 hours continuous glucose measures, without specifying when it was collected; 12 trials collected the continuous glucose measures at less than 24 weeks; 17 trials shared their fasting OGTT and 19 trials shared their 2 hours post prandial OGTT at 24-30 weeks; 8 trials shared their fasting OGTT and 7 trials shared their 2 hours post prandial OGTT at greater than 30 weeks. Amongst women with GDM, the most common outcomes available were caesarean section (2,706 women, 50 trials) and preterm birth (2,457 women, 45 trials).

Table 4.2: Details of outcome measures for all pregnant women and in women with GDM reported in eligible trials that contributed to the IPD

Outcomes reported in trials	*Number of trials*	*Total number of women*	*Number of outcomes(GDM)*
GDM trial authors' definition	54	23,361	2,861
GDM NICE definition	22	11,990	2,013
GDM IADPSG definition	16	6,174	1,758
GDM modified IADPSG definition	24	13,186	2,090
Fasting OGTT	16	10,174	1,724
2 hours post prandial OGTT	16	10,678	1,674
Fasting OGTT at <24 weeks	12	1,810	281
2 hours post prandial OGTT at <24 weeks	12	2,036	280
Fasting OGTT at 24-30 weeks	17	5,647	991
2 hours post prandial OGTT at 24-30 weeks	19	6,037	1,009
Fasting OGTT at >30 weeks	8	1,205	86
2 hours post prandial OGTT at >30 weeks	7	1,134	71
Hypertensive disease	41	17,921	2,087
Preterm delivery	45	20,764	2,457
Caesarean section	50	22,448	2,706
SGA	43	17,509	2,055
LGA	42	17,275	2,038
Stillbirth	30	10,512	1,356
NICU admission	35	13,487	1,653

4.2.2. Findings of IPD meta-analysis

Table 4.3 and the forest plot in Figure 4.1 shows the effect of the lifestyle interventions on GDM according to the definition used by the trial author. 23,361 women from 54 trials contributed their data towards this outcome. Overall, the interventions reduced the odds of developing GDM by 10% on average (OR= 0.90; 95% CI= 0.8, 1.02). When taken individually, physical activity has the most impact – reducing the odds of GDM by 36% on average (OR= 0.64; 95% CI= 0.48, 0.85), followed by diet, which reduced the odds of GDM by 19% on average

(OR= 0.81; 95% CI= 0.69, 0.96). Mixed interventions showed a 5% increase in the odds of developing GDM on average (OR= 1.05; 95% CI= 0.91, 1.21). The 95% CIs for overall and mixed approach encompassed the null value of one, suggesting the possibility that the interventions might not have any effect on the odds of developing GDM. The effect of diet interventions appeared statistically significant with a 95% prediction interval ranging from OR 0.68 to 0.97.

Table 4.3: Effect of lifestyle interventions on GDM (trial authors' definition)

Intervention	**Number of trials**	**Number of women**	**OR (95% CI)**	**95% PI**	**I^2(%)**	**τ^2 (95% CI)**
Overall	54	23,361	0.90 (0.8, 1.02)	0.59, 1.38	24.5	0.04 (0.01, 1.3)
Diet	8	2,974	0.81 (0.69, 0.96)	0.68, 0.97	0	0 (0, 0.17)
Physical activity	18	4,435	0.64 (0.48, 0.85)	0.39, 1.05	0	0.04 (0, 0.43)
Mixed approach	28	15,952	1.05 (0.91, 1.21)	0.79, 1.40	21.3	0.02 (0, 0.12)

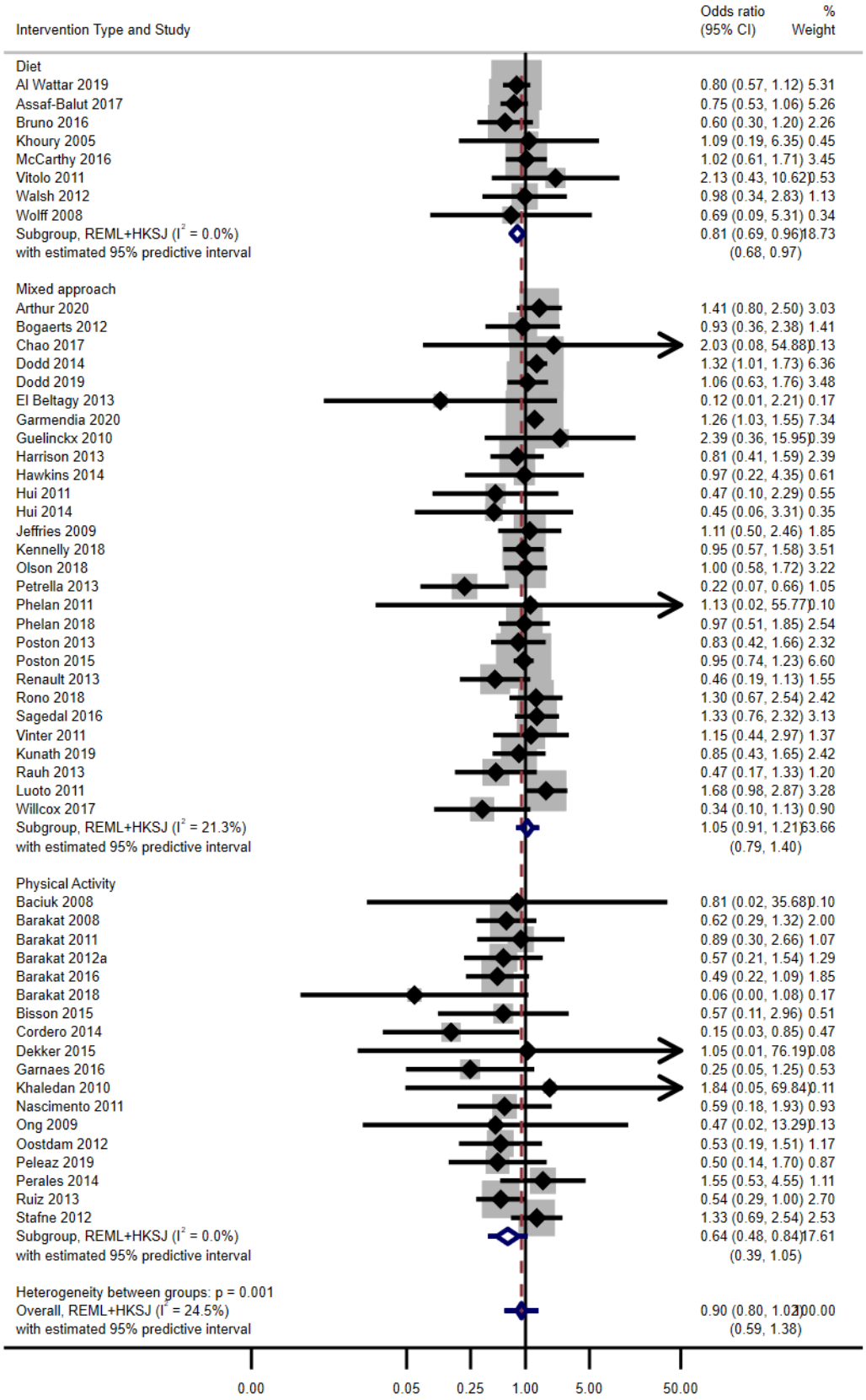


Figure 4.1: Forest plot showing the effect of lifestyle interventions on GDM (trial authors' definition)

Table 4.4 and the forest plot in Figure 4.2 shows the effect of the lifestyle interventions on GDM according to the NICE definition. The effect estimate for the overall interventions was based on 22 trials and reduced the odds of developing GDM by 2% on average (OR= 0.98; 95% CI= 0.84, 1.13). The 95% prediction interval suggested that in a new patient, belonging to a population similar to those in the trials analysed, the potential effect could vary from a 30% decrease to a 36% increase in the odds of developing GDM. Diet and physical activity had similar effects in reducing the odds of GDM ((OR= 0.7; 95% CI= 0.33, 1.49) and (OR= 0.65; 95% CI= 0.18, 2.31) respectively. Mixed interventions increased the odds of developing GDM by 10% on average (OR= 1.10; 95% CI= 0.98, 1.23). All the 95% CIs contained the value of one, indicating the possibility that the interventions might not influence the odds of developing GDM. The prediction intervals for diet and physical activity interventions were notably broad due to a smaller number of trials contributing to the meta-analyses.

Table 4.4: Effect of lifestyle interventions on GDM (NICE definition)

Intervention	**Number of trials**	**Number of women**	**OR (95% CI)**	**95% PI**	**I^2(%)**	**τ^2 (95% CI)**
Overall	22	11,990	0.98 (0.84, 1.13)	0.7, 1.36	18	0.02 (0, 0.13)
Diet	3	1,812	0.7 (0.33, 1.49)	0.08, 6.47	39	0 (0, 2.8)
Physical activity	5	977	0.65 (0.18, 2.31)	0.04, 11.49	27.8	0.6 (0, 8.8)
Mixed approach	14	9,201	1.1 (0.98, 1.23)	0.99,1.24	0	0 (0, 0.06)

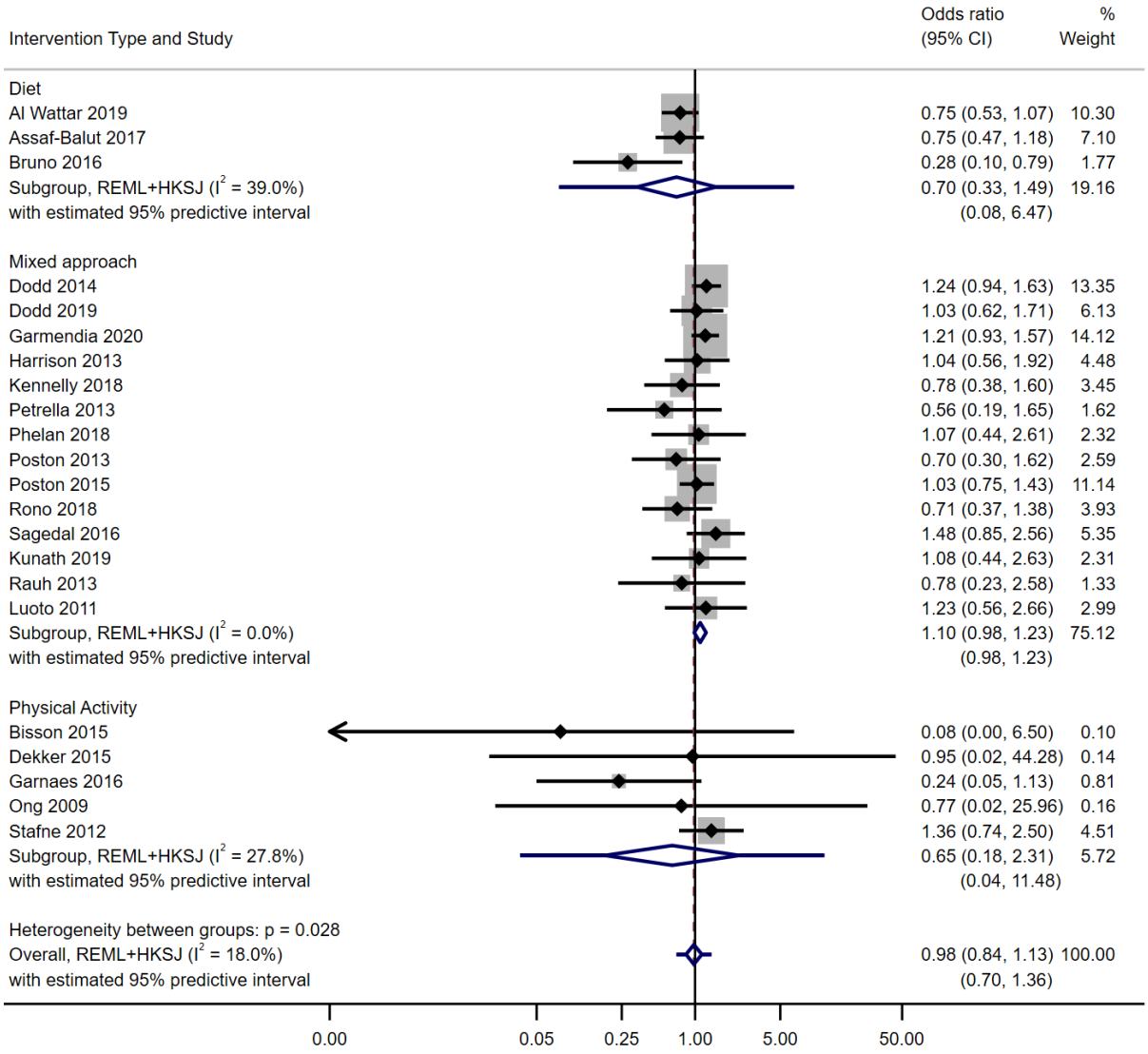


Figure 4.2: Forest plot showing the effect of lifestyle interventions on GDM (NICE definition)

and the forest plot in Figure 4.3 shows the effect of the lifestyle interventions on GDM according to the IADPSG definition. Overall, the interventions lowered the odds of developing GDM by 14% on average (OR= 0.86; 95% CI= 0.75, 0.97). This was based on IPD from 16 trials. The level of heterogeneity was very low, and the resulting 95% prediction interval suggested that the potential positive effect in a new patient (from a comparable population to those in the trials analysed) could vary from a 3% to a 25% reduction in the odds of developing GDM.

Taken individually, diet and physical activity on average showed a decrease in the odds of developing GDM by 29% and 8% on average ((OR= 0.71; 95% CI= 0.06, 7.88) and (OR= 0.92; 95%, CI= 0.28, 3.08) respectively). However, for mixed interventions, there was a smaller reduction in the odds of GDM by 11% on average (OR= 0.89, 95% CI= 0.77, 1.02). In all cases there is a possibility that the interventions do not have any effect on the odds of developing GDM, as all their confidence intervals overlapped with the null value of one. Prediction intervals were not generated for diet, as there were less than 3 studies contributing to the meta-analysis. The prediction interval for physical activity was also notably wide, as it had only had 3 trials.

Table 4.5: Effect of lifestyle interventions on GDM (IADPSG definition)

Intervention	**Number of trials**	**Number of women**	**OR (95% CI)**	**95% PI**	**I^2(%)**	**τ^2 (95% CI)**
Overall	16	6,174	0.86 (0.75, 0.97)	0.75, 0.97	0	0 (0, 0.07)
Diet	2	895	0.71 (0.06, 7.88)	undefined	0	0 (0, 14.9)
Physical activity	3	55	0.92 (0.28, 3.08)	0.03,32.47	0	0 (0, 13.85)
Mixed approach	11	5,224	0.89 (0.76, 1.03)	0.76,1.04	0	0 (0, 0.08)

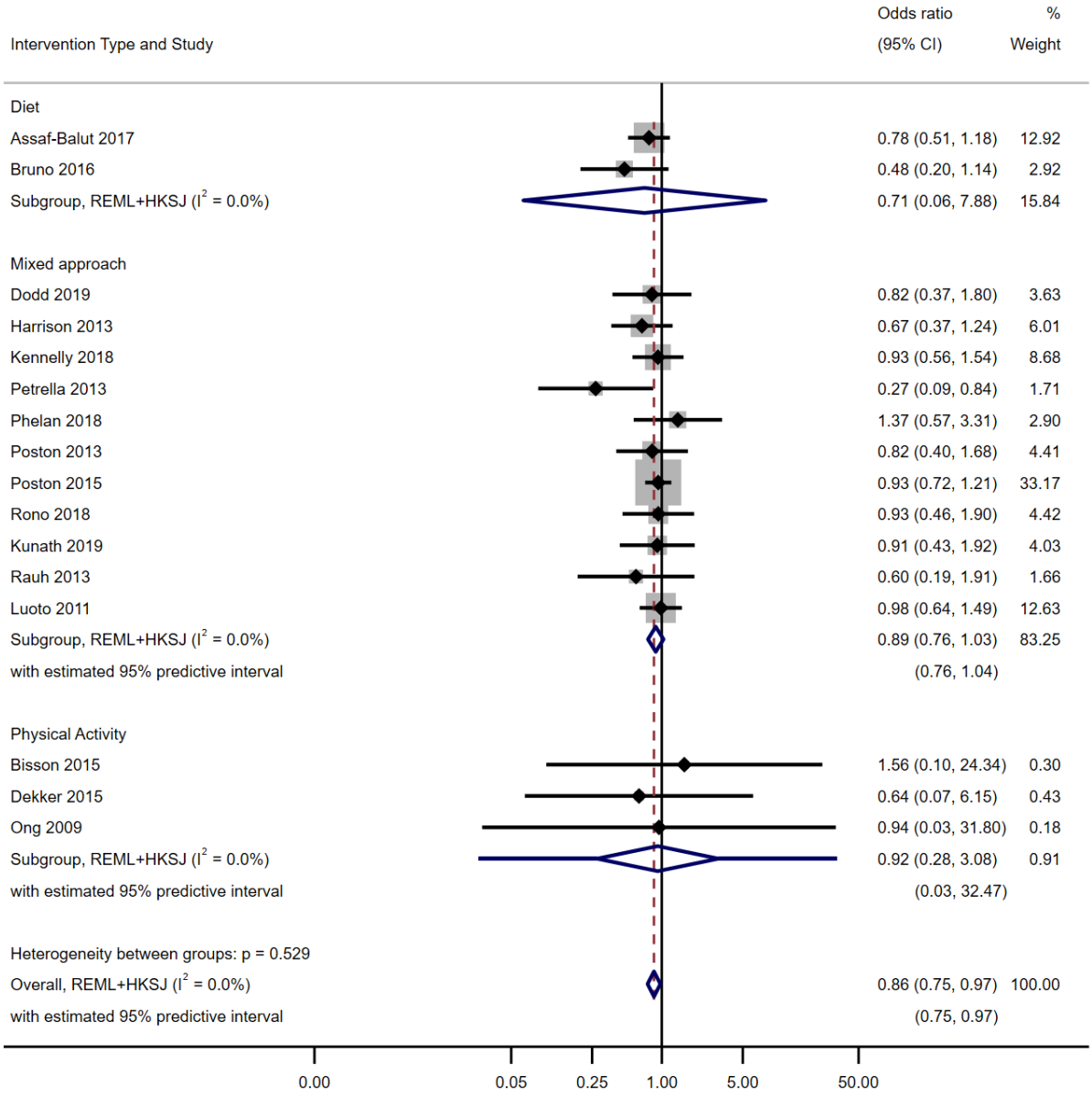


Figure 4.3: Forest plot showing the effect of lifestyle interventions on GDM (IADPSG definition)

Table 4.6 and the forest plot in Figure 4.4 shows the effect of the lifestyle interventions on GDM according to the modified IADPSG definition. The meta-analysis for the overall intervention was based on 24 trials and showed, on average, an 8% decrease in the odds of developing GDM (OR= 0.92, 95% CI= 0.78, 1.1). The 95% prediction interval suggested that the potential impact on a new patient (from a similar population to those in the trials analysed)

could vary widely, ranging from a 48% reduction to a 64% increase in the odds of developing GDM. This indicates significant uncertainty in the findings, partly due to notable heterogeneity among the included trials, with an estimated τ^2=0.07 and I^2 =51.4%.

Taken individually, the effects of the three interventions varied: while both diet and physical activity interventions showed a reduction in the odds of developing GDM on average ((OR= 0.64, 95% CI= 0.32, 1.3) and (OR= 0.88, 95% CI= 0.7, 1.09) respectively), mixed interventions showed an increase in the odds of developing GDM on average by 8% (OR= 1.08, 95% CI= 0.89, 1.31). However, all 95% confidence intervals overlapped with the null value of one, suggesting the potential for the interventions to have no effect on the odds of developing GDM. Prediction intervals were notably wide for diet interventions, which only had 3 trials contributing to the meta-analysis.

Table 4.6: Effect of lifestyle interventions on GDM (modified IADPSG definition)

Intervention	**Number of trials**	**Number of women**	**OR (95% CI)**	**95% PI**	**I^2(%)**	**τ^2 (95% CI)**
Overall	24	13,186	0.92 (0.78, 1.1)	0.52, 1.64	51.4	0.07 (0.02, 0.23)
Diet	3	1,891	0.64 (0.32, 1.3)	0.08, 5.11	48.9	0 (0, 2.78)
Physical activity	7	1,940	0.88 (0.7, 1.09)	0.7, 1.1	0	0 (0, 0.53)
Mixed approach	14	9,355	1.08 (0.89, 1.31)	0.68, 1.72	38.9	0.04 (0, 0.21)

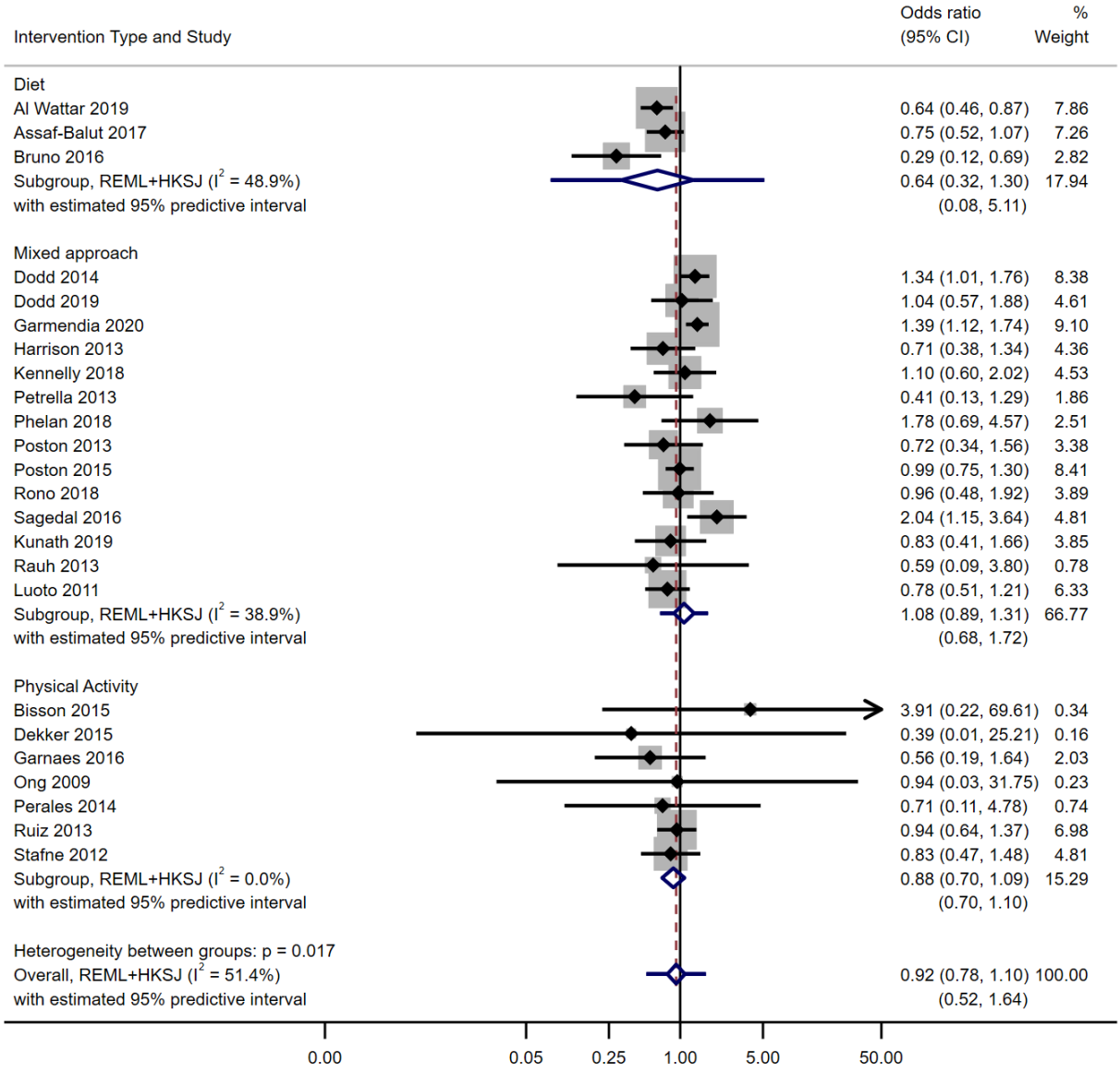


Figure 4.4: Forest plot showing the effect of lifestyle interventions on GDM (modified IADPSG definition)

Table 4.7 and the forest plot in Figure 4.5 to Figure 4.10 shows the effect of the lifestyle interventions on GDM as defined by the continuous glucose measure. 26 trials contributed their IPD for fasting and 2-hour post-prandial glucose levels at gestational ages less than 24 weeks. Overall, the intervention reduced fasting glucose levels by an average of 0.0047 mmol/L (MD= -0.0047, 95% CI= -0.04, 0.03). The 95% prediction interval suggested that the

potential effect in a new patient (from a similar population to those in the trials analysed) could vary from a reduction of 0.04 mmol/L to an increase of 0.03 mmol/L in fasting glucose levels. At two hours, the effect was slightly increased (MD= -0.01, 95% CI= -0.08, 0.06), although both the 95% CI and PI continued to overlap with the null value of zero, indicating that the intervention potentially had no effect on glucose levels at this time point.

The fasting and 2-hour post-prandial glucose levels was also analysed at other timepoints: such as, in women with gestational age between from 24 to 30 weeks and in women with gestational age exceeding 30 weeks. For women with gestational age 24 to 30 weeks, there was a reduction in the 2-hour glucose levels by an average of 0.07 mmol/L (MD= -0.07, 95% CI= -0.12, -0.01). For all other groups, the summary effect estimates remained minimal and statistically insignificant (at the 5% significance level). Statistical heterogeneity was minimal in all analyses, with a maximum average between-study variance of 0.01.

Table 4.7: Effect of lifestyle interventions on GDM (continuous glucose levels)

Time	Gestational age	Number of trials	Number of women	MD	95% PI	I^2(%)	τ^2 (95% CI)
0hr	<24wks	26	16,622	-0.004 (-0.04, 0.03)	-0.04, 0.03	0	0.00 (0.00, 0.01)
2hr	<24wks	26	17,558	-0.01 (-0.08, 0.06)	-0.23, 0.21	46.3	0.01 (0, 0.04)
0hr	24-30wks	16	8,225	-0.01 (-0.05, 0.02)	-0.05, 0.02	0	0.00 (0.00, 0.00)
2hr	24-30wks	18	8,749	-0.07 (-0.12, -0.01)	-0.20, 0.07	0	0.00 (0.00, 0.02)
0hr	>30wks	8	4,437	-0.01 (-0.05, 0.03)	-0.05, 0.03	0	0.00 (0.00, 0.04)
2hr	>30wks	7	4,282	-0.03 (-0.22, 0.16)	-0.38, 0.33	13	0.01 (0.00, 0.27)

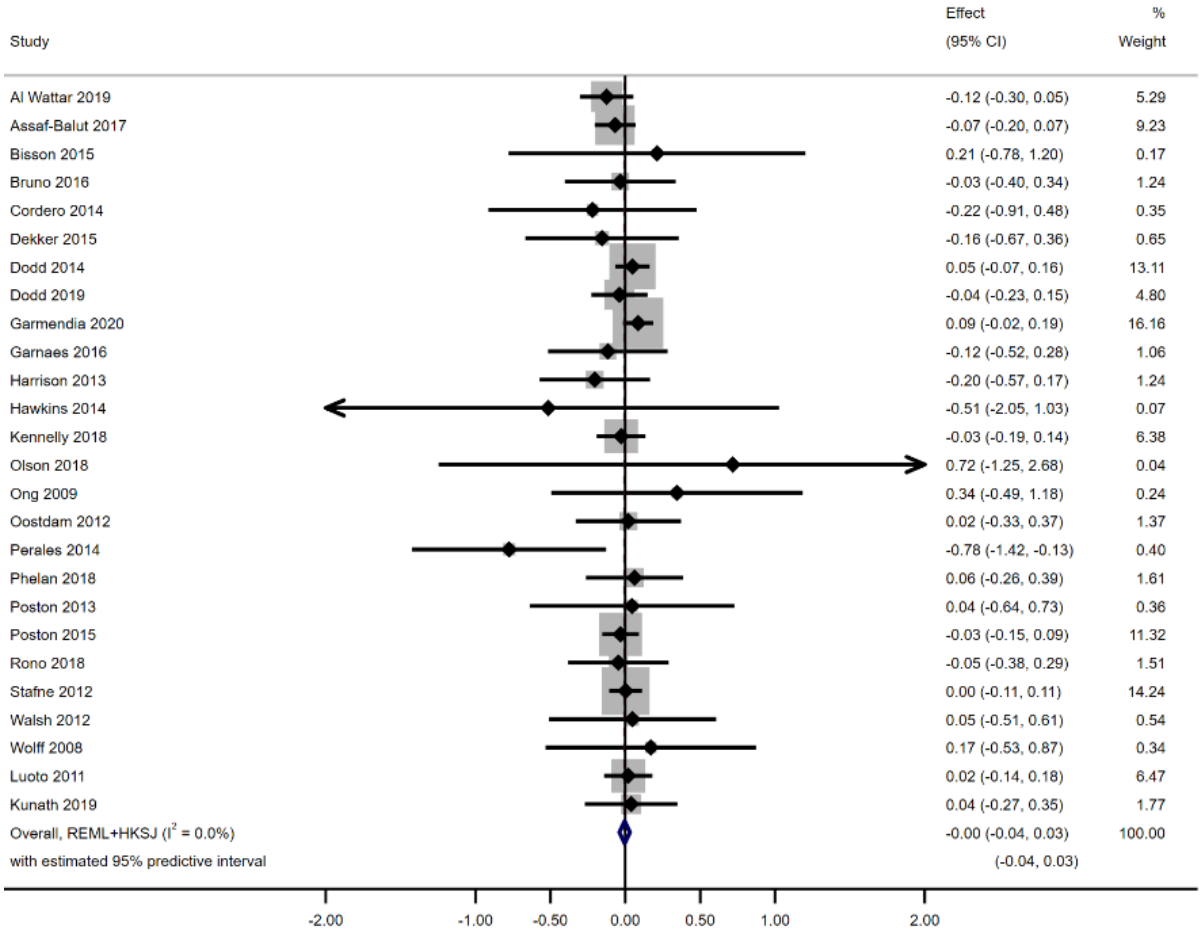


Figure 4.5: Forest plot showing the effect of lifestyle interventions on GDM (continuous 0-hour glucose levels) taken at less than 24 weeks

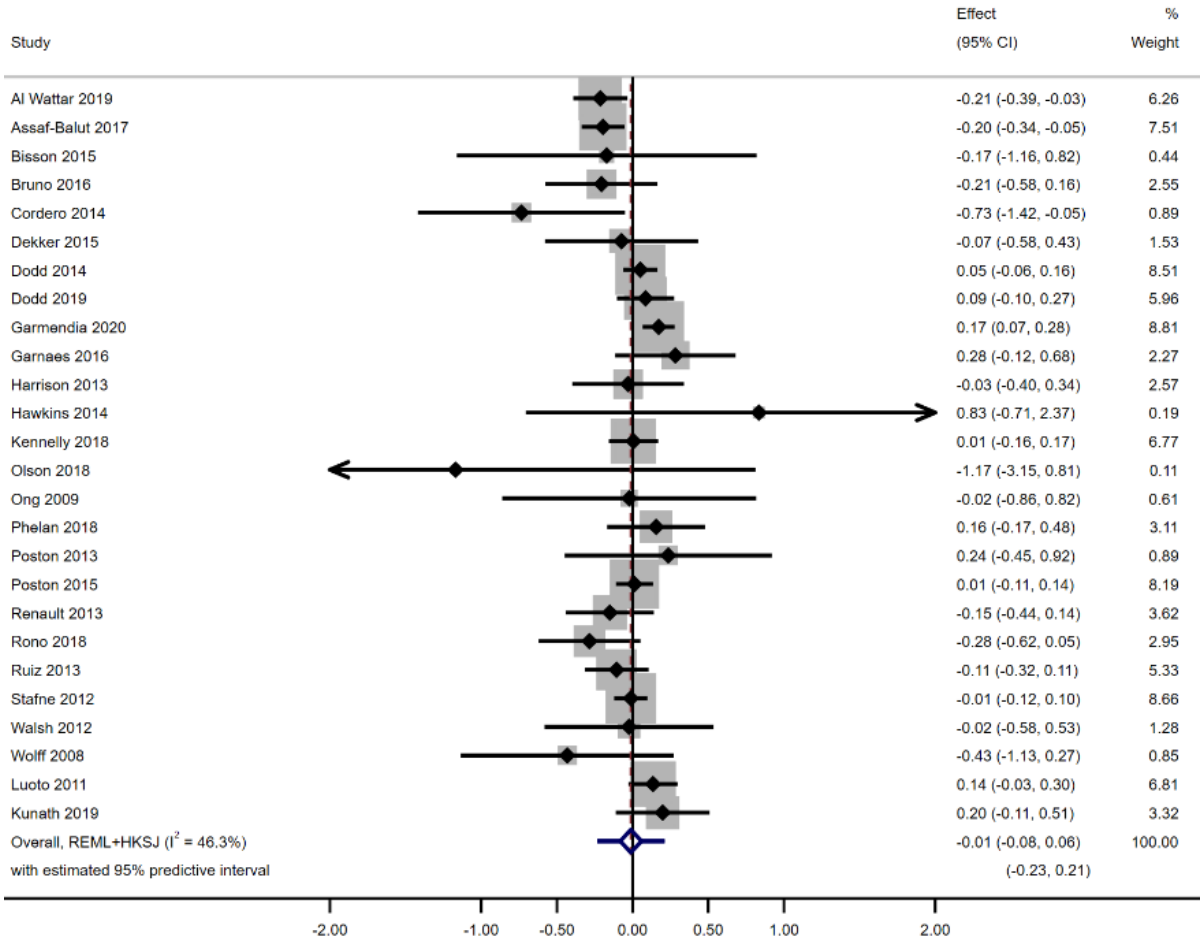


Figure 4.6 : Forest plot showing the effect of lifestyle interventions on GDM (continuous 2 hours glucose levels) taken at less than 24 weeks

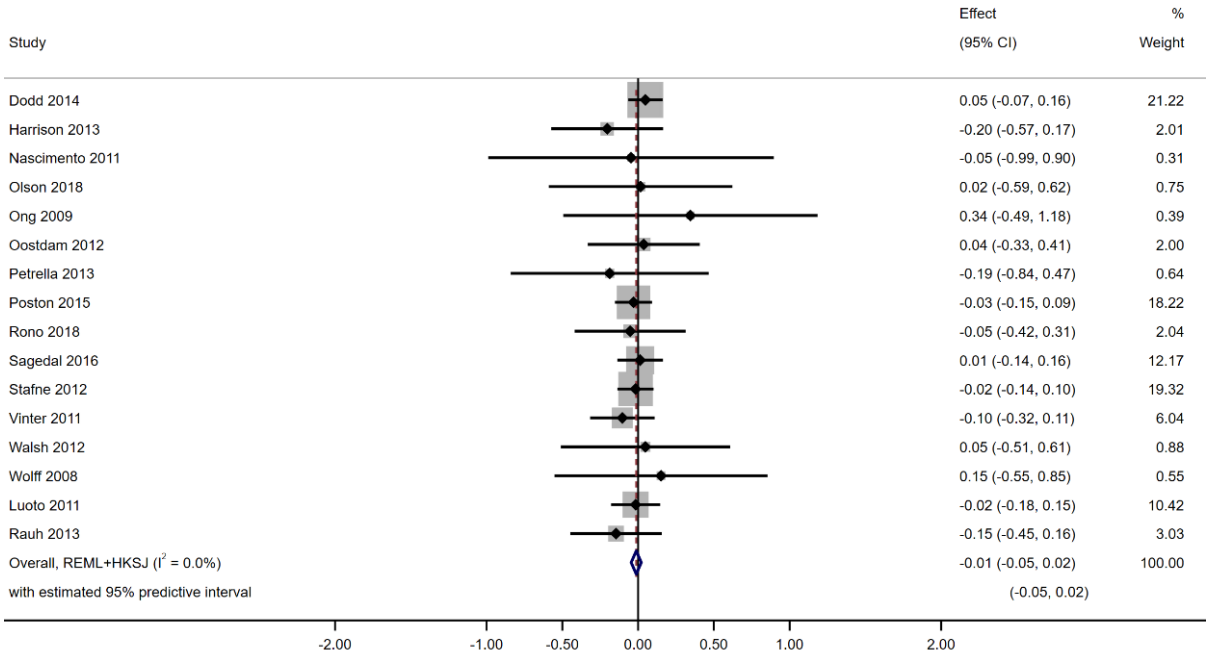


Figure 4.7: Forest plot showing the effect of lifestyle interventions on GDM (continuous 0-hour glucose levels) taken between 24-30 weeks

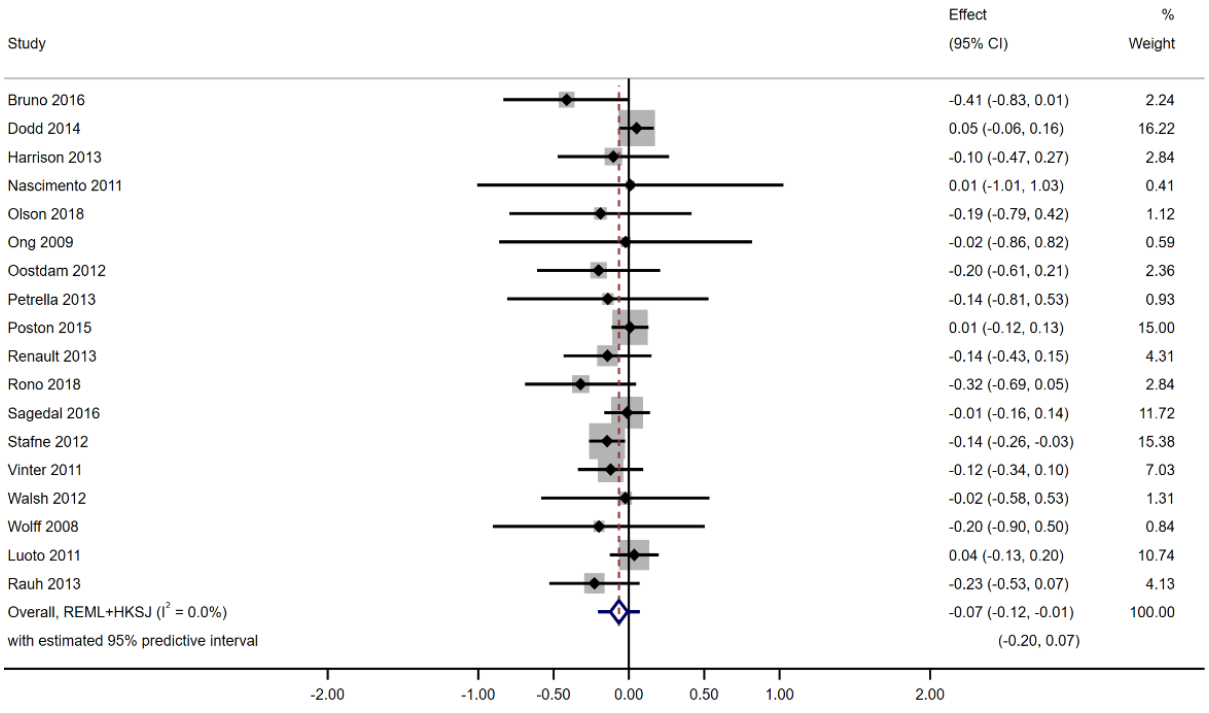


Figure 4.8: Forest plot showing the effect of lifestyle interventions on GDM (continuous 2 hours glucose levels) taken between 24-30 weeks

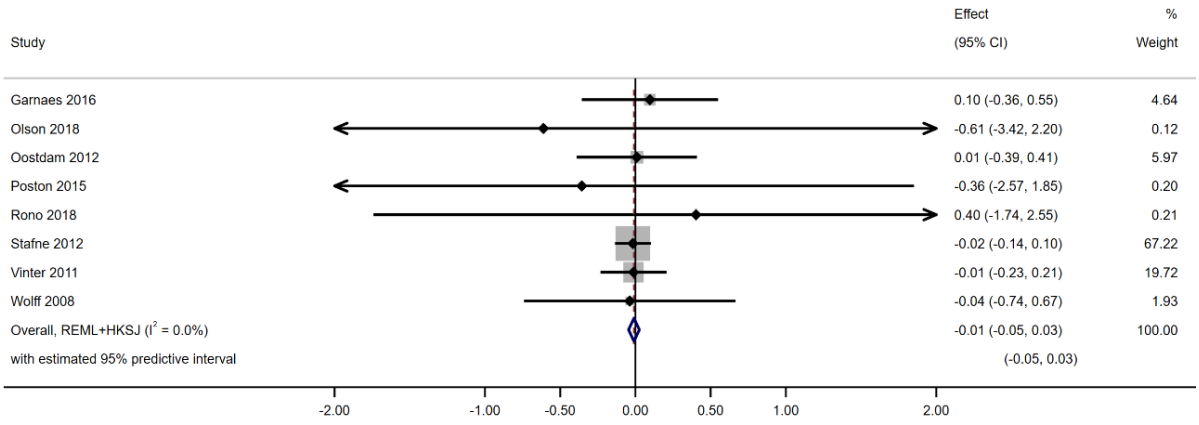


Figure 4.9: Forest plot showing the effect of lifestyle interventions on GDM (continuous 0-hour glucose levels) taken after 30 weeks

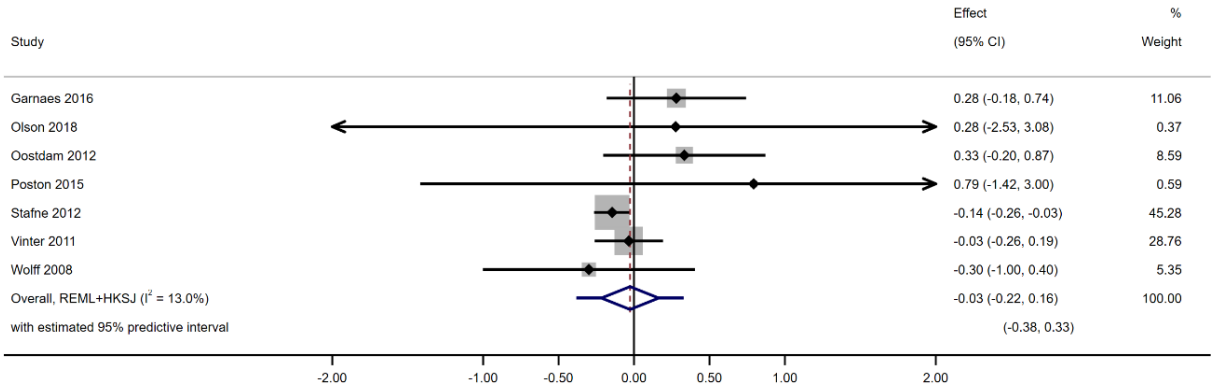


Figure 4.10 : Forest plot showing the effect of lifestyle interventions on GDM (continuous 2 hours glucose levels) taken after 30 weeks

4.2.3. Sensitivity analysis

4.2.3.1.Adding non-IPD trials to IPD meta-analysis

When the aggregate data from trials which did not share their IPD were added to the IPD meta-analysis, the lifestyle interventions reduced the odds of developing GDM (trial authors' definition) by 20% (OR= 0.80, 95% CI= 0.73, 0.88) on average (*Table 4.8*). However, the

prediction interval was very broad, indicating that a new patient (from a similar population to the trials included in the meta-analysis) could experience a 54% decrease to a 38% increase in the odds of developing GDM. This indicated a significant uncertainty in the result, in part because of the heterogeneity between the included trials, with an estimated τ^2=0.07 and I^2=33.6%.

Physical activity showed a statistically significant intervention effect estimates (OR= 0.64, 95% CI= 0.53, 0.76) when IPD and non-IPD trials were combined. The estimated PI also indicated a potential benefit to a new patient (from a similar population to the trials included in the meta-analysis), as it was entirely below one. Diet and mixed approach both showed a reduction in the odds of developing GDM ((OR= 0.79, 95% CI= 0.62, 1) and (OR= 0.92, 95% CI= 0.82, 1.04) respectively) but both their PI encompassed the null value of 1.

Out of the 47 non-IPD trials, 11 trials used the IADPSG definition for GDM. Adding the aggregate data from these trials to the IPD meta-analysis showed a 17% reduction in GDM (OR= 0.83, 95% CI= 0.73, 0.94), a 3% increase in effect compared with the IPD only analysis (). Mixed approach showed a statistically significant result (OR= 0.84, 95% CI= 0.72, 0.98) when both IPD and non-IPD trials were combined. The 95% prediction interval (0.71, 0.98) was also below the null value, suggesting a potential benefit in a new patient (from a similar population to the trials included in the meta-analysis). However, even though diet and physical activity indicated a reduction in the odds of developing GDM, the CI and PI still encompassed the null value of one and thus was not statistically significant and had the potential to have no effect (*Table 4.8*).

Among the 46 non-IPD trials, 1 trial 264 used the NICE definition and 1 trial 265 used the modified IADPSG definition. Adding the aggregate data from these trials did not change the results much from the main results, with only the IPD trials (

Table 4.4 and Table 4.6). The forest plots for each analysis have been presented in Appendix 15.

Table 4.8: Effect of lifestyle interventions on developing GDM (IPD + aggregate data)

Intervention	Number of trials	Number of women	OR (95% CI)	95% PI	I^2(%)	τ^2 (95% CI)
GDM (trial authors' definition)						
Overall	102*	34,932	0.80 (0.73, 0.88)	0.46, 1.38	33.6	0.07 (0.03, 0.15)
Diet	17	5,058	0.79 (0.62, 1)	0.44, 1.41	41.2	0.06 (0, 0.37)
Physical activity	36	9,683	0.64 (0.53, 0.76)	0.42, 0.97	4.2	0.3 (0, 0.23)
Mixed approach	49	20,191	0.92 (0.82, 1.04)	0.59, 1.43	23.4	0.04 (0, 0.14)
GDM (NICE definition)						
Overall	23	12,041	0.98 (0.85, 1.14)	0.71, 1.33	17.9	0.017(0, 0.12)
Diet	4	1,863	0.72 (0.41, 1.27)	0.33, 1.55	42.7	0 (0,2.68)
Physical activity	5	977	0.65 (0.18, 2.31)	0.04, 11.48	27.8	0.6 (0, 8.8)
Mixed approach	14	9,201	1.1 (0.98, 1.23)	0.98, 1.23	0	0.0 (0, 0.06)
GDM (IADPSG definition)						
Overall	27	8,465	0.83 (0.73, 0.94)	0.65, 1.05	0	0.01 (0, 0.1)
Diet	6	2,228	0.83 (0.53, 1.29)	0.32,2.16	56.1	0.09 (0, 0.78)
Physical activity	5	420	0.93 (0.69, 1.25)	0.66, 1.31	0	0 (0, 1.44)
Mixed approach	16	5,817	0.84 (0.72, 0.98)	0.71,0.98	0	0 (0, 0.12)
GDM (modified IADPSG definition)						
Overall	25	13,453	0.93 (0.79, 1.09)	0.53, 1.62	49.3	0.07 (0.02, 0.21)
Diet	3	1,891	0.64 (0.32, 1.3)	0.08, 5.11	48.9	0 (0, 2.78)
Physical activity	7	1,940	0.88 (0.7, 1.09)	0.7, 1.1	0	0 (0, 0.53)
Mixed approach	15	9,622	1.07 (0.89, 1.29)	0.69, 1.67	35	0.03 (0, 0.19)

*Total number of studies is not 100 as in this case it includes one study three times (Simmons 2016) corresponding to three intervention arms: diet, physical activity and mixed

4.2.3.2.Restricting IPD meta-analysis to only trials with a low risk of bias

After excluding IPD trials with a high risk of bias, there were 33 trials eligible for synthesis (previously 54). The results of the meta-analysis have been shown in . Here the outcome GDM was defined by the trial authors' definition. The overall summary effect remained comparable to the main analysis, showing a slight decrease in the odds of developing GDM by 6% on average (OR= 0.94, 95% CI= 0.82, 1.08). These findings suggest that evidence derived from this subgroup of trials aligns with the larger set of trials, including those considered to have high risk of bias.

When trials with a high risk of bias were excluded, the summary effect for diet interventions remained consistent with the main analysis with only a slight decrease in effect estimate (OR= 0.89, 95% CI= 0.69, 1.16), but with increased uncertainty, reflected in a wider 95% CI and PI, now encompassing the null value. For physical activity, the summary effect after removing trials with a high risk of bias yielded an OR of 0.59 (95% CI= 0.43, 0.82), indicating an increased effect compared to the summary result using all available trials. Heterogeneity was reduced in this subset for physical activity, with τ^2 estimated as zero. Notably, the 95% PI was estimated as (0.43, 0.82), indicating potential benefit in a new patient, consistent with the findings when combining IPD and aggregate data as discussed earlier. In the case of mixed interventions, the subset of low/medium risk of bias IPD trials showed reduced heterogeneity (τ^2= 0, 95% CI= 0, 0.09), and a 95% PI of (1.01, 1.29), indicating a shift towards a potentially negative effect. The forest plots for each analysis have been presented in Appendix 16.

Table 4.9: Effect of lifestyle interventions on GDM (trial authors' definition) (low risk of bias IPD trials)

Intervention	Number of trials	Number of women	OR (95% CI)	95% PI	I^2(%)	τ^2 (95% CI)
All	33	15,547	0.94 (0.82, 1.08)	0.64, 1.39	15	0.03 (0, 0.13)
Diet	5	1,930	0.89 (0.69, 1.16)	0.66, 1.21	0	0 (0, 0.56)
Physical activity	11	2,993	0.59 (0.43, 0.82)	0.43, 0.82	0	0 (0, 0.44)
Mixed	17	10,624	1.14 (1.01, 1.29)	1.01, 1.29	0	0 (0, 0.09)

4.2.3.3.Publication bias

The contour-enhanced funnel plots depicted in Figure 4.11, Figure 4.12, and Figure 4.13 were used to investigate the presence of small study effects. Figure 4.11 for GDM as defined by trial authors showed no evidence of asymmetry, suggesting that smaller trials likely had similar intervention effects compared to larger ones. This lack of asymmetry was noted even with the addition of aggregate data from non-IPD trials to the IPD meta-analysis (Figure 4.12) and with the exclusion of trials with a high risk of bias (Figure 4.13). Thus, it was reasonable to conclude that there was no evidence which suggested the presence of publication bias. Similar results can be observed for other definitions of GDM and the corresponding funnel plots can be seen in Appendix 17.

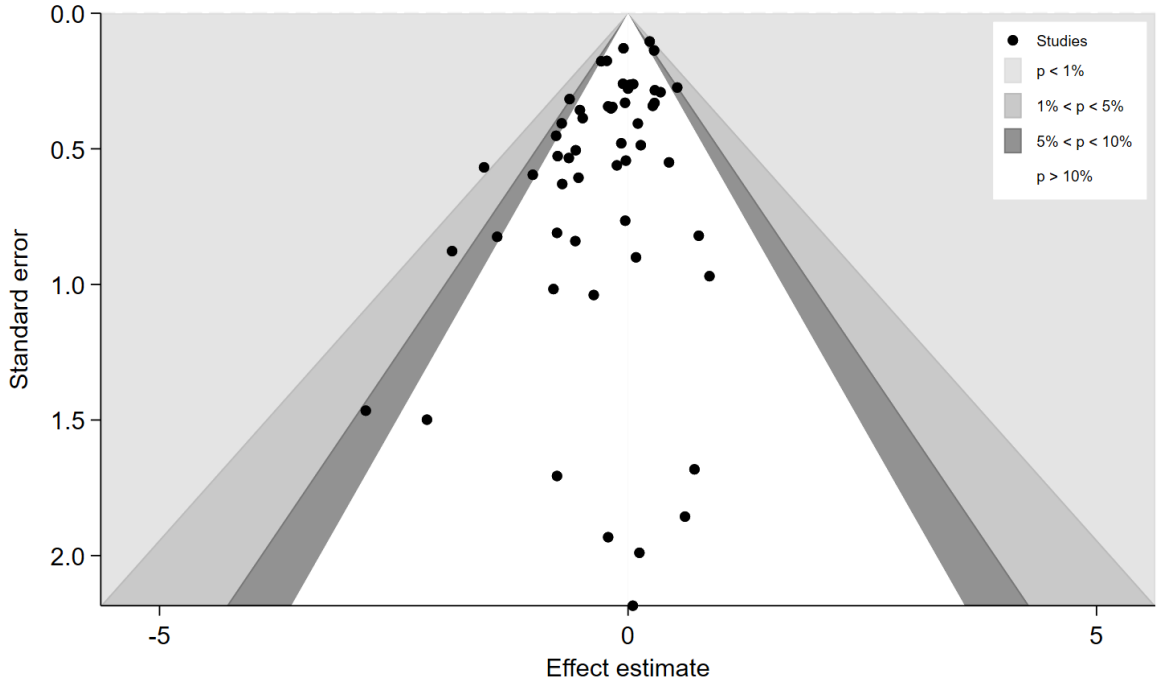


Figure 4.11 - Contour-enhanced funnel plot for overall intervention effects on GDM as defined by trial authors (IPD only)

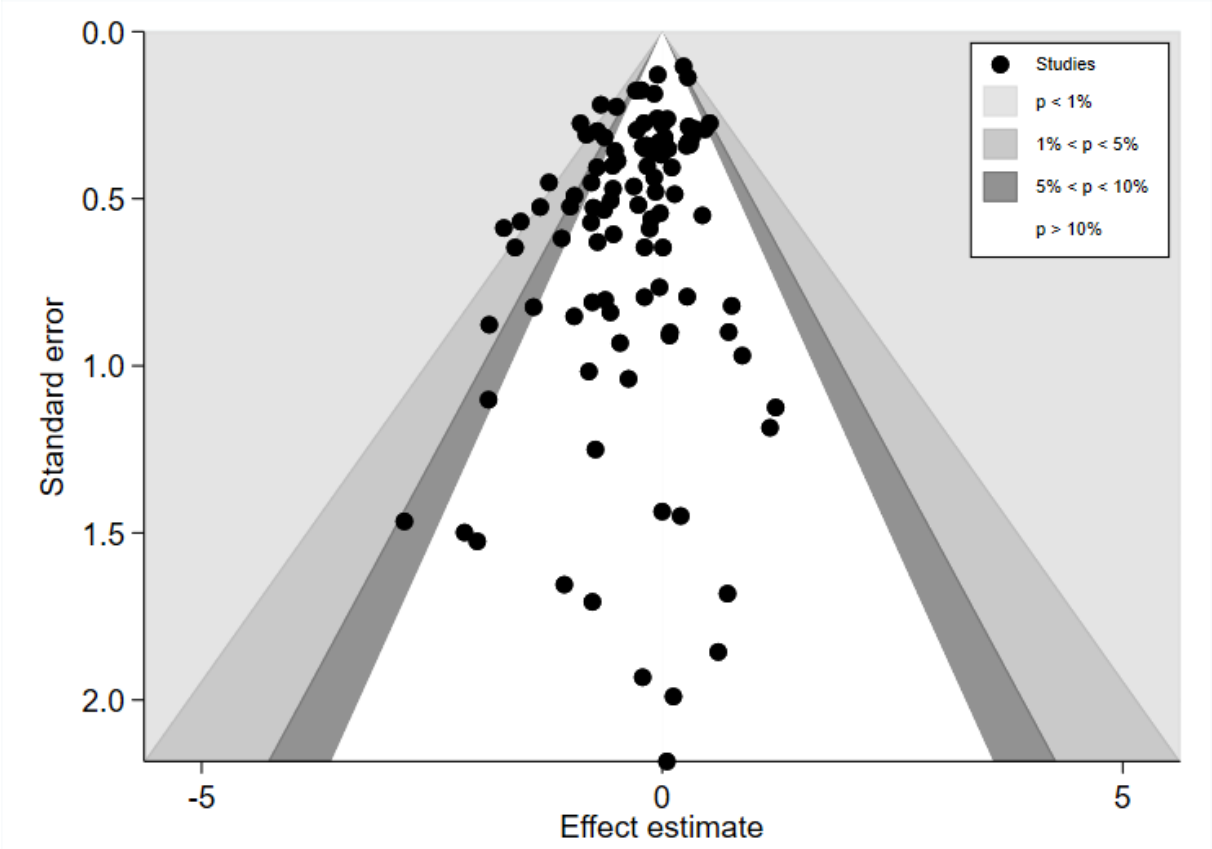


Figure 4.12 - Contour-enhanced funnel plot for overall intervention effects on GDM as defined by trial authors (IPD & aggregate data)

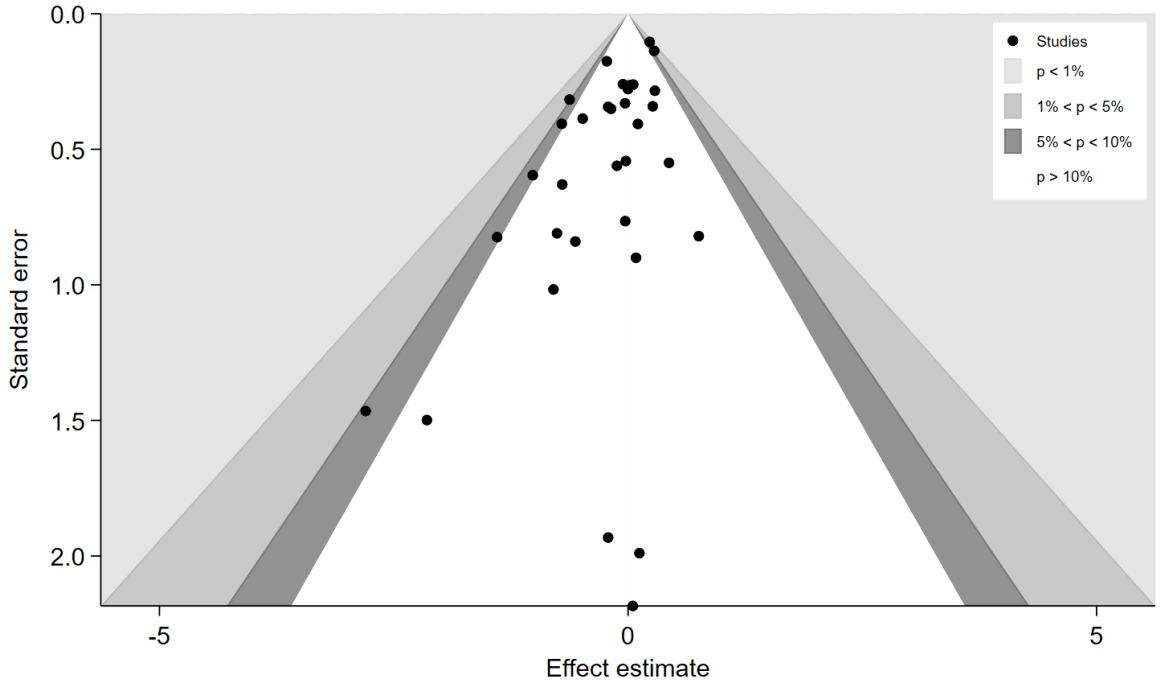


Figure 4.13 - Contour-enhanced funnel plot for overall intervention effects on GDM as defined by trial authors (IPD trials classified at low/medium risk of bias)

4.3. Summary

This IPD meta-analysis contained data from 54 trials for GDM according to trial authors' definition, 22 trials for GDM according to NICE definition, 16 trials for GDM according to the IADPSG definition, 24 trials for GDM according to the modified IADPSG definition, and 26 trials for continuous glucose measurements. Overall, lifestyle interventions showed a reduction in the odds of developing GDM. On average, there was a 10% reduction in the odds of developing GDM according to trial authors' definition (OR= 0.90; 95% CI= 0.8, 1.02); a 2% reduction in the odds of developing GDM according to NICE definition (OR= 0.98; 95% CI= 0.84, 1.13); a 14% reduction in the odds of developing GDM according to IADPSG definition (OR= 0.86; 95% CI= 0.75, 0.97); and an 8% reduction in the odds of developing GDM according to the modified

IADPSG definition (OR= 0.92, 95% CI= 0.78, 1.1). There was also a slight decrease observed in the continuous glucose measurements (both fasting and 2-hour post-prandial OGTT), but there was uncertainty in the effects of the intervention in this case, as indicated by the 95% PI.

Taken individually, physical activity showed the most impact in reducing the odds of developing GDM. On average, there was a 36% reduction in the odds of developing GDM according to trial author's definition (OR= 0.64; 95% CI= 0.48, 0.85); a 35% reduction in the odds of developing GDM according to the NICE definition (OR= 0.65; 95% CI= 0.18, 2.31); an 8% reduction in the odds of developing GDM according to the IADPSG definition (OR= 0.92; 95%, CI= 0.28, 3.08); and a 12% reduction in the odds of developing GDM according to the modified IADPSG definition (OR= 0.88; 95%, CI= 0.7, 1.09).

Diet based interventions also showed considerable reduction in the odds of developing GDM. On average, there was a 19% reduction in the odds of developing GDM according to trial authors' definition (OR= 0.81; 95% CI= 0.69, 0.96); a 30% reduction in the odds of developing GDM according to NICE definition (OR= 0.7; 95% CI= 0.33, 1.49); a 29% reduction in the odds of developing GDM according to IADPSG definition (OR= 0.71; 95% CI= 0.06, 7.88); and a 36% reduction in the odds of developing GDM according to modified IADPSG definition (OR= 0.64, 95% CI= 0.32, 1.3). However, there was lesser certainty in these results as the number of diet-based trials contributing their data to the meta-analysis was consistently low.

On the other hand, mixed interventions mostly increased the odds of developing GDM. On average, there was a 5% increase in the odds of developing GDM according to trial authors' definition (OR= 1.05; 95% CI= 0.91, 1.21); a 10% increase in the odds of developing GDM according to NICE definition (OR= 1.10; 95% CI= 0.98, 1.23); an 11% reduction in the odds of developing GDM according to IADPSG definition (OR= 0.89, 95% CI= 0.76, 1.03); and an 8% increase in the odds of developing GDM according to the modified IADPSG definition (OR= 1.08, 95% CI= 0.89, 1.31).

The results of the main IPD meta-analysis were supported by additional sensitivity analysis. Firstly, when aggregate data were added from trials which did not share their IPD to the main IPD, it resulted in a 20% reduction in the odds of developing GDM according to the trial authors' definition (OR= 0.80, 95% CI= 0.73, 0.88); and a 17% reduction in the odds of developing GDM (IADPSG definition) (OR= 0.83, 95% CI= 0.73, 0.94). Physical activity also continued to emerge at the top among the other individual types of intervention when the IPD and non-IPD trials were combined, with a 36% reduction in the odds of developing GDM according to the trial authors' definition (OR= 0.64, 95% CI= 0.53, 0.76) and a 7% reduction in the odds of developing GDM according to the IADPSG definition (OR= 0.93, 95% CI= 0.69, 1.31). The NICE definition and the modified IADPSG definition also showed considerable reductions (35% and 12% respectively), but most of this was based on the trials which contributed their IPD as there was only 1 additional trial in each case contributing their aggregate data.

Secondly, running the IPD meta-analysis with only the trials with low risk of bias (as estimated by the Risk of Bias 2011 tool) showed results consistent with the main analysis. There was a 6% reduction in the odds of developing GDM (OR= 0.94, 95% CI= 0.82, 1.08) for the overall interventions, and a 41% reduction in the odds of developing GDM (OR= 0.59, 95% CI= 0.43, 0.82) for physical activity taken separately.

Lastly, there was no evidence of the presence of small study effects and publication bias in GDM as defined by the trial authors' definition. This was true even when the aggregate data from non-IPD trials were added to the IPD meta-analysis, and when the trials with a high risk of bias were excluded from the IPD meta-analysis.

The implications of these results have been discussed in detail in Chapter 7.

Chapter 5

5. Exploring GDM: Differential Effects, Maternal and Neonatal Complications, TIDieR Components, and Network Meta-Analysis

In this chapter, I have investigated the effect of the lifestyle interventions on specific subgroups of women, and the effect of the interventions on maternal and neonatal outcomes on women with GDM. I have also tried to understand how the differences in the components of the TIDieR framework affected the intervention effect estimates. Lastly, I have conducted a network meta-analysis to rank the interventions in terms of their effectiveness in preventing GDM. I have presented all the results along with their interpretations in the later sections of the chapter.

5.1. Methods

The methods used in this Chapter is the same as that previously described in Chapter 2 and Chapter 4. I used the same IPD dataset which was obtained in Chapter 4 to assess the differential effects of the interventions; to evaluate the effect of the interventions in maternal and neonatal complications; and to conduct the network meta-analysis. For the TIDieR analysis, I extracted data from all the IPD trials according to the TIDieR framework based on the intervention characteristics.

5.1.1. Differential effect by subgroups (treatment-covariate interactions)

I looked at whether the intervention effect would be modified by differences in a woman's baseline characteristics. To do so, I included and summarised the treatment-covariate interaction terms in the two-stage meta-analysis framework. The interaction term was explained as the change in intervention effect for a 1-unit change in the covariate. In each case, I adjusted for age and baseline BMI.

The continuous variables (age and baseline BMI) were dichotomised according to pre-specified, clinically relevant cut-off points, to make their interpretations in the clinical setting easier. However, I also analysed them as continuous variables to avoid the pitfalls of arbitrary dichotomisation. [93]

The covariates analysed were as follows:

- Age (in years)
- Age (defined as >=20 years vs <20 years)
- Baseline BMI (in kg/m^2)
- Baseline BMI (defined as overweight vs normal, obese vs normal)
- Ethnicity (defined as Caucasian vs non-Caucasian)
- Parity (defined as nulliparous vs multiparous)

- Education (defined as middle vs low, high vs low), where low is defined as less than 12 years of education, middle is defined as 12 years of education or A-levels equivalent and high is defined as at least university educated or graduate.

5.1.2. Maternal and Neonatal Complications in women with GDM

I looked at the effect of the interventions on some maternal and neonatal complications on women with GDM, as given below:

- maternal complications: hypertensive diseases, caesarean section and preterm birth
- offspring complications: stillbirth, large for gestational age (LGA), small for gestational age (SGA) and admission to the neonatal unit (NICU)

For each of these outcomes, I followed the two-stage IPD meta-analysis method described in Chapter 2, by restricting the analysis to the subset of women with GDM. All analyses were adjusted for age and baseline BMI.

5.1.3. Meta-regression of intervention characteristics using TIDieR framework

I mapped the components of the interventions from each study which shared IPD according to the TIDieR framework. I performed meta-regression analysis to explore whether the effect of the intervention differed according to the components of the TIDieR framework. The model was adjusted for age and baseline BMI. The analysis was conducted for the overall effect of the intervention as well as by stratifying the data according to type of intervention (diet,

physical activity and mixed). When more than one groups were compared, the reference group for the comparison was the one with the most frequent category overall in the trials.

5.1.4. Network Meta-Analysis

A network meta-analysis (NMA) was performed. The outcome was chosen to be trial authors' definition of GDM, as this outcome had the largest evidence base. A multivariate random-effects meta-analysis framework with a REML estimation was implemented using the 'network' library in Stata. This approach allowed for the integration of both direct and indirect evidence in evaluating the effects of different interventions on GDM, assuming a common between-study variance across all intervention comparisons (thus implying a +0.5 between-study correlation for each pair of intervention effects). Sensitivity to relaxing this assumption was examined using model fit statistics. Summary effect estimates and corresponding 95% CIs were derived for each pairwise comparison of interventions in the network.

Based on the results, the ranking of intervention types was determined using resampling methods based on the approximate posterior distribution of intervention effects. Rankings were quantified by probabilities of each intervention being ranked from first to last, along with mean rank and its associated 95% CI. Network diagrams and rankograms were used to visually represent the network structure and intervention rankings.

To assess the consistency assumption, which states that direct and indirect evidence are concordant on average, each intervention comparison with both direct and indirect evidence

was evaluated. This involved estimating direct and indirect evidence separately and comparing them using Wald tests. Inconsistency was inferred if the global test across all evidence yielded a p-value below 0.05.

Furthermore, the impact of intervention components was explored by extending the standard NMA to a network meta-regression. Each component of interventions was introduced individually as a study-level categorical covariate to assess whether intervention effects varied according to these components. Components of the TIDieR framework assessed included:

- Theory (Yes, No)
- Resources (Combination, None, Self-monitoring tool, Written resource/other)
- Intervention Facilitator (Allied Health, Fitness Specialist, Medical, Researcher, Unsupervised/ eHealth)
- Prior Training (Yes, No/Not reported (NR))
- Structure (Group, Individual, Individual & Group)
- Intervention Method (Face to face, Remote, Face to Face & Remote)
- Location (Exercise Centre, Hospital/Antenatal Clinic, Non-Clinical setting)
- Number of sessions (1-5, 6-10, 11-25, >25)
- Duration (0 - 12 weeks, 13 - 24 weeks, 25-40 weeks, NR)
- Ongoing support (Yes, No)

5.2. Results

5.2.1. Interaction Effects

shows the covariate treatment interaction effect estimates for developing GDM (trial authors' definition). Among all the potential effect modifiers assessed, only mothers' education was found to be statistically significant at the 5% level. The analysis revealed similar outcomes for the interaction effect between education and intervention when comparing middle to low education levels (OR: 0.68, 95% CI: 0.51, 0.90) and high to low education levels (OR: 0.71, 95% CI: 0.54, 0.93), suggesting a decrease in the odds of developing GDM among those with middle or higher education levels in the intervention group. This positive effect persisted when examining the 95% PI for the summary effects. Almost all trials contributed data towards continuous age and continuous BMI (52 and 54 trials respectively). These were analysed by assuming a linear effect. However, for both, no interaction effect was observed for per unit increase in age or BMI, with both showing the same effect estimates of approximately (OR: 1.00, 95% CI: 0.98, 1.02). Forest plots for all treatment-covariate interaction effects have been provided in Appendix 19.

Table 5.1: Treatment-covariate interactions for GDM (trial authors' definition)

Item	Number of trials	Number of women	Treatment–covariate interaction OR (95% CI)	95% PI	I^2(%)	τ^2 (95% CI)
Age						
Per year of age	52	23,161	1.00 (0.99, 1.01)	0.98, 1.03	0	0.00 (0.00, 0.00)

>=20 vs <20	24	17,320	1.00 (0.74, 1.36)	0.74, 1.36	0	0.00 (0.00, 0.79)
Baseline BMI category						
Per unit of BMI	54	23,361	1.00 (0.98, 1.02)	0.98, 1.02	0	0.00 (0.00, 0.00)
Overweight vs Normal	33	16,711	0.98 (0.74, 1.29)	0.50, 1.90	0	0.09 (0.00, 0.64)
Obese vs Normal	48	21,080	0.90 (0.72, 1.11)	0.72, 1.12	0	0.00 (0.00, 0.37)
Ethnicity						
Non-Caucasian vs. Caucasian	18	8,733	0.98 (0.71, 1.34)	0.71, 1.34	0	0.00 (0.00, 0.41)
Parity						
Multiparous vs. Nulliparous	40	19,574	0.88 (0.75, 1.03)	0.75, 1.03	0	0.00 (0.00, 0.17)
Mother's education						
Middle vs Low	33	10,887	0.68 (0.51, 0.90)	0.51, 0.90	0	0.00 (0.00, 0.49)
High vs Low	32	10,794	0.71 (0.54, 0.93)	0.54, 0.93	0	0.00 (0.00, 0.41)

Table 5.2 shows the covariate treatment interaction effect estimates for developing GDM (NICE definition). When using this definition, none of the interaction effects were statistically significant for any of the potential effect modifiers assessed. Continuous age and continuous BMI data were present in a considerable number of trials (22 trials). A linear effect was assumed for continuous covariate interactions, and no interaction effect was observed for per unit increase in age or BMI, with both showing an effect estimate of (OR: 1, 95% CI: 0.99, 1.02). However, women who were categorised as non-White showed the largest reduction in the odds of developing GDM – around 27% on average (OR: 0.73, 95% CI: 0.42, 1.26) compared to those from a non-White ethnic background. Forest plots for all treatment-covariate interaction effects has been provided in Appendix 20.

Table 5.2: Treatment-covariate interactions for GDM (NICE definition)

Item	Number of trials	Number of women	Summary treatment–covariate interaction OR (95% CI)	95% PI	I^2(%)	τ^2 (95% CI)
Age						
Per year of age^	22	11,990	1.00 (0.99, 1.02)	0.99, 1.02	0	0 (0, 0)
>=20 vs <20	13	10,461	1.15 (0.87, 1.51)	0.87, 1.51	0	0 (0, 0.73)
Baseline BMI category						
Per unit of BMI^	22	9,462	1.00 (0.99, 1.02)	0.99, 1.02	3.5	0 (0, 0)
Overweight vs Normal	16	7,965	1.11 (0.67, 1.83)	0.34, 3.56	23.9	0.23 (0, 1.43)
Obese vs Normal	16	9219	1.07 (0.69, 1.68)	0.4, 2.87	16.3	0.17 (0, 1.19)
Ethnicity						
Non-White vs. White	10	5,736	0.73 (0.42, 1.26)	0.34, 1.57	25.4	0.05 (0, 1.3)
Parity						
Multiparous vs. Nulliparous	14	9,072	0.98 (0.77, 1.24)	0.77, 1.25	0	0 (0, 0.37)
Mother's education						
Middle vs Low	8	4312	1.3 (0.78, 2.15)	0.77, 2.19	0	0 (0, 1.12)
High vs Low	8	4293	1.15 (0.68, 1.96)	0.67, 1.99	0	0 (0, 1.35)

5.2.2. Maternal and Neonatal Complications in women with GDM

Table 5.3 shows the effect of lifestyle interventions on maternal and neonatal complications in women with GDM (trial authors' definition). Among women who received lifestyle interventions during pregnancy and subsequently developed GDM, there was no significant decrease in the odds of developing hypertensive disease, preterm birth, caesarean section, stillbirth, SGA, LGA or NICU admission compared to controls who also developed GDM. According to the individual types of interventions, physical activity-based interventions showed a significant increase in the odds of developing hypertensive disease (OR: 1.78, 95%

CI: 1.25, 2.51; 13 studies, 276 women), preterm delivery (OR: 2.28, 95% CI: 1.24, 4.22, 11 studies, 251 women), and SGA (OR: 1.60, 95% CI: 1.15, 2.22; 13 studies, 274 women). Conversely, diet-based interventions reduced the likelihood of having LGA (OR: 0.25, 95% CI: 0.13, 0.48; 6 studies, 241 women) and preterm delivery (OR: 0.36, 95% CI: 0.18, 0.74; 6 studies, 246 women) compared to controls who developed GDM. Forest plots for all maternal and neonatal complications has been provided in Appendix 21.

Table 5.3: Effect of lifestyle interventions on maternal and offspring complications in women with GDM

Outcome	**Intervention**	**No. of studies**	**No. of women**	**OR (95% CI)**	**95% PI**	**I^2(%)**	**τ^2 (95% CI)**
Hypertensive disease	All	45	2,830	1.09 (0.90, 1.31)	0.90, 1.31	0	0.00 (0.00, 0.23)
	Diet	8	475	0.89 (0.46, 1.75)	0.45, 1.79	0	0.00 (0.00, 2.72)
	Physical activity	13	276	**1.78 (1.25, 2.51)**	**1.25, 2.52**	0	0.00 (0.00, 1.32)
	Mixed	24	2079	1.06 (0.83, 1.35)	0.83, 1.35	0	0.00 (0.00, 0.39)
Preterm birth	All	40	2,446	0.88 (0.67, 1.17)	0.67, 1.17	0	0.00 (0.00, 0.50)
	Diet	6	246	**0.36 (0.18, 0.74)**	**0.17, 0.78**	0	0.00 (0.00, 5.01)
	Physical activity	11	251	**2.28 (1.24, 4.22)**	**1.23, 4.25**	0	0.00 (0.00, 1.72)
	Mixed	22	1,932	0.78 (0.57, 1.06)	0.57, 1.06	0	0.00 (0.00, 0.51)
Caesarean section	All	43	2,693	0.98 (0.85, 1.13)	0.85, 1.13	0	0.00 (0.00, 0.12)
	Diet	8	438	1.13 (0.93, 1.38)	0.92, 1.39	0	0.00 (0.00, 1.13)
	Physical activity	13	274	0.82 (0.45, 1.48)	0.45, 1.49	0	0.00 (0.00, 1.31)
	Mixed	22	1,981	0.98 (0.80, 1.19)	0.77, 1.25	0	0.00 (0.00, 0.19)
Stillbirth	All	22	1,260	0.95 (0.78, 1.14)	0.78, 1.14	0	0.00 (0.00, 0.86)

	Diet	4	177	0.71 (0.29, 1.78)	0.21, 2.46	0	0.00 (0.00, 18.27)
	Physical activity	4	79	1.43 (0.60, 3.39)	0.44, 4.60	0	0.00 (0.00, 11.32)
	Mixed	14	1,004	0.91 (0.78, 1.06)	0.78, 1.07	0	0.00 (0.00, 1.45)
Small for gestational age	All	34	1,750	1.17 (0.92, 1.49)	0.92, 1.49	0	0.00 (0.00, 0.51)
	Diet	6	241	0.89 (0.18, 4.35)	0.03, 26.97	9.9	1.13 (0.00, 13.99)
	Physical activity	13	274	**1.60 (1.15, 2.22)**	**1.15, 2.23**	0	0.00 (0.00, 1.26)
	Mixed	15	1,235	1.19 (0.93, 1.51)	0.93, 1.52	0	0.00 (0.00, 0.71)
Large for gestational age	All	36	2,029	1.01 (0.80, 1.28)	0.80, 1.28	0	0.00 (0.00, 0.22)
	Diet	6	241	**0.25 (0.13, 0.48)**	**0.12, 0.51**	0	0.00 (0.00, 2.89)
	Physical activity	13	274	0.96 (0.56, 1.66)	0.56, 1.67	0	0.00 (0.00, 1.29)
	Mixed	17	1,514	1.11 (0.86, 1.44)	0.86, 1.44	0	0.00 (0.00, 0.21)
NICU admission	All	26	1,626	0.98 (0.78, 1.24)	0.78, 1.24	0	0.00 (0.00, 0.32)
	Diet	5	365	0.68 (0.40, 1.16)	0.37, 1.25	0	0.00 (0.00, 4.36)
	Physical activity	3	56	0.64 (0.12, 3.52)	0.00, 97.41	0	0.00 (0.00, 27.36)
	Mixed	18	1,205	1.07 (0.81, 1.43)	0.81, 1.43	0	0.00 (0.00, 0.44)

5.2.3. TIDieR analysis

When the lifestyle interventions from the trials which shared their IPD were broken down to their core components as described by TIDieR framework, it was found that the majority of the interventions were:

- not based on theory (65%, 35/54), [266–300]
- were administered individually (51%, 28/54), [266,274,275,277,279,282,284–286,289,292–294,298,300–313]
- primarily through face-to-face interactions (83%, 45/54), [266–277,279,282–295,297–300,302–307,309,310,312,314–318]
- and did not include additional resources for participants (68%, 36/54). [266–269,271–276,279–285,287–292,294,295,297–300,302,305,310,312,314–316,318]
- The facilitators were predominantly allied health staff (72%, 39/54). [267–277,279–281,284,287,289–293,295–297,299–303,305,309,310,313,315–320]
- The facilitators often did not undergo training for delivering the intervention, or such training was not documented in the studies (65%, 34/54). [266–269,271–277,280–284,286,288,290–295,297–299,303,305,308–310,313,315,317,318]
- Most interventions commenced during early pregnancy (before 20 weeks gestation) (72%, 39/54),[267–269,271–279,282,284,285,288,290–295,299–301,305–307,309–311,314–319] and
- took place in hospital settings or antenatal clinics (76%, 40/54). [267–277,279–287,289–307,311–318,320]

I have provided the intervention characteristics according to TIDieR framework for all the trials which shared their IPD in Appendix 18. I have presented the meta-regression results summarising how the intervention effects changed according to intervention components in the tables: overall (*Table 5.4*), diet (*Table 5.5*), physical activity (), , and mixed (*Table 5.7*)

interventions. A statistically significant association was observed between the structure of intervention and the prior training received by the intervention providers with GDM (trial authors' definition). Delivery of the intervention in a group format was associated with a greater reduction in the odds of developing GDM (OR: 0.81; 95% CI: 0.68, 0.97) compared to individual delivery. Also, when providers had no prior training specific to the intervention, there was a greater reduction in the odds of developing GDM (OR: 0.82; 95% CI: 0.69, 0.96) compared to cases where training was provided. None of the other intervention components showed a significant difference in developing GDM.

Table 5.4: Association of overall lifestyle intervention TIDieR component subgroups with GDM.

Core component	**n (%)**	**OR**	**CI 95%**	**Comparison p-value**	**Global p-value**
Structure					
Individual	25 (47.2%)	1.02	(0.89, 1.17)	(ref)	-
Group	28 (52.8%)	0.81	(0.68, 0.97)	0.048	
Number of sessions					
Low + moderate	20 (38.5%)	0.95	(0.82, 1.11)	(ref)	-
High	32 (61.5%)	0.80	(0.62, 1.03)	0.230	
Theory					
No	35 (64.8%)	0.86	(0.73, 1.01)	(ref)	-
Yes	19 (35.2%)	1.00	(0.83, 1.20)	0.230	
Resources					
Combination + Other resources	17 (31.5%)	1.03	(0.88, 1.21)	(ref)	0.100
None	27 (50.0%)	0.85	(0.69, 1.04)	0.135	
Self-Monitoring tool	10 (18.5%)	0.72	(0.52, 1.00)	0.057	
Method					
Face to face	45 (86.5%)	0.90	(0.79, 1.03)	(ref)	-
Face to face + Remote	7 (13.5%)	1.00	(0.71, 1.41)	0.593	
Facilitator					
Allied health staff	39 (76.5%)	0.84	(0.72, 0.98)	(ref)	0.204
Medical staff	6 (11.8%)	1.14	(0.85, 1.53)	0.076	

Other	6 (11.8%)	0.91	(0.59, 1.38)	0.745	
Prior training					
No/NR	35 (67.3%)	0.83	(0.71, 0.98)	(ref)	-
Yes	17 (32.7%)	1.04	(0.89, 1.21)	0.049	
Location					
Hospital/ Antenatal clinic	40 (75.7%)	0.92	(0.81, 1.05)	(ref)	0.445
Exercise centre	8 (15.1%)	0.77	(0.51, 1.15)	0.385	
Other	5 (9.4%)	1.10	(0.74, 1.66)	0.401	
Duration					
Moderate	18 (34.0%)	1.03	(0.86, 1.24)	(ref)	0.228
High	20 (37.7%)	0.85	(0.69, 1.05)	0.174	
Low	15 (28.3%)	0.81	(0.62, 1.05)	0.134	
Ongoing support					
No	37 (69.8%)	0.89	(0.76, 1.04)	(ref)	-
Yes	16 (30.2%)	0.97	(0.79, 1.18)	0.520	
Gestational age					
<20	37 (68.5%)	0.87	(0.76, 1.00)	(ref)	-
≥20	17 (31.5%)	1.04	(0.85, 1.27)	0.164	

Table 5.5: Association of diet-based interventions TIDieR component subgroups with GDM.

Core component	**N (%)**	**OR**	**95% CI**	**Comparison p-value**	**Global p-value**
Structure					
Individual	2 (25.0%)	0.84	(0.54, 1.55)	(ref)	-
Group	6 (75.0%)	0.77	(0.51, 1.16)	0.699	
Number of sessions					
Low + moderate	8 (100%)	0.81	(0.64, 1.04)	-	-
High	0 (0%)	-	-	-	-
Theory					
No	7 (87.5%)	0.82	(0.60, 1.12)	(ref)	-
Yes	1 (12.5%)	0.80	(0.52, 1.23)	0.899	
Resources					
Combination + Other resources	4 (50.0%)	1.07	(0.61, 1.89)	(ref)	0.366
None	3 (37.5%)	0.77	(0.56, 1.06)	0.252	
Self-Monitoring tool	1 (12.5%)	0.60	(0.24, 1.50)	0.223	

Method					
Face to face	8 (100%)	0.81	(0.64, 1.04)	-	-
Face to face + Remote	0 (0%)	-	-	-	-
Facilitator					
Allied health staff	6 (75.0%)	0.77	(0.57, 1.02)	(ref)	0.375
Medical staff	1 (12.5%)	1.02	(0.52, 2.01)	0.362	
Other	1 (12.5%)	2.12	(0.26, 17.53)	0.272	
Prior training					
No/NR	6 (75.0%)	0.82	(0.60, 1.13)	(ref)	-
Yes	2 (25.0%)	0.79	(0.52, 1.21)	0.876	
Location					
Hospital/ Antenatal clinic	8 (100%)	0.81	(0.64, 1.04)	-	-
Exercise centre	0 (0%)	-	-	-	-
Other	0 (0%)	-	-	-	-
Duration					
Moderate	2 (57.1%)	0.87	(0.59, 1.28)	(ref)	0.633
High	1 (14.3%)	0.60	(0.22, 1.61)	0.381	
Low	4 (28.6%)	0.79	(0.49, 1.27)	0.665	
Ongoing support					
No	6 (75.0%)	0.77	(0.54, 1.10)	(ref)	-
Yes	2 (25.0%)	0.86	(0.60, 1.23)	0.602	
Gestational age					
<20	6 (75.0%)	0.77	(0.58, 1.01)	(ref)	-
≥20	2 (25.0%)	1.09	(0.59, 2.01)	0.243	

Table 5.6: Association of physical activity-based interventions TIDieR component subgroups with GDM

Core component	**N (%)**	**OR**	**95%CI**	**Comparison p-value**	**Global p-value**
Structure					
Individual	3 (16.7%)	0.59	(0.13, 2.76)	(ref)	-
Group	15 (83.3%)	0.64	(0.47, 0.88)	0.911	
Number of sessions					
Low + moderate	3 (16.7%)	1.10	(0.60, 2.03)	(ref)	-

High	15 (83.3%)	0.56	(0.41, 0.77)	0.056	
Theory					
No	17 (94.4%)	0.66	(0.48, 0.90)	(ref)	-
Yes	1 (5.6%)	0.25	(0.04, 1.48)	0.269	
Resources					
Combination + Other resources	12 (66.7%)	0.63	(0.25, 1.55)	(ref)	0.733
None	4 (22.2%)	0.66	(0.46, 0.96)	0.901	
Self-Monitoring tool	2 (11.1%)	0.43	(0.14, 1.30)	0.581	
Method					
Face to face	18 (100%)	0.64	(0.47, 0.87)	-	-
Face to face + Remote	0 (0%)	-	-	-	-
Facilitator					
Allied health staff	16 (88.9%)	0.64	(0.47, 0.87)	(ref)	-
Medical staff	-	-	-	-	-
Other	2 (11.1%)	0.88	(0.06, 12.79)	0.805	
Prior training					
No/NR	15 (83.3%)	0.65	(0.45, 0.94)	(ref)	-
Yes	3 (16.7%)	0.58	(0.30, 1.13)	0.759	
Location					
Hospital/ Antenatal clinic	13 (72.2%)	0.70	(0.49, 1.00)	(ref)	0.533
Exercise centre	4 (22.2%)	0.47	(0.24, 0.91)	0.275	
Other	1 (5.6%)	0.47	(0.01, 18.21)	0.819	
Duration					
Moderate	2 (11.1%)	0.52	(0.25, 1.10)	(ref)	0.301
High	10 (55.6%)	0.58	(0.40, 0.84)	0.808	
Low	6 (33.3%)	0.89	(0.54, 1.49)	0.226	
Ongoing support					
No	16 (88.9%)	0.64	(0.45, 0.90)	(ref)	-
Yes	2 (11.1%)	0.63	(0.24, 1.63)	0.988	
Gestational age					
<20	13 (72.2%)	0.55	(0.39, 0.80)	(ref)	-
≥20	5 (27.8%)	0.83	(0.53, 1.30)	0.160	

Table 5.7: Association of mixed intervention TIDieR component subgroups with GDM.

Core component	N (%)	OR	CI 95%	Comparison p-value	Global p-value
Structure					
Individual	19 (70.4%)	1.11	(0.97, 1.27)	(ref)	-
Group	8 (29.6%)	1.00	(0.79, 1.26)	0.413	
Number of sessions					
Low + moderate	21 (80.8%)	1.03	(0.90, 1.18)	(ref)	-
High	5 (19.2%)	1.25	(0.99, 1.58)	0.153	
Theory					
No	11 (39.3%)	1.07	(0.88, 1.30)	(ref)	-
Yes	17 (60.7%)	1.06	(0.89, 1.26)	0.943	
Resources					
Combination + Other resources	19 (67.9%)	1.06	(0.92, 1.22)	(ref)	0.168
None	2 (7.1%)	1.27	(0.98, 1.63)	0.215	
Self-Monitoring tool	7 (25.0%)	0.84	(0.58, 1.20)	0.226	
Method					
Face to face	19 (73.1%)	1.10	(0.96, 1.27)	(ref)	-
Face to face + Remote	7 (26.9%)	0.99	(0.75, 1.29)	0.461	
Facilitator					
Allied health staff	17 (68.0%)	1.05	(0.87, 1.26)	(ref)	0.515
Medical staff	5 (20.0%)	1.15	(0.86, 1.55)	0.568	
Other	3 (12.0%)	0.88	(0.61, 1.28)	0.406	
Prior training					
No/NR	14 (53.8%)	0.94	(0.75, 1.18)	(ref)	-
Yes	12 (46.2%)	1.14	(0.98, 1.31)	0.166	
Location					
Hospital/ Antenatal clinic	19 (70.4%)	1.06	(0.92, 1.22)	(ref)	0.949
Exercise centre	4 (14.8%)	1.11	(0.66, 1.85)	0.861	
Other	4 (14.8%)	1.12	(0.76, 1.65)	0.778	
Duration					
Moderate	12 (42.9%)	1.15	(0.96, 1.38)	(ref)	0.179
High	9 (32.1%)	1.10	(0.89, 1.34)	0.732	
Low	7 (25.0%)	0.84	(0.63, 1.12)	0.070	
Ongoing support					
No	15 (55.6%)	1.12	(0.96, 1.30)	(ref)	-
Yes	12 (44.4%)	1.02	(0.84, 1.24)	0.462	

Gestational age					
<20	18 (64.3%)	1.04	(0.89, 1.21)	(ref)	-
≥20	10 (35.7%)	1.13	(0.90, 1.40)	0.535	

5.2.4. Network Meta Analysis

I created a connected network for GDM (trial authors' definition) to compare the three interventions (diet, physical activity, and mixed approach) against control. The analysis was based on 54 studies which provided their IPD. Of those, 8 studies compared control and diet-based interventions, 18 studies compared control and physical activity-based interventions and 28 studies compared control and mixed interventions. This has been represented diagrammatically in the network map provided below (Figure 5.1)

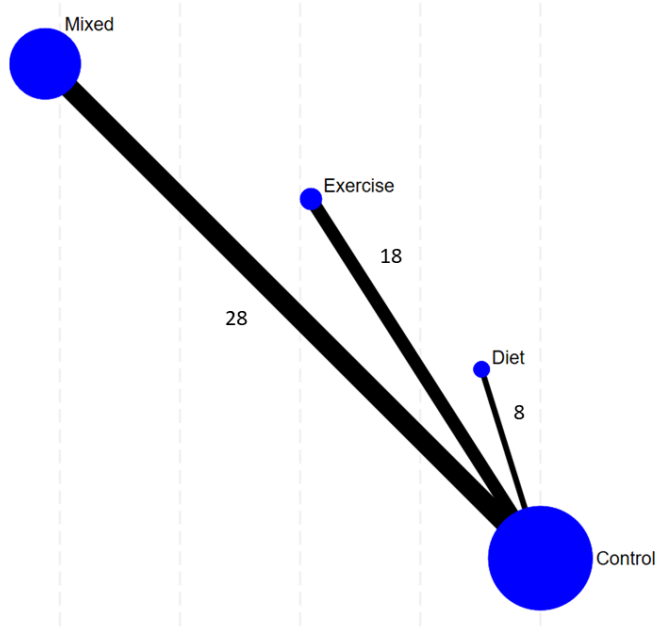


Figure 5.1: Network graph of included studies for GDM defined by trial authors, with thickness of lines and size of circles proportional to the number of trials and number of women, respectively.

Before carrying out the network meta-analysis, a global Wald test confirmed that the consistency assumption was upheld for the network ($p = 0.438$). Additionally, there was evidence of between-study variability, suggesting some level of heterogeneity among the studies in the network ($\tau = 0.103$).

The analysis showed that the summary effect estimates for direct comparisons were consistent with the results observed in the univariate IPD meta-analysis. The indirect intervention effects were estimated for all other comparisons in the network and has been tabulated in Table 5.8. It was seen that only the physical activity vs. mixed approach comparison was statistically significant. Physical activity showed a 39% reduction in the odds of developing GDM (OR 0.61, 95% CI 0.455 to 0.825) on average, in comparison to the mixed approach.

Table 5.8: Network meta-analysis results for all possible comparisons

Intervention 1	**Intervention 2**	**OR**	**95% CI**
Control	Diet	1.229	(0.975, 1.548)
Control	Physical activity	1.546	(1.182, 2.022)
Control	Mixed	0.947	(0.825, 1.087)
Physical activity	Control	0.647	(0.495, 0.846)
Physical activity	Diet	0.795	(0.557, 1.134)
Physical activity	Mixed	**0.613**	**(0.455, 0.825)**
Diet	Control	0.814	(0.646, 1.026)
Diet	Physical activity	1.258	(0.882, 1.794)
Diet	Mixed	0.771	(0.587, 1.013)
Mixed	Control	1.056	(0.920, 1.213)
Mixed	Diet	1.298	(0.988, 1.705)
Mixed	Physical activity	1.633	(1.211, 2.200)

Note: OR <1 favours intervention 1, OR >1 favours intervention 2

Table 5.9 provides a summary of how different interventions rank in terms of their effectiveness, from best to worst. It gives the probability of each intervention being ranked from best to worst, as well as the mean rank with an estimate of uncertainty (95% CI) obtained from simulations. Physical activity intervention has the highest mean rank (1.1, 95% CI 1, 2) and the highest probability (89%) of being ranked as the best intervention. This indicates that, on average, physical activity is considered the most effective intervention among the options studied. Mixed interventions have the lowest mean rank (3.8) and the highest probability (78.6%) of being ranked as the worst intervention. This implies that, on average, mixed interventions are considered less effective compared to the other interventions. Both diet and control interventions have less certainty in their mean rankings, as their 95% CIs span across three ranks. This means that there is more uncertainty about their effectiveness compared to

physical activity and mixed interventions. Despite the uncertainty surrounding the mean rankings, the evidence suggests that physical activity might offer benefits in reducing the odds of developing GDM compared to the other interventions assessed in the study. This conclusion was drawn based on evidence from both univariate IPD meta-analysis and network meta-analysis.

Table 5.9: Estimated probabilities (%) of each intervention having each rank & the mean rank with 95% confidence intervals for each intervention.

	Intervention			
Rank (%)	**Physical activity**	**Diet**	**Control**	**Mixed**
Best	89	11	0	0
2nd	11	83.1	3.4	2.5
3rd	0	3.1	78	18.9
Worst	0	2.8	18.6	78.6
Mean Rank (95% CI)	1.1 (1, 2)	2 (1, 3)	3.2 (2, 4)	3.8 (3, 4)

Lastly, network meta-regression models were fitted by incorporating study-level characteristics describing the components of interventions. The consistency assumption held true (global Wald test p-values were all greater than 0.45). The variability in effect sizes across different studies included in the analysis as captured by the between study variance, though small, was non-zero (τ range 0.069 to 0.132), indicating that there was some variability in effect sizes among the studies. Some component effects could not be estimated due to collinearity among the predictor variables describing the components of interventions. For the component effects that could be estimated, the effects were determined with uncertainty, as indicated by wide 95% CIs for both potentially beneficial and harmful effects. No components of interventions were found to have a statistically significant effect on the overall intervention effect.

5.3. Summary

In this chapter I explored the effects of the lifestyle interventions in a few different ways. When the effect of the interventions on different subgroups of women was studied, only mothers' education had a statistically significant impact on GDM as per trial authors' definition. Those with a middle and higher education level saw a large decrease in the odds of developing GDM compared to those with lower education levels ((OR: 0.68, 95% CI: 0.51, 0.90) and (OR: 0.71, 95% CI: 0.54, 0.93) respectively).

When using the NICE definition for GDM, none of the interaction effects were statistically significant for any of the potential effect modifiers assessed. However, women who were categorised as non-White showed the largest decrease in the odds of developing GDM compared to those of White ethnic background, by approximately 27% on average (OR: 0.73, 95% CI: 0.42, 1.26).

Next, I looked at the effect of the lifestyle interventions on different maternal and neonatal complications in women with GDM as defined by trial authors' definition. There was no significant decrease observed in the odds of developing hypertensive disease, preterm birth, caesarean section, stillbirth, SGA, LGA, or NICU admission among women with GDM who received the overall interventions compared to controls who also developed GDM. Women with GDM who had physical activity-based interventions experienced many adverse effects compared to controls with GDM. In this group of women, there was a significant increase in the odds of developing hypertensive disease (OR: 1.78, 95% CI: 1.25, 2.51), preterm delivery

(OR: 2.28, 95% CI: 1.24, 4.22), and SGA (OR: 1.60, 95% CI: 1.15, 2.22). However, diet-based interventions reduced the odds of developing LGA (OR: 0.25, 95% CI: 0.13, 0.48) and preterm delivery (OR: 0.36, 95% CI: 0.18, 0.74) compared to controls who developed GDM.

When the interventions were broken down to their core-components (according to TIDieR) and a meta-regression analysis was run to find the association between them and GDM (trial authors' definition), statistically significant associations were observed in the structure of intervention and the prior training received by the intervention providers. Implementing the intervention in a group setting was associated with a notable decrease in the odds of developing GDM (OR: 0.81, 95% CI: 0.68, 0.97) compared to individual delivery. Additionally, instances where intervention providers lacked prior training specific to the intervention, there was a greater decrease in the odds of developing GDM (OR 0.82, 95% CI 0.69 to 0.96) compared to cases where training was provided. No other components of the intervention demonstrated a significant difference in GDM development.

When a network meta-analysis was conducted to rank the different types of interventions, physical activity had the highest mean rank (1.1; 95% CI= 1, 2) and the highest probability (89%) of being ranked as the best intervention. On the other hand, mixed interventions had the lowest mean rank (3.8) and the highest probability (78.6%) of being ranked as the worst intervention. The implications of these results have been discussed in detail in Chapter 7.

Chapter 6

6. Economic Evaluation of prediction model for Fetal Growth Restriction (FGR)

In this chapter, I have presented the methods and results of the economic evaluation conducted to assess the relative cost-effectiveness of three different approaches used in detecting fetal growth restriction (FGR) during pregnancy. The three approaches were: (1) no routine testing of FGR; (2) using symphysis fundal height (SFH) and ultrasound scans and (3) using the IPPIC prediction model. I have discussed the IPPIC prediction model previously in the Chapter 1 (Section 1.3.2) My work builds on the economic model provided in the National Institute of Health and Care Excellence (NICE) guidelines[75], which at the time of writing the thesis is more than a decade old. I have extended the NICE model to include the prediction model to predict the risk of developing FGR, which was created as part of the International Prediction of Pregnancy Complications (IPPIC) Health Technology Assessment. [321] The aim of this research is to help decision makers in health care resource settings determine which strategy provides the greatest effectiveness at the most reduced cost in detecting FGR during pregnancy and look at the relative incremental cost-effectiveness ratios (ICERs) of the different strategies.

6.1. Methods

The general methods used in the cost-effectiveness analysis has been explained in Chapter 2. In this section, I have presented some finer details related to the methodology of the cost-effectiveness analysis.

The individuals in the economic evaluation model were independent of each other and the time from entry into the model until delivery of fetus was less than nine months. Hence, I did not have to adjust for discounting. Also, there were no recurring events. Therefore, I adopted a decision tree model, which was the most suitable model in this situation. The model was constructed using Microsoft Excel® and has been depicted in Figure 6.1. I considered the perspective of the National Health Service (NHS) and did not consider any private out-of-pocket costs to women or productivity losses.

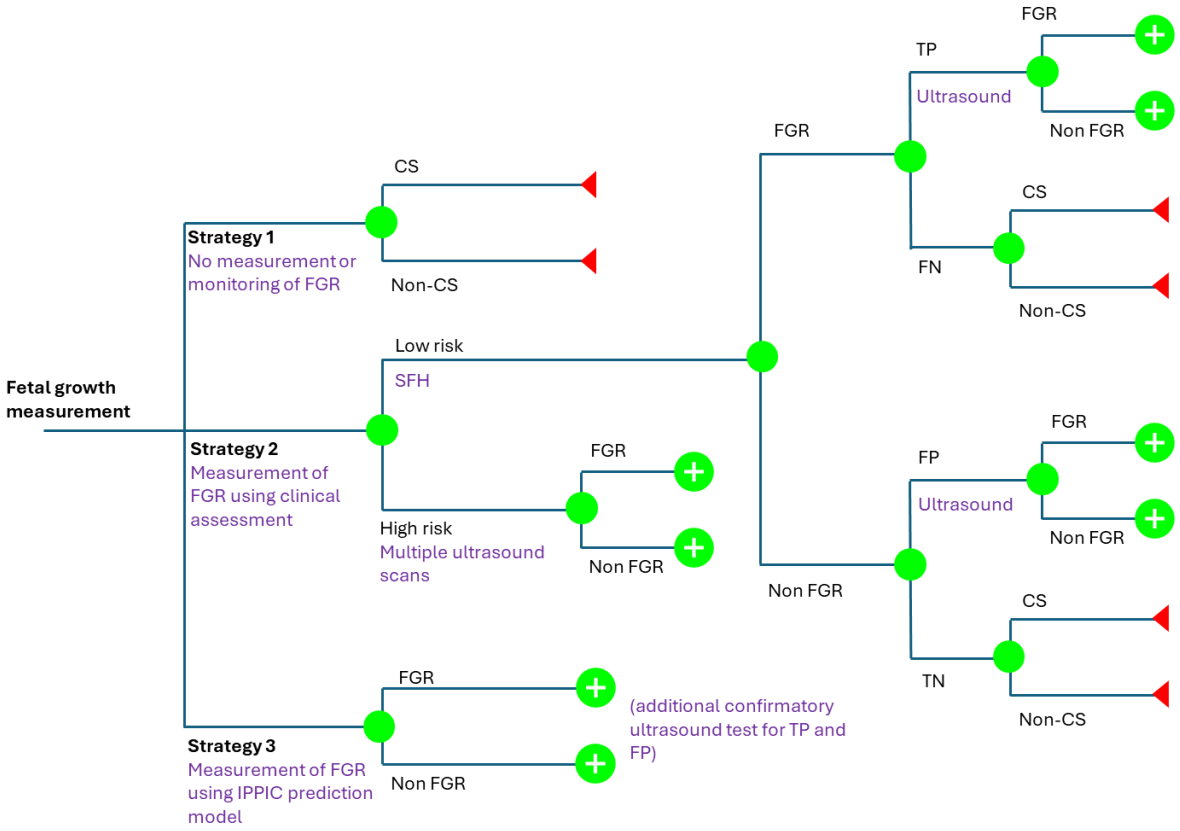


Figure 6.1: The decision tree for measuring and monitoring FGR

Note: Here, ● denotes a chance node, ◀ denotes a terminal node and ⊕ denotes a branch which has been collapsed due to brevity.

6.1.1. Study population

I only considered nulliparous women in the UK with singleton pregnancies, and the outcomes were from the perspective of the infant.

6.1.2. Model structure

At the time of entry into the model, the health care provider has three alternative options for measuring FGR: no routine testing, measurement of FGR using clinical assessment (followed by SFH and ultrasound scans), and measurement of FGR using IPPIC prediction model. These strategies formed the three main branches of my decision tree.

For Strategy 1, the two main pathways were: the pregnant woman either went on to deliver a baby via caesarean section or via non-caesarean section methods. This was chosen as the final outcome in my model, in line with the previous NICE model. I did not consider stillbirth, neonatal death, livebirth or NICU admission as my final outcomes due to the lack of reliable clinical data in Strategy 2 and Strategy 3.

In Strategy 2, I considered that FGR was diagnosed via clinical assessment. Women were first identified as being high risk (HR) or low risk (LR) based on clinical assessment. All low risk women received an SFH measurement. All the women who tested positive for this SFH measurement went on to have an ultrasound measurement. All those who tested negative for the SFH measurement went to have a delivery via caesarean section or non-caesarean methods. All high-risk women went on to have multiple ultrasound scans until delivery.

After each test, there were two outcomes for the baby: either the baby truly had FGR or truly did not have FGR. Simultaneously, at each test juncture, the baby could have been given a correct diagnosis or an incorrect diagnosis. Thus, at each testing a baby had four possible outcomes: being correctly identified as FGR (True Positive, TP), incorrectly identified as not FGR (False negative, FN), incorrectly identified as FGR (False positive, FP), or correctly

identified as not FGR (True Negative, TN). Following each of these identifications, the pregnant woman followed the same pathway and had the same final outcomes, i.e., caesarean section or non-caesarean section.

In strategy 3, I considered that FGR was detected using the IPPIC prediction model. I only considered the prediction model where the outcome variable was binary: FGR or no FGR, (Model 1). I have not considered the prediction model where the outcome was a continuous variable: birthweight of baby (Model 2), as I would have to dichotomise this variable into a binary variable (FGR or no FGR), which would be redundant (same as Model 1). This pathway started with the same two options -- baby being detected with FGR or no FGR using the model, and ended with caesarean section or non-caesarean section births. I have considered that those who were diagnosed with FGR using the prediction model would have had a confirmatory ultrasound test, and have accounted for this in the costs section.

6.1.3. Inputs to model

The parameters for the model were populated from multiple sources from the existing literature. If unavailable, expert opinion was sought. The quality of the data source was assessed using the following criteria: data obtained from published articles, systematic reviews, meta-analyses, other economic evaluations, and national registers, were considered as 'high quality'; if data were unavailable, expert opinion was sought for plausible values, or proxy data were used, it was considered as 'low quality'. Whenever possible, all the data were

from the latest available estimates. All input parameters and their quality are presented in Table 6.1, Table 6.2 and *Table 6.3*.

6.1.4. Probabilities

The majority of the baseline probabilities were populated using the Hospital Episode Statistics 2018-2019 [322] published by the NHS. Probabilities were also used from other published literature, which has been listed in Table 1 along with the quality of the source of the information. I used proxy variables when no statistics were available for the intended variables. Expert opinion was sought to ensure that these proxy variables were as reasonable as possible and made sense in a clinical setting. However, due to the lack of verifiable data, these parameters have been marked as low quality. For example, the probability of detecting FGR using the different methods should have ideally been different for each method. But due to sparse data being available, this has been approximated by the general probability of detecting FGR.

The sensitivity and specificity of the prediction model was obtained at the threshold probability of 0.08 from the IPPIC HTA report (table reproduced in Appendix 24). This threshold probability was deemed to be the most plausible value to explain model performance. The choice for the threshold probability was guided by the desire to obtain a high enough specificity without losing out on the sensitivity (sensitivity = 67.8%, specificity = 98.7%). The calculations for probabilities have been shown in Appendix 22.

Table 6.1: Model inputs for probabilities and diagnostic test performances

Parameter	Proxy variable	Value	Source	Quality
CS		0.2951	Hospital Episode Statistics 2018-2019 [322]	High
Non-CS		0.7049	Hospital Episode Statistics 2018-2019 [322]	High
CS (FGR)		0.9000	Assumption	Low
FGR (SFH)	FGR	0.0300	Vieira 2019 [323], NICE guidelines [75]	Low
FGR (ultrasound)	FGR	0.0300	Vieira 2019 [323], NICE guidelines [75]	Low
FGR (prediction model)	FGR	0.0300	Vieira 2019 [323], NICE guidelines [75]	Low
Sensitivity of SFH measurement		0.59	Pay 2015 [324]	High
Specificity of SFH measurement		0.9700	Pay 2015 [324]	High
Sensitivity of ultrasound scan		0.5556	Haragan 2015 [325]	High
Specificity of ultrasound scan		0.9598	Haragan 2015 [325]	High
Sensitivity of prediction model		0.6780		Low
Specificity of prediction model		0.9870		Low
Probability of high-risk women using clinical assessment		0.25	Assumption	Low
Number of serial USS for high-risk women		5	Assumption	Low

6.1.5. Costs

Costs have been presented in pounds sterling in 2019-20 prices. The majority of the unit costs were obtained from the National Schedule of Reference Costs: main schedule [326]. If the data were unavailable for the mentioned year, it was inflated using the NHS Cost Inflation Index (NHSCII) pay and prices indices [327] from the previously available years. If direct cost values

were unavailable, they were calculated using weighted averages, as shown in Appendix 23. The cost of the prediction model was assumed to be £0, as there is no additional associated cost which needed to be employed by the healthcare provider for its use. However, an additional cost of a confirmatory ultrasound scan was assigned to those identified as FGR using the prediction model (True Positive and False Positive), as it would serve as a further confirmation to predict FGR.

Table 6.2: Model inputs for costs

Parameter	Value	Source	Quality
Prediction model	£0.00	Assumption	Low
Delivery by CS	£3,976.91	National schedule of reference costs [326]	High
Delivery by Non-CS	£2,099.34	National schedule of reference costs [326]	High
SFH measurement	£4.87	Personal Social Services Research Unit (PSSRU) 2006 [328]	High
Ultrasound fetal growth scan	£57.07	National schedule of reference costs [326]	High

6.1.6. Outcomes

Ideally, with health economics models we can compare different interventions using outcomes based on robust clinical and health-related quality of life (HRQoL) data such as the quality-adjusted life year (QALY). However, due to the lack of reliable clinical and HRQoL data, my model does not do that. Instead, I have taken a similar approach to the NICE model[75], and considered the number of preventable perinatal deaths attributable to FGR for the study to be cost-effective for the measurement and monitoring of fetal growth.

Following this decision, assumptions were made regarding how many perinatal deaths could be prevented for every known 1,000 FGR fetuses using each strategy. Around 60,000 small for gestational age (SGA) babies are born every year, of which a third (approx. 18,050) are expected to have intrauterine growth restriction[75]. Unfortunately, 50% of these babies do not survive even with any intervention. Of the remaining, we can expect around 10% (903) babies survive when using Strategy 1 (no testing), around 25% (2256) babies survive when using Strategy 2 (SFH+ ultrasound) and around 50% (4513) babies survive when using Strategy 3 (prediction model). In other words, for every 1,000 known FGR fetuses, approximately 50 perinatal deaths could be prevented using Strategy 1, 125 perinatal deaths could be prevented using Strategy 2 and 250 perinatal deaths could be prevented using Strategy 3.

Table 6.3: Model inputs for perinatal deaths averted (outcomes)

Perinatal deaths saved for every 1000 FGR babies	**Value**	**Source**	**Quality**
Strategy 1: No measurement or monitoring of FGR	50	Assumption	Low
Strategy 2: Measurement of FGR using SFH measurement and ultrasound	125	Assumption	Low
Strategy 3: Measurement of FGR using Prediction model	250	Assumption	Low

6.1.7. Analysis

The following analysis were planned for the cost-effectiveness analysis:

Cost-effectiveness: reference case / base-case analysis

For the base-case analysis, I used a decision analytical model using a deterministic approach to conduct the cost-effectiveness analysis from the perspective of the NHS. Costs have been presented in 2019-20 prices and outcomes have been presented as the number of the perinatal deaths avoided. The results have been presented in terms of an incremental cost-effectiveness ratio (ICER) which is the cost per perinatal death avoided.

Cost-effectiveness: sensitivity analyses

A sensitivity analysis was conducted by varying the performance of the prediction model. In the base-case scenario, the model sensitivity was 67.8% and the model specificity was 98.7%. However, I also wanted to examine how the cost-effectiveness analysis results would change, if the prediction model gave perfect information (i.e., 100% sensitivity and 100% specificity) and if it performed only as good as a coin toss (i.e., 50% sensitivity and 50% specificity).

Resource Impact Assessment

Apart from conducting a formal cost-effectiveness analysis for an intervention, at times, it is beneficial to conduct a resource impact assessment (RIA). This formal assessment helps to understand and quantify the costs or savings expected from implementing that guideline [329]. This cost and savings may be in the form of cash or non-cash impact for both providers and commissioners. An example of a non-cash impact is improving capacity building that does not result directly in saving money. Impact assessment also incorporates the changes in costs and savings related to changes in number of staff being employed, necessary staff training, changes in facilities required, changes in patient flows, and changes in demand of the service.

However, before conducting the formal resource impact assessment, it was imperative to conduct an Evaluability Assessment[330]. This would address whether an impact assessment is required in the first place, whether it is expected to provide additional information, and if required, what methodology would be the most appropriate.

6.2. Results

6.2.1. Base case analysis

Table 6.4 provides the results of the base-case cost-effectiveness analysis. For this analysis, the different pathways have been ordered in terms of increasing cost. Compared to Strategy 1 of not testing for FGR, Strategy 3 of using a prediction model was the most cost-effective approach. On average, this strategy was associated with only a slight increase in cost with the largest number of perinatal deaths avoided. For every additional death prevented, it cost only an additional £1,062.80. Detecting FGR using ultrasound and SFH was not supported by this analysis, as its additional benefits were not justified by the increase in costs. Hence it has been dominated by Strategy 3 (strategy 3 is cheaper and more effective than strategy 2).

Table 6.4: Base-case cost-effectiveness results

Strategy	**Expected cost**	**Perinatal deaths saved for every 1000 FGR babies**	**Incremental cost**	**Incremental effect**	**ICER**

No measurement or monitoring of FGR	£2,653,364.4	50			
Measurement of FGR using Prediction model	£2,865,925.1	250	£212,560.65	200	£1,062.80
Measurement of FGR using SFH measurement and ultrasound	£3,444,371.4	125	£578,446.28	-125	Dominated

6.2.2. Sensitivity analysis

The results of the sensitivity analysis have been presented shown in *Table 6.5*. For 100% model sensitivity and 100% model specificity, i.e., when the prediction model provided perfect information regarding who would go on to develop FGR, it cost only an additional £1,023.49 for every additional death prevented compared with Strategy 1 and in line with the base-case results. When the model performance was lowered to being as good as chance, i.e., 50% model sensitivity and 50% model specificity, the results changed slightly. Using the prediction model cost an additional £5,330.07 for every additional death prevented compared with Strategy 2. This increased cost was due to the reduced model performance. Also, at high model performance, Strategy 2 was not cost-effective, but at reduced model performance it was cost-effective, with an ICER of £10,546.76 per additional death saved compared to no monitoring.

Table 6.5: Sensitivity analysis of the cost-effectiveness analysis

Strategy	**Expected cost**	**Perinatal deaths saved for every 1000 FGR babies**	**Incremental cost**	**Incremental effect**	**ICER**
When sensitivity = specificity =100%					
No measurement or monitoring of FGR	£2,653,364.4	50			
Measurement of FGR using Prediction model	£2,858,063.2	250	£204,698.79	200	£1,023.49
Measurement of FGR using SFH measurement and ultrasound	£3,444,371.4	125	£586,308.14	-125	Dominated
When sensitivity = 50% = specificity =50%					
No measurement or monitoring of FGR	£2,653,364.4	50			
Measurement of FGR using SFH measurement and ultrasound	£3,444,371.4	125	£791,006.93	75	£10,546.76
Measurement of FGR using Prediction model	£4,110,630.6	250	£666,259.25	125	£5,330.07

6.2.3. Resource Impact Assessment

Following the evaluability assessment, it was evident that no additional resource impact was expected, other than the impact associated with what has been described in the cost-effectiveness analysis. This is because, there were no further costs associated with either hiring more staff or training staff to use the prediction model. Staff at hospitals are already trained to use prediction models for other diseases. Any additional facilities would have also not been required, nor were patient flows expected to change in the next five years. Thus, it was decided that the impact assessment was not required for the prediction model.

6.3. Summary

In conclusion, it is seen that among the three methods assessed, using the IPPIC prediction model is the most cost-effective method for monitoring FGR, particularly when the model operates at high levels of accuracy. It's implementation, while costing a negligible amount to the NHS has the potential to save many infant lives. However, the actual choice of method may also be influenced by other factors such as availability, practitioner expertise, and patient preferences.

It should be noted that as with most economic evaluations, there is a limitation in our research. A few parameters in this analysis were populated using expert opinion of clinicians and various subject experts due to lack of clinical data. Even though it allowed me to conduct an economic evaluation where there was none, the use of such an approach introduced

uncertainty in the model. I have tried to adjust for this by conducting a sensitivity analysis, however, the best way to eliminate these errors would be via the use of robust clinical data.

Chapter 7

7. Discussions and Conclusions

In this chapter, I have presented a summary of all the important findings from each of the chapters in this thesis. I have also discussed the strengths and limitations of the research. The results were compared to the existing evidence, and the relevance of the results in clinical practice were presented. Finally, I identified gaps in the current research and provided recommendations for future research.

7.1. Summary of findings

The systematic review found 100 eligible studies which assessed the effectiveness of lifestyle interventions on GDM and included data on more than 34,000 women. It resulted in the collection of the largest IPD database (54 trials with 24,693 women) on lifestyle interventions during pregnancy, which can be utilised to explore many complications of pregnancy and maternal outcomes.

Table 7.1: Summary of findings for effect of lifestyle interventions on different definitions of GDM

Intervention	No. of trials	No. of women	OR (95% CI)	95% PI	I^2(%)	τ^2 (95% CI)
GDM (trial authors' definition)						

Overall	54	23,361	0.90 (0.8, 1.02)	0.59, 1.38	24.5	0.04 (0.01, 1.3)
Diet	8	2,974	0.81 (0.69, 0.96)	0.68, 0.97	0	0 (0, 0.17)
Physical activity	18	4,435	0.64 (0.48, 0.85)	0.39, 1.05	0	0.04 (0, 0.43)
Mixed approach	28	15,952	1.05 (0.91, 1.21)	0.79, 1.40	21.3	0.02 (0, 0.12)
GDM (NICE definition)						
Overall	22	11,990	0.98 (0.84, 1.13)	0.7, 1.36	18	0.02 (0, 0.13)
Diet	3	1,812	0.7 (0.33, 1.49)	0.08, 6.47	39	0 (0, 2.8)
Physical activity	5	977	0.65 (0.18, 2.31)	0.04, 11.49	27.8	0.6 (0, 8.8)
Mixed approach	14	9,201	1.1 (0.98, 1.23)	0.99,1.24	0	0 (0, 0.06)
GDM (IADPSG definition)						
Overall	16	6,174	0.86 (0.75, 0.97)	0.75, 0.97	0	0 (0, 0.07)
Diet	2	895	0.71 (0.06, 7.88)	undefined	0	0 (0, 14.9)
Physical activity	3	55	0.92 (0.28, 3.08)	0.03,32.47	0	0 (0, 13.85)
Mixed approach	11	5,224	0.89 (0.76, 1.03)	0.76,1.04	0	0 (0, 0.08)
GDM (modified IADPSG definition)						
Overall	24	13,186	0.92 (0.78, 1.1)	0.52, 1.64	51.4	0.07 (0.02, 0.23)
Diet	3	1,891	0.64 (0.32, 1.3)	0.08, 5.11	48.9	0 (0, 2.78)
Physical activity	7	1,940	0.88 (0.7, 1.09)	0.7, 1.1	0	0 (0, 0.53)
Mixed approach	14	9,355	1.08 (0.89, 1.31)	0.68, 1.72	38.9	0.04 (0, 0.21)
GDM (continuous glucose levels)						
OGTT Test at GA	**No. of trials**	**No. of women**	**MD**	**95% PI**	**I^2(%)**	**τ^2 (95% CI)**
0hr at <24wks	26	34,278	-0.004 (-0.04, 0.03)	-0.04, 0.03	0	0.00 (0.00, 0.01)
2hr at <24wks	26	35,257	-0.01 (-0.08, 0.06)	-0.23, 0.21	46.3	0.01 (0, 0.04)
0hr between 24-30wks	16	22,547	-0.01 (-0.05, 0.02)	-0.05, 0.02	0	0.00 (0.00, 0.00)
2hr between 24-30wks	18	23,624	-0.07 (-0.12, -0.01)	-0.20, 0.07	0	0.00 (0.00, 0.02)
0hr at >30wks	8	12,569	-0.01 (-0.05, 0.03)	-0.05, 0.03	0	0.00 (0.00, 0.04)

2hr at >30wks	7	12,049	-0.03 (-0.22, 0.16)	-0.38, 0.33	13	0.01 (0.00, 0.27)

For all definitions of GDM, lifestyle interventions reduced the odds of developing GDM, ranging from a 2% reduction (NICE definition) to a 14% reduction (IADPSG definition), on average. Taken individually, physical activity had the most impact, ranging from an 8% (IADPSG definition) to a 36% (trial authors' definition) reduction in the odds of developing GDM. Diet also had a considerable impact, reducing the odds of developing GDM from 19% (trial authors' definition) to 36% (modified IADPSG). The results for mixed interventions changed depending on the definition used: it showed a reduction in the odds of developing GDM (by 11% using IADPSG definition) and showed an increase in the odds of developing GDM (5% using trial authors' definition, 10% using NICE definition, 8% using modified IADPSG definition). The reason why mixed interventions tended to be less successful in reducing the odds of developing GDM could be attributed to the challenge of simultaneously adopting multiple behaviour change interventions, which could have impacted adherence and compliance with the intervention. When the effect of the intervention was assessed on continuous glucose measurements (fasting and 2-hour OGTT), it had the potential to either reduce or increase the glucose levels. This indicated that the intervention had no effect on the outcomes.

Adding the aggregate data from the trials which did not contribute their IPD and restricting the IPD meta-analysis to only trials with a low risk of bias, did not alter the main results: lifestyle interventions continued to show a reduction in the odds of developing GDM and physical activity showed the greatest reduction among the individual interventions. Also,

there was no evidence of small study effects – meaning that the smaller trials likely had similar intervention effects compared to larger ones and there was likely no publication bias.

The overall impact of the intervention did not differ among pregnant women with respect to their age, baseline BMI, ethnicity, and parity. Only mothers' education emerged as statistically significant, resulting in a notable decrease in the odds of developing GDM among women with middle or higher education levels compared to those with low education levels, when both sets of women received the intervention. This showed that the interventions might not be reaching the populations who need it the most – specifically, women with low levels of education. Public health bodies should therefore tune their strategy to make these interventions more accessible, so that women with lower education levels may also benefit in reducing their risk of developing GDM.

Despite the lack of statistical significance, women categorised as non-white ethnicity showed the largest decrease in the odds of developing GDM (NICE definition) compared to those from white Caucasian backgrounds, when both groups received the same interventions. Tailored interventions for this subgroup of women may be more effective in preventing GDM and improving maternal and neonatal health outcomes. However, the wide confidence interval suggests uncertainty in this estimate, which in turn, indicates that the effect of ethnicity on GDM may vary across different populations or under different circumstances.

Among women with GDM, the interventions did not result in any significant decrease in the odds of developing maternal and neonatal complications. However, despite these findings

from my IPD meta-analysis, it should be noted that in almost all the included trials, maternal and neonatal complications in women with GDM were not the primary outcomes. Therefore, it is essential that future studies look at the effect of lifestyle interventions in managing the risks associated with these complications in women with GDM to get a clearer picture. Taken individually, physical activity-based interventions showed a significant increase in the odds of developing hypertensive disease, preterm delivery, and SGA babies in women with GDM. At first glance, this seems to suggest that physical activity interventions may have unintended adverse effects on these outcomes, highlighting the need for careful consideration and monitoring of such interventions during pregnancy. However, we need to exercise caution in this interpretation. This is because we do not know whether women continued with intervention after developing GDM. Additionally, it is not known whether those who experienced the complications were the ones who didn't stick to the physical activity plan, or whether any other intervention to manage GDM once diagnosed were offered to the women to prevent adverse complications. In contrast, diet-based interventions showed a decrease in the odds of having LGA babies and preterm delivery compared to controls, in women with GDM. This indicates a potentially beneficial effect of diet-based interventions in managing these particular outcomes among women with GDM. However, further research is warranted to better understand the mechanisms underlying these associations and to optimise intervention strategies to improve maternal and neonatal health outcomes in this population.

When the interventions were analysed with respect to the TIDieR framework, significant differences were found related to the structure of interventions (individual vs group) and prior training of the intervention provider (No/Not Reported vs Yes) with the odds of developing

GDM. None of the other components showed a significant difference in the odds of developing GDM.

The results from the NMA showed that physical activity-based interventions might be more effective or have a more favourable impact on GDM prevention than the other interventions examined. However, it is important to acknowledge that there is uncertainty surrounding the mean rankings of different interventions assessed in the study. This uncertainty implies that there is variability in the effectiveness of the interventions and this needs to be addressed via future research.

Another objective of my thesis was to find out the most cost-effective method of detecting FGR. As discussed in the Introduction, FGR is a serious complication of high-risk pregnancies in general and GDM in particular. There still exists a lack of consensus in its definition, detection, screening and prediction. Towards this end, the IPPIC FGR prediction model addresses the gaps in evidence. This model was already found to have minimal miscalibration and was clinically useful over a wide range of predicted probability thresholds. There was only a concern in understanding whether it would prove to be cost-effective. Further, not just the IPPIC prediction model, these gaps exist in the cost-effectiveness research of all methods of detecting FGR. There is limited knowledge on whether a method is economically viable, even if it performs well under clinical settings. To address this, I conducted a cost-effectiveness analysis for different methods in detecting FGR, from the perspective of the NHS in the UK. From the results of the decision analytical model, it was found that the IPPIC prediction model was the most cost-effective method of detecting FGR compared to strategies of no screening

and using SFH and ultrasound scans, particularly when the prediction model operated at high levels of accuracy.

7.2. Strengths and limitations

The biggest strength of this thesis is the IPD meta-analysis which comprises the largest dataset to date with over 24,000 women, which significantly improves precision and reliability of the results compared to aggregate data meta-analysis.[331] By obtaining access to the raw participant data, I could standardise variables (including harmonising prognostic factors and outcome definitions), effectively address missing data and carry out subgroup analysis. Individual trials cannot estimate subgroup effects as they have relatively small sample sizes and thereby lack the necessary power. Aggregate data meta-analysis is also limited in exploring subgroup effects, as participant level information is not available, and the subgroup effects from individual trials are rarely reported in sufficient detail. These limitations were addressed in my IPD meta-analysis and substantially enhanced the reliability of the findings.[332]. The beneficial effects of lifestyle interventions seen in preventing GDM, particularly physical activity-based interventions, were consistent across all definitions and sensitivity analyses. This showed that the findings were reliable and robust. Additionally, by conducting a network meta-analysis, I was able to compare the efficacy of the interventions, which showed that physical activity was the most effective. This finding will be crucial for informing health policy decisions in prioritising interventions based on their potential impact on GDM prevention.

This piece of research also has some limitations. Firstly, IPD was not obtained for all the identified trials, including most recently published studies, due to time constraints of completing the PhD. This could have potentially impacted the precision of the results. However, the proportion of women in trials which did not share their IPD was substantially lower than the trials for which the IPD was obtained.

Secondly, while the thesis investigated various definitions of GDM, such as NICE, IADPSG, and modified IADPSG, there was a severe lack of raw oral glucose tolerance test (OGTT) results for every required time point across all included IPD trials. Thus, I was not able to redefine or recalculate the GDM diagnosis for the various diagnostic criteria for all the included IPD trials. This in turn restricted the number of IPDs contributing to the analysis of GDM outcomes based on alternative diagnostic criteria. If the test results had been incorporated into the IPD meta-analysis it might have enhanced the precision of the estimates for other GDM outcome definitions. This underscores the significant influence that GDM diagnostic criteria can have on the potential effectiveness of any intervention to prevent the disease. Future trials should not only report binary GDM outcomes but also collect raw individual OGTT test results, as these values would be important for subsequent IPD meta-analysis.[333]

Thirdly, there was a under-reporting on the ethnicity of the women in the IPD meta-analysis. A third of the trials sharing their IPD did not include this information, and among those that did, most of the population was predominantly White. Consequently, the effects of ethnicity within specific subcategories in the non-White group could not be examined due to the broad range of definitions used in the individual studies. It is imperative that disaggregated ethnicity

data be collected and reported in individual studies to facilitate a better understanding of the findings. This will help in ensuring that interventions do not exacerbate existing inequalities.

The IPD obtained in this study were insufficient to determine the optimal components and delivery methods of interventions. The variation in intervention components and delivery observed across trials may have contributed to the heterogeneity in these findings.

Lastly, information on adherence and compliance with intervention was not analysed due to limited data availability. Had this information been available in all the trials, it would have given a better indication of the relative effectiveness of the interventions.

This thesis also explored the cost-effectiveness of different strategies to detect FGR. Its biggest strength is that this economic evaluation contributes to the limited evidence pool by following realistic clinical pathways for pregnant women in the UK. However, due to lack of robust clinical data to populate all the probabilities in the model, there is some amount of uncertainty introduced in the results. This can be eliminated with the publication of more robust clinical information and sensitivity analysis where other model parameters (including effectiveness data, model structure and model cost) are changed. The model could be extended to account for complications affecting mothers and babies post-delivery. Babies born with FGR often require prolonged NICU admissions, which can impact the cost-effectiveness outcomes. However, in this thesis, incorporating these pathways was not feasible due to a lack of reliable clinical data on associated costs and probabilities. More comprehensive data could have helped me to accurately capture the economic impacts. Future research focusing on these

areas could enhance the robustness and applicability of the model. Another limitation is that no internal or external validation of the model was performed due to the limitations in time involved in a PhD. These limitations can be addressed in future research.

7.3. Comparison to existing evidence

At present, there are no national or international guidelines recommending interventions for preventing GDM, most probably due to the uncertainty surrounding the effectiveness of lifestyle interventions.[334] Our results align with previous IPD and aggregate data meta-analysis, indicating that lifestyle interventions during pregnancy—particularly those emphasising physical activity—can mitigate the risk of GDM, with enhanced benefits observed when physical activity is initiated early in pregnancy. [143,261,335] Meta-analyses focusing on dietary interventions for GDM prevention have also indicated a reduction in risk, especially among overweight and obese women.[336] However, unlike IPD analyses, aggregate data meta-analyses lack the ability to adjust for baseline prognostic factors, potentially impacting the accuracy of effect estimates. Moreover, these studies fail to quantify the expected benefits for specific subgroups of women with risk factors such as high BMI, advanced maternal age, minority ethnic backgrounds, and low socioeconomic status.[337] The quality of evidence from these reviews is deemed low due to discrepancies in definitions, small sample sizes resulting in imprecise estimates, and statistical heterogeneity arising from the use of aggregate data. [338]

Using the IPD meta-analysis, robust estimates for preventing GDM (for various diagnostic criteria) were generated, with minimal heterogeneity compared to previously published reviews. My analysis did not reveal any beneficial effects in GDM prevention with the mixed approach, consistent with findings from prior reviews.[331] Among women with middle to high levels of education, a notable decrease in odds of developing GDM was observed compared to those with lower education levels, indicating a potential association between intervention effectiveness and socioeconomic status. This common trend in individually focused interventions highlights a concern within behavioural science regarding socioeconomic disparities.[339,340] This underscores the necessity for tailored approaches that consider socioeconomic factors when developing and implementing preventive strategies. Also, a significant difference was found in the GDM outcomes, based on the structure of the interventions and the prior trainings of the facilitators, according to subgroups outlined in the TIDieR framework. Interventions delivered in group formats demonstrated a greater reduction in the odds of developing GDM compared to those delivered individually. This may be attributed to the social support and shared learning experiences among peers within a group setting, which can motivate behavioural changes.[341] The social dynamics introduced by group settings may also foster positive peer pressure, further encouraging adherence to the intervention.

7.4. Relevance to clinical practice

Currently, there is a lack of widespread practice-level protocols or policy-level guidance focused on pregnancy and the prevention of GDM. The emphasis remains primarily on

screening and treating diagnosed cases rather than prevention. Notably, the Diabetes Prevention Programme (DPP) in the UK does not include the prevention of gestational diabetes within its framework.[342] This IPD meta-analysis offers evidence supporting the reduction of GDM through lifestyle interventions administered during antenatal care. It is advisable to encourage women to adopt any lifestyle intervention that is convenient and available, particularly emphasizing physical activity, as it demonstrated the most significant benefit in reducing the risk of GDM. The notable reduction in GDM risk observed with physical activity-based intervention may be partly attributed to the contrast between the typically more sedentary standard care control groups and the active intervention arm. During pregnancy, women often experience decreased levels of physical activity compared to when they are not pregnant,[335] underscoring the importance of physical activity in GDM prevention. There is a high prevalence of GDM and its associated complications in both women and their and offsprings. Therefore, even a slight shift in the population distribution can have considerable public health impacts if widely implemented.

The focus of research should now shift towards implementation science methodologies, which can help translate research findings into equitable, culturally appropriate, and scalable interventions integrated within supportive health systems and policy frameworks. While this study demonstrated the effectiveness of physical activity-based interventions in preventing GDM, the risks of certain outcomes such as hypertensive disease, preterm delivery and small-for gestational-age babies were paradoxically higher in women who still went on to develop GDM. These discrepancies may stem from variations in intervention adherence and post-diagnosis management, factors which were not accounted for in this study and may differ

across various settings. Clinical management strategies aimed at reducing complications may inadvertently elevate risks such as preterm birth. [343]

When we look at other complications of pregnancy such as FGR, methods such as repeated ultrasound scans and SFH measurements are currently the standard in detecting the disease. Based on my cost-effectiveness analysis, these methods have higher costs with limited returns. On the other hand, the IPPIC risk prediction model can identify individuals at risk for FGR utilising various factors such as maternal characteristics, medical history, and biomarkers before clinical symptoms manifest (early detection). Implementing the risk prediction model is cost-effective and could be conducted as part of routine practice.

7.5. Research recommendations

While this IPD meta-analysis confirms that lifestyle interventions can significantly reduce the risk of gestational diabetes, it reveals that women from higher socioeconomic backgrounds experience greater benefits compared to those from lower socioeconomic backgrounds. This discrepancy persists despite individuals from more disadvantaged backgrounds being predisposed to higher baseline risks due to factors such as increased obesity rates,[344] limited access to nutritious foods, and reduced availability of recreational facilities like gyms.[345] Understanding the behavioural, social, and structural determinants influencing engagement and adherence to interventions is crucial for advancing health equity. This knowledge can help in the customisation of programs to improve uptake of interventions and maximise health benefits across all socioeconomic strata.

Although I did try to explore the impact of socioeconomic status using mother's education as an indicator, there are other socioeconomic factors which were not explored due to data unavailability. Future research should investigate factors such as, deprivation deciles, to gain a more comprehensive understanding of how interventions can support women from lower socioeconomic backgrounds, improve gestational diabetes outcomes, and address long-term health implications for both mothers and children. Future studies should focus on identifying barriers and facilitators at various levels, including individual, interpersonal, community, organizational, and policy levels, to inform adaptations that optimise engagement and outcomes across diverse populations. Research is also required to identify the intersection between socioeconomic status and ethnicity to identify specific cultural factors influencing intervention effectiveness, so that these can be addressed while designing interventions in future programs. There is also a need for more trials to be conducted in more diverse settings and populations, particularly low-middle income countries. More importantly, better funding and collaborative channels should be opened up globally so that study authors from these countries are encouraged to share their IPD. While conducting this research, I found authors from these countries to be less likely to respond to emails, or most likely to stop responding once data is requested. More efforts should be made to make the trial authors aware of the benefits of participating in IPD collaborative groups.

Research investigating customised lifestyle interventions tailored to socioeconomic indicators and individual risk profiles could improve the accuracy of preventive strategies. The adoption of technology for delivering lifestyle interventions is becoming increasingly popular and has

the potential to lower the costs associated with implementing interventions on a large scale.[346] Nevertheless, the efficacy and acceptability of technology-driven solutions should be thoroughly assessed following their development and deployment.

GDM poses lifelong metabolic risks with implications spanning across generations. However, investigating the effects of lifestyle interventions on long-term maternal and offspring outcomes was not within the scope of this thesis. Lifestyle interventions that decrease gestational diabetes rates may potentially offer protective benefits against obesity, impaired glucose tolerance, metabolic syndrome, and type 2 diabetes throughout the child's life, mitigating increasing population trends. These potential multi-generational advantages may then be quantified with the use of well-designed observational follow-up studies. Future researchers in this field can use the platform established by the i-WIP Collaborative Network [261] to prioritise objectives, harmonise variables, plan studies, and impact public policies.

As discussed before, different countries and institutions have different definitions for diagnosing GDM. A uniform definition of GDM would be useful in many ways: firstly, it would improve consistency in clinical practice. Healthcare providers across different regions would be using the same standards for diagnosing and managing GDM, thus reducing the risks of misdiagnosing or underdiagnosing patients. Secondly, it would improve the comparability and monitoring of disease status across studies, enhancing global research and clinical outcomes. However, there are many barriers towards achieving a standardised definition. Diverse findings across studies complicate consensus on thresholds and diagnostic criteria. Some countries also struggle to implement uniform guidelines due to financial or logistical

challenges. It might also be required to tailor the diagnostic criteria to different ethnicities and risk factors, to reflect local health risks accurately. Future research should be undertaken in this sector keeping these issues in mind, to come up with a standardised definition for GDM.

Efforts should also be taken to standardise definitions of lifestyle interventions —such as those involving diet, physical activity, and mixed interventions. At present there is a wide variation in the definitions, as implemented by the trial author. Dietary interventions ranged from broad dietary guidelines to highly structured meal plans, with varying levels of macronutrient and micronutrient restrictions. Physical activity-based interventions also ranged from general guidelines of increased levels of activities, to more structured classes supervised by a trainer, with varying intensity, duration, and frequency. Similarly, mixed approach could be a simple combination of diet and physical activity or could also involve counselling, education, motivational interviewing, or cognitive-behavioural therapy, delivered in person, by phone, or through digital platforms. Standardised definitions minimise ambiguity, ensuring all stakeholders share a common understanding, which benefits all parties involved. For example, participants benefit from clearer instructions and expectations, leading to better adherence and potentially improved outcomes. Uniform definitions will also make it easier for researchers to replicate the interventions more accurately in order to ensure that findings can be validated and generalised across diverse populations. Aggregating data through systematic reviews and meta-analyses will also be easier. Policymakers and health organisations can also use standardised definitions to develop precise recommendations for public health strategies and then monitor trends and conduct impact evaluations of those

initiatives. These issues are especially important for 'mixed interventions' which suffers from a lot of heterogeneity in their definitions.

Of late, researchers have been placing greater importance upon assessing the integrity of the trials being included in an IPD meta-analysis.[347] This involves filtering out untrustworthy trials which have intentional or unintentional errors and biases, based on low-quality, falsified, or fraudulent data. Including these trials can distort the evidence base, leading to potential research waste.[348] While conducting this IPD meta-analysis, I followed the current guidance for best practice [93] by checking for sequence generation, data consistency, data completeness, and baseline imbalance to assess integrity. These data cleaning steps usually aim to resolve issues to include data and do not provide information on which studies not to include in the evidence base due to trustworthiness concerns. However, due to the lack of a formal tool, [349] I did not carry out a systematic data integrity check.

A recent paper by Hunter et al., [350] proposes a new tool for detecting integrity issues in IPD from randomised trials. It includes both aggregate data specific domains (7 domains, 13 items) and IPD-specific domains (8 domains, 18 items), with decision rules. The aggregate data domains include retraction notices and expressions of concern, provision of IPD, communication, ethics approval, trial registration / protocol, randomisation, plausibility. The IPD domains include unusual or repeated data patterns, baseline characteristics, correlations, date violations, patterns of allocation, internal and external inconsistencies, and plausibility of data. Each of the items can be rated as having either no issues, some/minor issue(s), or many/major issue(s), leading to the final inclusion/exclusion of the trial in the evidence base.

Future research needs to be conducted where each of the trials in the present IPD should be assessed using such tools to identify the presence of fraudulent data, if present.

Another recommendation for future research would be to incorporate the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) framework to this IPD meta-analysis evaluate the certainty or quality of evidence for a specific outcome.[351,352] This tool categorises evidence into four levels: high, moderate, low, and very low certainty and could therefore provide more insight into how trustworthy the recommendations from research like this thesis are. These ratings are determined by assessing five key domains: risk of bias, inconsistency in results, indirectness of evidence, imprecision in estimates, and potential publication bias.

The IPPIC FGR prediction model has been shown to perform well and has been validated. However, it can still benefit from further research, which can focus on: improving generalisability by externally validating and recalibrating the model in diverse populations; finding methods to better integrate the model into existing clinical workflows for decision-making; and prospectively monitoring the model performance to detect potential calibration drifts. Future recommendations in terms of the health economic evaluation includes investing more funding into generating the clinical estimates generally used in cost-effectiveness analysis. It should also focus on designing better clinical pathways that closely resemble real world settings and consider implementation strategies for successful adoption of these interventions in healthcare settings. Specifically, a sensitivity analysis can be conducted by

varying the cost of the prediction model to reflect the start-up cost involved in bringing a new test or technology to widespread use.

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9. Appendices

Appendix 1: The search strategy used for the systematic review

The search strategy used for Medline (via Ovid) is as follows:

1. Pregnancy/
2. pregnan*.tw.
3. Gravidity/
4. gravid*.tw.
5. gestation*.tw.
6. Pregnant Women/
7. pregnant wom#n.tw.
8. (child adj3 bearing).tw.
9. childbearing.tw.
10. matern*.tw.
11. or/1-10
12. Weight Gain/ph [Physiology]
13. weight gain*.tw.
14. Weight Loss/ph [Physiology]
15. weight loss*.tw.
16. weight change*.tw.
17. Obesity/dh, me, ph, pc, px, th [Diet Therapy, Metabolism, Physiology, Prevention & Control, Psychology, Therapy]
18. obes*.tw.
19. Adiposity/ph [Physiology]
20. adipos*.tw.
21. Overweight/dh, me, ph, pc, px, th [Diet Therapy, Metabolism, Physiology, Prevention & Control, Psychology, Therapy]
22. overweight*.tw.
23. Body Mass Index/
24. bmi.tw.
25. or/12-24
26. exp Randomized Controlled Trial/
27. "randomized controlled trial".pt.
28. "controlled clinical trial".pt.
29. (random$ or placebo$).tw,sh.
30. ((singl$ or double$ or triple$ or treble$) and (blind$ or mask$)).tw,sh.
31. single-blind method/
32. double-blind method/
33. or/26-32
34. 11 and 25 and 33
35. exp Animals/
36. (rat$ or mouse or mice or hamster$ or animal$ or dog$ or cat$ or bovine or sheep or lamb$).af.

37. 35 or 36
38. Humans/
39. human$.tw,ot,kf.
40. 37 or 38
41. 37 not (37 and 40)
42. 34 not 41

The same search strategy was also adapted for Cochrane Central, HTA, and Pascal is as follows:

(((Pregnancy)
OR (pregnan*)
OR (Gravidity)
OR (gravid*)
OR (gestation*)
OR (Pregnant Women)
OR (pregnant wom$n)
OR (child bearing)
OR (child)
OR (bearing)
OR (childbearing)
OR (matern*))

AND

((Weight Gain)
OR (weight gain*)
OR (Weight Loss)
OR (weight loss*)
OR (weight change*)
OR (Obesity)
OR (obes*)
OR (Adiposity)
OR (adipos*)
OR (Overweight)
OR (overweight*)
OR (Body Mass Index)
OR (bmi))

AND

((Randomized Controlled Trial)
OR ("randomized controlled trial")
OR ("controlled clinical trial")
OR ((random$ OR placebo$))

OR (((singl$ OR double$ OR triple$ OR treble$) AND (blind$ OR mask$)))
OR (single-blind method)
OR (double-blind method)))

AND NOT (Animals OR rat$ OR mouse OR mice OR hamster$ OR animal$ OR dog$ OR cat$ OR bovine OR sheep OR lamb$)

Appendix 2: List of variables sought for iWIP GDM IPD meta-analysis

Variables
Height in cm
Pre-pregnancy weight in kg
Pre-pregnancy BMI
Early pregnancy weight in kg
Early pregnancy BMI
Gestational age at baseline (weeks)
Gestational age at baseline (days)
Gestational age at follow-up (weeks)
Gestational age at follow-up (days)
Follow-up weight in kg
Follow-up BMI
Total weight gain in kg
Weight post delivery
Babies birth weight in gr
Age in years
Land of birth
Parity
Socio-economic status
Race/Ethnicity
Education Mum detail
Education Mum (lower/ middle/ high
Current smoker
Ex-smoker (pre pregnancy)
Allocation
Unit of randomisation
Type of intervention
Details of intervention
Exercise detail
Diet detail
Adherence
Number of fetuses
GA at delivery in weeks
Mode of delivery
Number of times giving birth before this pregnancy
Number of prior pregnancies
Previous Miscarriages
Gravidity (no. of times pregnant)
Obesity (>30 BMI)
Previous large baby (4.5kg+)

Previous GDM
Family history of diabetes
Baseline GDM
Baseline DM
Baseline PIH
Baseline hypertension
GDM test value
GDM test unit
Type of GDM test
OGTT glucose load
OGTT test 0 hour
OGTT test 1 hour
OGTT test 2 hours
OGTT test 3 hours
Time of OGTT test
GA at testing for OGTT
Gestational diabetes
GA at diagnosis of GDM
Management of GDM (diet, metformin, insulin)
Pregnancy induced hypertension
Pre-Eclampsia
Preterm delivery
Caesarean section
Thrombo-embolism
Admission to HDU/ITU
Intrauterine death
Neonatal death
Perinatal death
Neonatal hypoglycaemia
Apgar score at 1 minute
Apgar score at 5 minutes
Small for gestational age
Large for gestational age
Admission to NICU
Shoulder dystocia
Respiratory distress syndrome
Birth trauma

Appendix 3: Data Extraction Template

Variables
Study
Country
Settings
Year
Language
Method of randomisation
Allocation concealment
Blinding
Inclusion criteria
Type of intervention
Details of intervention
Details of control
Primary outcome
Secondary outcomes
Treatment in case of developing GDM
Sample size of controls: Randomised
Sample size of controls: Completed
Number of events in control group
Sample size of interventions: Randomised
Sample size of interventions: Completed
Number of events in intervention group
Definition used to diagnose GDM

Appendix 4: Study characteristics (in brief) for all included trials

Study	Country	Intervention	BMI Category	Number of women
Studies contributing IPD (n=54)				
Al Wattar 2019	UK	Diet	Any BMI category	1252
Arthur 2020	Australia	Mixed	Any BMI category	396
Assaf-Balut 2017	Spain	Diet	Any BMI category	1000
Baciuk 2008	Brazil	Physical Activity	Any BMI category	71
Barakat 2008	Spain	Physical Activity	Any BMI category	160
Barakat 2011	Spain	Physical Activity	Any BMI category	80
Barakat 2012a	Spain	Physical Activity	Any BMI category	290
Barakat 2016	Spain	Physical Activity	Any BMI category	840
Barakat 2018	Spain	Physical Activity	Any BMI category	429
Bisson 2015	Canada	Physical Activity	Obese and above	50
Bogaerts 2012	Belgium	Mixed	Obese and above	197
Bruno 2016	Italy	Mixed	Overweight and above	131
Chao 2017	USA	Mixed	Overweight and above	41
Cordero 2014	Spain	Physical Activity	Any BMI category	257
Dekker 2015	Australia	Physical Activity	Obese and above	35
Dodd 2014	Australia	Mixed	Overweight and above	2142
Dodd 2019	Australia	Mixed	Normal only	641
El Beltagy 2013	Egypt	Mixed	Obese and above	96
Garmendia 2020	Chile	Mixed	Normal and above	4631
Garnaes 2016	Norway	Physical Activity	Overweight and above	91
Guelinckx 2010	Belgium	Mixed	Obese and above	195

Harrison 2013	Australia	Mixed	Overweight and above	228
Hawkins 2014	USA	Mixed	Overweight and above	68
Hui 2011	Canada	Mixed	Any BMI category	190
Hui 2014	Canada	Mixed	Any BMI category	113
Jeffries 2009	Australia	Mixed	Any BMI category	286
Kennelly 2018	Ireland	Mixed	Overweight and above	565
Khaledan 2010	Germany	Physical Activity	Any BMI category	44
Khoury 2005	Norway	Diet	Any BMI category	290
Kunath 2019	Germany	Mixed	Normal and above	2261
Luoto 2011	Finland	Mixed	Overweight and above	442
McCarthy 2016	Australia	Diet	Overweight and above	382
Nascimento 2011	Brazil	Physical Activity	Overweight and above	80
Olson 2018	USA	Mixed	Normal and above	1126
Ong 2008	Australia	Physical Activity	Any BMI category	12
Oostdam 2012	The Netherlands	Physical Activity	Overweight and above	121
Pelaez 2019	Spain	Physical Activity	Any BMI category	345
Perales 2014	Spain	Physical Activity	Any BMI category	184
Petrella 2013	Italy	Mixed	Overweight and above	63
Phelan 2011	USA	Mixed	Normal and above	401
Phelan 2018	USA	Mixed	Overweight and above	264
Poston 2013	UK	Mixed	Obese and above	164
Poston 2015	UK	Mixed	Obese and above	1555
Rauh 2013	Germany	Mixed	Normal and above	250
Renault 2013	Denmark	Mixed	Obese and above	283
Rono 2018	Finland	Mixed	Obese and above	128
Ruiz 2013	Spain	Physical Activity	Any BMI category	962

Sagedal 2016	Norway	Mixed	Normal and above	591
Stafne 2012	Norway	Physical Activity	Any BMI category	702
Vinter 2011	Denmark	Mixed	Obese and above	360
Vitolo 2011	Brazil	Diet	Any BMI category	321
Walsh 2012	Ireland	Diet	Any BMI category	800
Willcox 2017	Denmark	Mixed	Overweight and above	100
Wolff 2008	Denmark	Diet	Obese and above	66
Studies that did not contribute IPD (n=46)				
Abdel-Aziz 2018	Egypt	Diet	Any BMI category	147
Barakat 2012	Spain	Physical Activity	Any BMI category	83
Barakat 2013	Spain	Physical Activity	Any BMI category	428
Barakat 2014	Spain	Physical Activity	Any BMI category	200
Barakat 2019	Spain	Physical Activity	Any BMI category	456
Barquiel 2023	Spain	Mixed	Obese and above	169
Brownfoot 2016	Australia	Mixed	Any BMI category	782
Buckingham 2019	USA	Mixed	Normal and above	47
Cahill 2018	USA	Mixed	Overweight and above	240
Chan 2018	Hong Kong	Mixed	Overweight and above	220
Da Silva 2017	Brazil	Physical Activity	Obese and above	639
Deng 2022	China	Mixed	Overweight and above	84
Ding 2021	China	Mixed	Overweight and above	215
Eslami 2018	Iran	Mixed	Overweight and above	140
Ferrara 2020	USA	Mixed	Overweight and above	394
Gonzalez-Plaza 2022	Spain	Physical Activity	Obese and above	150
Hajian 2020	Iran	Mixed	Overweight only	66
Herring 2016	USA	Mixed	Overweight and above	56

Horn 2018	USA	Mixed	Overweight and above	281
Jing 2015	China	Mixed	Any BMI category	262
Ko 2014	USA	Physical Activity	Any BMI category	1196
Kong 2014	USA	Physical Activity	Overweight and above	37
Korpi-Hyovalti 2012	Finland	Diet	Overweight and above	54
Liu 2022	USA	Mixed	Overweight and above	217
McDonald 2021	USA	Physical Activity	Normal and above	74
Michalopoulou 2023	UK	Diet	Obese and above	51
Okesene-Gafa 2019	New Zealand	Diet	Obese and above	230
Parat 2019	France	Mixed	Overweight and above	206
Perales 2016a	Spain	Physical Activity	Any BMI category	241
Polley 2002	USA	Mixed	Normal and above	110
Price 2012	USA	Physical Activity	Any BMI category	62
Quinlivan 2011	Australia	Diet	Overweight and above	124
Rakhshani 2012	India	Mixed	Obese and above	68
Roland 2023	Denmark	Physical Activity	Normal and above	219
Sadiya 2022	UAE	Mixed	Obese and above	63
Seneviratne 2016	New Zealand	Physical Activity	Overweight and above	74
Simmons 2016	United Kingdom, Ireland, Netherlands, Austria, Poland, Italy, Denmark, and Belgium	Mixed	Obese and above	388
Thornton 2009	USA	Mixed	Obese and above	232
Tomic 2013	Croatia	Physical Activity	Any BMI category	334
Trak-Fellermeier 2020	Puerto Rico	Mixed	Overweight and above	31
Uria-Minguito 2022	Spain	Physical Activity	Any BMI category	260

Vesco 2014	USA	Mixed	Any BMI category	114
Wang 2016	China	Physical Activity	Overweight and above	265
Wang 2023	China	Diet	Any BMI category	519
Xu 2021	China	Diet	Any BMI category	348
Xu 2023	China	Diet	Overweight and above	251

Appendix 5: Detailed clinical characteristics of the randomised controlled trials (IPD)

Al Wattar, 2019	Method of randomisation: 1:1 ratio via a password-protected online data management system. Used minimisation to balance the groups for maternal BMI, parity, and ethnicity. Allocation concealment: Random elements allocated to ensure allocation concealment Blinding: Not reported	Inclusion criteria: · Pregnant women ≥ 16 years · <18 weeks' gestation · Singleton pregnancy · Able to consume nuts and olive oil · Proficient in written and spoken English Exclusion criteria: · History of preexisting diabetes · Gestational diabetes · Chronic renal disease · Autoimmune disease · If they were taking lipid-altering drugs such as statins at the time of booking Number of participants: Intervention, n = 627 Control, n = 625 Type of intervention: Diet	ESTEEM intervention was based on a Mediterranean-style diet: provided participants in the intervention arm with mixed nuts (30 g/day of walnuts, hazelnuts, and almonds) and extra virgin olive oil (0.5 L/week) as the main sources of cooking fat. The trial dietitian and trained researchers delivered the intervention over 3 face-to-face sessions, which included a personalised one-on-one session at 18 weeks' gestation, and 2 further group sessions at 20 and 28 weeks using pre-piloted presentations. In the first visit, the 24-hour food recall technique was used to identify any changes that were needed in the participants' diet to follow a Mediterranean-style pattern. The intervention was made culturally sensitive by providing cooking advice through a bespoke recipe book. Instead, incorporated elements of the Mediterranean diet into the local cuisine by codesigning the recipes with community teams (food-	Received dietary advice as per UK national recommendations for antenatal care and weight management in pregnancy	Maternal outcomes: · GDM · GWG · Pre-eclampsia · Maternal admission to high dependency or intensive care unit · Antepartum haemorrhage · Mode of delivery · Preterm delivery · Maternal anaemia Neonatal outcomes: · Stillbirths · Neonatal deaths · Small-for-gestational age fetus (<10th percentile) · Admission to the neonatal care unit · Birth weight · Hypoxic ischaemic · Encephalopathy

			academy.co.uk). Where possible, we involved women's partners to participate in these sessions. In between the face-to-face sessions, women were followed up twice with phone calls at 24 and 32 weeks' gestation to reinforce the dietary goals and to assess their general health. Adherence was marked by the number of sessions attended.		
Arthur, 2020	Method of randomisation: The lead researcher generated the random allocation sequence Allocation concealment: Sequentially numbered opaque envelopes were used Blinding: Non-blinded study	Inclusion criteria: Women in the second trimester of a singleton pregnancy booking in to deliver in an outer metropolitan hospital in Queensland (Redcliffe Hospital). Exclusion criteria: · Poor English proficiency · Multiple pregnancies · Previous bariatric surgery · Pre-existing medical disease	Women allocated to the treatment group were provided with the same information as controls but were additionally provided with a set of digital scales and a weight diary with instruction to record their weight each day. However, these scales were provided as an incentive to join the trial only and were not standardized.	The women allocated to the control group received written and verbal information regarding appropriate weight gain in pregnancy. The institute of Medicine (IOM) guidelines regarding weight gain in pregnancy are explicitly displayed	Primary outcome: · Percentage weight change above target range (as defined by the IOM guidelines) Secondary outcomes: · GWG Maternal clinical characteristics: · Gestational diabetes · Hypertension or pre-eclampsia · Gestational age at delivery · Method of

		(including diabetes hypertension or renal disease and smoking) Number of participants: Intervention, n = 197 Control, n = 199 Type of intervention: Mixed		in the standardized Queensland Health pregnancy handheld health record provided to all women undertaking public hospital led antenatal care in Queensland and these were discussed with the women enrolled.	delivery · Estimated blood loss Perinatal clinical characteristics: · Weight · Length · Head circumference · APGAR 1 min · APGAR 5 min · Admission to Special · Care Nursery (SCN) · Length of stay in SCN · Fetal distress

Assaf-Balut, 2017	Method of randomisation: Stratified randomization with permutated block-randomization, stratified by age (18-29, 30-34 and >=35), pregestational body mass index (BMI) (<25, 25-29.9 and >=30 kg.m2), parity (1 or >1), and ethnicity (Caucasian, Hispanic and other), in an allocation ratio of (1:1) in blocks of 4-6 Allocation concealment: Not reported Blinding: Participants, staff and the dietician were aware of the allocation assignments. Statistician and research assistant blinded	Inclusion criteria: · Women attending their first gestational visit at 8±12 GW (Visit 0) with FBG < 92 mg/dL. · 18 years old · Single gestation Exclusion criteria: · Gestational age at entry >14 GW · Intolerance to nuts or EVOO · Medical conditions or pharmacological therapy Number of participants: Intervention, n = 500 Control, n = 500 Type of intervention: Mixed	Both the intervention group (IG) and control group (CG) were given the same basic MedDiet recommendations: >=two servings/day of vegetables, >= three servings/day of fruit (avoiding juices), three servings/day of skimmed dairy products, wholegrain cereals, two-three servings of legumes/week, moderate to high consumption of fish; a low consumption of red and processed meat, avoidance of refined grains, processed baked goods, pre-sliced bread, soft drinks and fresh juices, fast foods and precooked meals. They were also recommended to walk >=30 minutes/day. These recommendations were given to women by different parties, depending on the group they were allocated to. In one hand, participants allocated to IG received lifestyle guidance from dieticians one week after inclusion in a unique 1-hour group session. The key IG recommendation was a daily consumption of at least 40 mL of EVOO and a handful (25-30g) of pistachios. To ensure the	All recommendations same as the intervention arm. Except, Controls were advised by midwives to restrict consumption of dietary fat, including EVOO and nuts. These recommendations are provided in local antenatal clinics as part of the available guidelines in pregnancy standard care.	Primary outcome: · GDM Secondary outcomes: · GWG · Pregnancy- induced hypertension · Caesarean section (CS) · Perineal trauma · Shoulder dystocia · Preterm delivery (< 37 GW) · Neonates SGA (small for gestational age,<10 percentile) and LGA (large for gestational age, >90 percentile) according to national charts · Admissions to the Neonatal Intensive Care Unit (NICU)

			consumption of the minimum amount recommended, women were provided at Visit 1 and 2 with 10 L of EVOO and 2 Kg of roasted pistachios each. This way, they had available 1L of EVOO and 150g of roasted pistachios weekly, throughout the pregnancy. The number of visits for the study was alike in both groups. All women were followed-up at first ultrasound visit (Visit 1), at 24±28 GW (Visit 2), third trimester evaluation at 36±38 GW (Visit 3) and at delivery. Nutritional guidance was reinforced at each visit for both groups. Dietary recommendations were individualized at each visit depending on GWG (according to first trimester BMI), in the context of usual recommendations. These recommendations were given in aims to reduce the caloric content of their diet when GWG exceeded the goal, by either the dietician (IG) or the midwife (CG).		

Baciuk, 2008	Method of randomisation: Computer-generated randomisation list of numbers. Volunteers were enrolled sequentially and randomised to one of the two study groups Allocation concealment: Each sequential number corresponded to a sealed opaque envelope containing the information on the randomisation group. Blinding: Outcome assessors	Inclusion criteria: · Pregnant women of < 20 weeks of pregnancy Singleton pregnancy · No gestational risk factors · Received prenatal care at the research institution and intended to give birth there Exclusion criteria: · Practising regular physical exercise · Two or more Caesarean sections · Clinical and/or laboratory diagnoses (neurological, cardiovascular, pulmonary, musculoskeletal or endocrine disorders any disorder that could represent a risk to the woman's health, such as morbid obesity, severe anaemia or vaginal bleeding during pregnancy) Number of participants: Intervention, n=34 Control, n=37 Type of intervention: Physical activity	The counsellors were trained for the study by recording conversations with 10 pregnant women, followed by feedback on performance by other members of the research team. Physical activity (water aerobics): the intervention was the regular, moderate practice of water aerobics for 50 minutes three times a week in an indoor swimming pool with water warmed at 28–30 °C. Water aerobics was initiated following the first physical evaluation and continued up to delivery. The moderate intensity of exercises during the sessions was assured by monitoring patients' heart rate using a heart rate monitor and kept around 70% of one's predicted maximum heart rate.	No intervention	Outcomes: · GDM · Request for analgesia · Caesarean section · Apgar score at 1 minute of ≥ 7 Vaginal delivery · Preterm birth (< 37 weeks) · Low birthweight (< 2500 g), Adequacy of neonatal weight to gestational age · Length of labour (minutes), Birthweight, Gestational age, Weight gain · Body fat (%) · Fat-free mass (%) BMI

Barakat, 2008	Method of randomisation: Not reported Allocation concealment: The investigator responsible for randomly assigning participants did not know in advance which group the next person would be allocated to, and was not part of the assessment Blinding: Outcomes assessors	Inclusion criteria: · Singleton and uncomplicated pregnancy · Not at high risk for preterm delivery (no history of recurrent spontaneous preterm birth, i.e. number of previous preterm deliveries ≤ 1) · Aged 25–35 years · Sedentary before gestation (not exercising > 20 minutes on > 3 days/week) Exclusion criteria: · Not under medical follow-up throughout the entire pregnancy period · Women not planning to give birth in the same obstetrics hospital associated with the study · Women with any serious medical condition preventing them from exercising safely Number of participants: Intervention, n = 80 Control, n = 80 Type of intervention: Physical activity	The programme consisted of 35- to 40-minute sessions thrice weekly from 12–13 weeks of gestation to end of pregnancy (38–39 weeks), with an estimated average of 80 sessions per participant. They were supervised by a trained fitness specialist with each group consisting of 10–12 women. The venue was spacious and well-lit with favourable conditions (altitude 600 m, temperature 19–21 °C and humidity 50–60%). The sessions were accompanied by music. The exercise activity was of light to moderate intensity with a target heart rate of ≤ 80% of maximum predicted heart rate for age (220 – age). All participants were provided with heart rate monitors. Each session included a warm-up (8 minutes), a core session (20 minutes) and a cool-down period (8 minutes). Warm-up and cool-down components involved light stretching exercises for limbs, neck and trunk. In addition, the cool-down period included relaxation exercises. The core portion involved toning and very mild resistance exercises. Toning included shoulder shrugs	The women were asked to maintain their level of activity.	Outcomes: · GDM · GWG · Preterm deliveries · Birthweight · Macrosomia · Birth length · Head circumference · Ponderal index · Apgar score at 1 minute · Apgar score at 5 minutes

			and rotations, arm elevations and leg lateral elevations, pelvic rocks and tilts. The resistance exercises included one set of 10–12 repetitions of each of (1) abdominal curls and (2) the below exercises using barbells (3 kg/exercise) or low to medium resistance bands: bicep curls, arm side lifts and extensions, shoulder elevations, bench press, seated lateral row, leg circles and lateral leg elevations, knee (hamstring) curls and extensions, ankle flexions and extensions. Exercises such as jumping, ballistics, extreme stretching and joint overextension were avoided		

Barakat, 2011	Method of randomisation: Use of a random number table Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Pregnant women in first trimester attending the hospital associated with the study Exclusion criteria: · Not planning to deliver in the same department · Not receiving medical follow-up throughout the pregnancy · Absolute contraindication to aerobic activity in pregnancy · Haemodynamically significant heart disease · Restrictive lung disease · Recent pulmonary embolism (previous 5 years) · Cervical incompetence/cerclage · Multiple pregnancy · Risk of premature labour · PIH/PE · Thrombophlebitis · Acquired infectious disease · Intrauterine growth restriction · Major blood disorders · Absence of prenatal control Number of participants: Intervention, n = 40	The programme consisted of 35- to 45-minute sessions thrice weekly from 6–9 weeks of gestation to the end of pregnancy (38–39 weeks), with an estimated average of 85 sessions per participant. The participants were supervised by a trained fitness specialist with each group consisting of 10–12 women. The venue was spacious and well-lit with favourable conditions (altitude 600 m, temperature 19–21 °C and humidity 50–60%). High room temperatures and humid environment were avoided. The sessions were accompanied by music. The exercise activity was of light to moderate intensity with a target heart rate of ≤ 70% of maximum predicted heart rate for age (220 – age). All participants were provided with heart rate monitors. Each session included a warm-up (7–8 minutes), a core session (25 minutes) and a cool-down period (7–8 minutes). Warm-up and cool-down components involved light stretching exercises for limbs, neck and trunk. In addition, the cool-down period included relaxation and pelvic floor	Standard care	Outcomes: · GDM · GWG · Gestational age at delivery · Type of delivery (normal, instrumental, Caesarean) · Delivery lacerations type · Systolic and diastolic blood pressure · 1-hour glucose level · Birthweight · Macrosomia · Apgar score at 1 minute · Apgar score at 5 minutes

		Control, n = 40 Intervention type: Physical activity	exercises. The core portion involved toning and very mild resistance exercises. Toning included shoulder shrugs and rotations, arm elevations and leg lateral elevations, pelvic rocks and tilts. The resistance exercises included one set of 10–12 repetitions of each of (1) abdominal curls and (2) the below exercises using barbells (3 kg/exercise) or low- to medium- resistance bands: bicep curls, arm side lifts and extensions, shoulder elevations, bench press, seated lateral row, leg circles and lateral leg elevations, knee (hamstring) curls and extensions, ankle flexions and extensions. Exercises such as jumping, ballistics, extreme stretching and joint overextension were avoided. Supine exercises were limited to 2 minutes and exercises involving the Valsalva manoeuvre were avoided. Care was taken to ensure adequate nutrition prior to exercise sessions		

Barakat, 2012a	Method of randomisation: Computer-generated list of random numbers Allocation concealment: Not reported Blinding: Randomisation procedure including sequence generation, allocation concealment, and implementation was made for three different authors to facilitate blinding.	Inclusion criteria: · Healthy uncomplicated singleton pregnancy Exclusion criteria: · Absolute obstetrical contraindication to exercise, [as per ACOG (2002)] · Plans to deliver baby elsewhere · Not receiving antenatal care throughout the pregnancy Participating in another physical activity programme, Regular exercise before pregnancy (four or more times per week) Number of participants: Intervention, n = 138 Control, n = 152 Type of intervention: Physical activity	The programme consisted of 40- to 45-minute sessions thrice weekly from 6 to 9 weeks of gestation to end of pregnancy (38–39 weeks), with an estimated average of 85 sessions per participant. The participants were supervised by a trained fitness specialist with each group consisting of 10–12 women. The venue was spacious and well-lit with favourable conditions (altitude 600 m, temperature 19–21 °C and humidity 50–60%). The sessions were accompanied by music The exercise activity was of light to moderate intensity with a target heart rate of ≤ 70% of maximum predicted heart rate for age (220 – age). All participants were provided with heart	Standard Care	Outcomes: · GDM · GWG · Type of delivery (normal, instrumental, Caesarean) · Gestational age at delivery · Preterm delivery (< 37 weeks) · Blood pressure · 1-hour glucose tolerance test · Birthweight/length · pH of the umbilical cord blood · Apgar score

			rate monitors. Each session included a warm-up (7–8 minutes), a core session (25 minutes) and a cool-down period (7–8 minutes). Warm-up and cool-down components involved light stretching exercises for limbs, neck and trunk The core portion included exercises for arms and abdomen, and aerobic dance to improve posture, strengthen muscles of labour and pelvic floor and prevent lower back pain		

Barakat, 2016	Method of randomisation: The randomisation list was obtained by computer-generated random allocation with a 1:1 ratio Allocation concealment: The allocations were sealed in numbered white envelopes, which were kept in the midwifery facility. Blinding: Not reported	Inclusion criteria: · Women with singleton and uncomplicated pregnancies (no type 1, 2 diabetes or GDM at baseline) · Without history or risk of preterm delivery Exclusion criteria: · Women not planning to give birth in the same obstetric hospital · Women having any serious medical conditions (contraindications) · Women not under medical follow-up throughout pregnancy. Number of participants: Intervention, n=420 Control, n=420 Type of intervention: Physical activity	During pregnancy, the EG trained for three days a week with sessions lasting 50-55 minutes. The training started from weeks 9-11 of pregnancy and continued until the end of the third trimester (weeks 38-39). The program included aerobic exercise, aerobic dance, muscular strength, and flexibility, and met the standards set by ACOG. Women used an HR monitor to ensure HR remained below 70% of the age-predicted maximum. Each session had a gradual warm-up and cool-down period lasting 10-12 minutes, with the main exercise session lasting 25-30 minutes. One set (10–12 reps) was performed using barbells or low-to-medium resistance bands. Exercises in the supine position were not performed for more than 2 minutes.	Women in the control group received general advice from their healthcare provider about the benefits of physical activity. The control group participants had the same number of visits with their healthcare providers as the exercise group during their pregnancy.	Primary outcome: · Pregnancy-induced hypertension Secondary outcomes: · GDM · GWG · Birth weight · Macrosomia (birth weight was >4,000g) · Low birth weight was defined as <2500g.

Barakat, 2018	Method of randomisation: A computer-generated list of random numbers was used to allocate the participants into the study groups. Allocation concealment: The researcher who was in charge of randomly assigning participants to each group did not know in advance which treatment the next person would receive. Blinding: The randomization blinded process (sequence generation, allocation concealment and implementation) was performed by three different authors.	Inclusion criteria: · Women with singleton and uncomplicated pregnancies (no type 1, 2 diabetes or GDM at baseline), · With no history or risk of preterm delivery (i.e.1 previous preterm delivery) · Not participating in any other trial Exclusion criteria: · Women with severe medical conditions (contraindications) that prevent them from exercising safely. · Women not planning to give birth in the same obstetric hospital · With no medical follow-up throughout pregnancy. Number of participants: Intervention, n=227 Control, n=202 Type of intervention: Physical activity	Pregnant women in the intervention group participated in a supervised moderate exercise program three days per week (55–60 min per session) from the 9th to 11th week to the end of the third trimester. Each participant was expected to attend 83-85 group training sessions and used a heart rate monitor to ensure their heart rate was under 70% of the age-predicted maximum. The exercise program met the standards set by the American Congress of Obstetricians and Gynecologists and included sections such as warm-up, aerobic resistance, muscle strengthening, balance exercises, stretching, pelvic floor strengthening, and relaxation. Exercises were performed using barbells or elastic bands, and exercises in the supine position were not performed for more than 2 minutes.	The women in the control group (CG) received standard care during their pregnancy. They had scheduled visits with their obstetricians and midwives every 4-5 weeks until the 36-38th week of pregnancy, and then weekly until delivery, as per hospital protocol. They were given general nutrition and physical activity advice by their healthcare providers. The women were not discouraged from exercising on their own during pregnancy. However, the CG women were asked about their exercise habits once each trimester using a "Decision Algorithm" over the phone, similar to	Primary outcome: · Data corresponding to labour and delivery · Duration of stages, Spontaneous/assisted vaginal delivery · Use of epidural Secondary outcomes: · GDM · GWG · Maternal gestational age · Birth weight · Apgar Scores · pH of the umbilical cord blood

				our previous studies. Question#1: Since the beginning of pregnancy, have you exercised in your leisure time, in a supervised program or on your own? a Answer: No. b Answer: Yes. Question #2: (if the previous response was “b”): Given 7 days a week, how many days per week did you exercise? a Answer: Less than 3 days. b Answer: 3 days or more. Question #3: (if the previous response was “b”): Taking into account the total duration of physical exercise continuously, how long did you exercise every day? a Answer: Less than 20 min each day.	

				b Answer: 20 min or more each day. Interpretation of the “Decision Algorithm”: Pregnant women in the control group who reached level b of these three questions, were excluded from the study.	

Bisson, 2015	Method of randomisation: Randomization was stratified according to parity and based on a computer-generated random numbers table. Allocation concealment: Sealed envelopes were kept in a secure place by a research assistant not involved in the study and provided to a kinesiologist at the time of allocation. Blinding: Due to the nature of the intervention, kinesiologists in charge of training and participants were not blinded to group assignment. However, all assessors and research assistants in charge of data entry and analyses were blinded to participants' allocation	Inclusion criteria: · Women recruited before the end of the 14th week of gestation at family practice obstetrical and ultrasound clinics and in the community. · Pre-pregnancy BMI >= 30.0 kg/m2 · Regardless of previous physical activity levels 18 years or older · Singleton pregnancy planning to deliver in participating hospitals Exclusion criteria: · Women with diabetes or chronic hypertension before pregnancy Number of participants: Intervention, n = 25 Control, n = 25 Type of intervention: Physical activity	The exercise group was offered a supervised exercise program starting at the 15th week of gestation with free membership in a hospital-based conditioning centre, where kinesiologists were always available for counselling. Participants were individually supervised once a week and invited to complete two more sessions/wk. Exercise prescription consisted of 3 weekly 1h sessions, for a total of 36 prescribed sessions over 12 wks. Each session included a 5–10 min warm-up on a stationary ergo cycle, a 15–30 min treadmill walk, a 20 min muscular work-out and a cool-down period. Duration of the cardiovascular training increased progressively from 15 min during the first week to 30 min by the end of the first month. The muscular work-out included dynamic exercises for both lower and upper limbs using the participant's own body weight, small weights, exercising balls and strength equipment with selective charges. Participants started with 1 set of 10–15 repetitions per exercise and progressed to 2 sets of 15	The control group was told to continue usual activities without being restrained from doing physical activity. Both groups were given a pamphlet about the benefits of physical activity and appropriate exercises for pregnant women.	Primary outcome: · Time spent at moderate and vigorous physical activity (MVPA) at 36 weeks of gestation. · Number of accelerometery counts/day (reflecting total activity) · Daily time spent at MVPA in periods >= 10 min · Physical activity in the previous month was measured at each visit using the Pregnancy Physical Activity Questionnaire (PPAQ) · Adherence to exercise Maternal outcomes: · GDM · GWG · Gestational age at delivery (wks) · Caesarean delivery · Gestational hypertension Newborn outcomes: · Birth weight, g · Placental weight, g · Birth weight Z-score · Large for gestational

			repetitions, with intensity adjusted to their tolerance level. To enhance motivation, the muscular work-out was modified every 4 weeks (twice during the intervention period). Exercise intensity was self-monitored with heart rate monitors (Polar FT4, Polar Electro, Finland) and the modified Borg Scale, with targets at 70% of peak heart rate (measured during the fitness test), and/or at a perceived exertion score of 3-5/10. Participants recorded duration and mean heart rate of each session from their monitors on their exercise log. On non-training days, women were advised to be as active as possible.		age · Small for gestational age · Birth length, cm · Head circumference, cm

Bogaerts, 2012	Method of randomisation: Women were randomly assigned to three groups Allocation concealment: Opaque envelopes Blinding: Not reported	Inclusion criteria: · Pregnant women with a BMI of ≥ 29 kg/m2(classified as obese Exclusion criteria: · Gestational age of > 15 weeks · Pre-existing type 1 DM · Multiple pregnancy primary need for nutritional advice · Incomplete knowledge of Dutch language Number of participants: Intervention 1 (Brochure group), n = 58 Intervention 2 (Lifestyle group), n = 76 Control, n = 63 Type of intervention: Mixed	Brochure group: a study-specific brochure containing information on diet and physical activity during pregnancy including tips to limit excessive GWG was provided Lifestyle intervention group: this group received the same brochure but additionally had four antenatal lifestyle intervention sessions. The sessions included a group of up to three women led by a midwife trained in motivational intervention techniques. Each session lasted 1.5 to 2 hours and occurred: before 15 weeks of pregnancy between 18 and 22 weeks between 24 and 28 weeks between 30 and 34 weeks The sessions focused on energy balance and energy expenditure, physical activity and other issues and queries related to pregnancy. The suggested dietary composition was based on national recommendations and included 50–55% carbohydrates, 30–35% fat and 9–11% protein intake. The lifestyle and dietary habits in relation to the participants' 7-day food diaries were discussed, including topics such as reading food labels and	Routine antenatal care as per national guideline 'prenatal care'.	Outcomes: · GDM · GWG (weight at delivery minus self-reported pre-pregnancy weight) · GWG at first trimester (weight at 14 weeks minus pre-pregnancy weight) · GWG at second trimester (weight at 22 weeks minus pre-pregnancy weight) · GWG at third trimester (weight at 34 weeks minus pre-pregnancy weight) · Anxiety (State and Trait Anxiety Inventory) · Depression (10-item Edinburgh Postnatal Depression Scale) · PIH · PE · Induction of labour · Method of delivery (vaginal, vacuum/forceps, elective Caesarean section and emergency Caesarean section) · Birthweight · Apgar score at 1 minute ·

			shopping methods. The intervention was based on the concept of motivational interviewing and the behaviour change model of Prochaska and others. The communication was directive and focused on intrinsic motivation to resolve discrepancies and conflicts about making changes without undue pressure. After each session the women were asked to set personal goals and identify behaviours that need changing. Positive reinforcement was provided to increase self-confidence by identifying and dealing with barriers to behavioural change		Apgar score at 5 minutes

Bruno, 2016	Method of randomisation: The randomisation list was obtained by computer-generated random allocation with a 1:1 ratio Allocation concealment: The allocations were sealed in numbered white envelopes, which were kept in the midwifery facility. Blinding: Not reported.	Inclusion criteria: · Pregnant women with a pre-pregnancy BMI ≥ 25 kg/m2 · Age >18 years · Singleton pregnancy Exclusion criteria: · Chronic diseases (including diabetes mellitus) · Previous GDM · Smoking habits (≥5 cigarettes per day), Hypertension · Medical conditions or dietary supplements that might affect body weight (i.e. thyroid diseases) Previous bariatric surgery, contraindications to exercise and intent to deliver outside of our hospital. Number of participants: Intervention, n=69 Control, n=62 Type of intervention: Mixed	Dietary intervention During enrolment, women attended a session with a dietitian lasting about an hour. The intervention group received a personalized diet (I) with a daily intake of 1500 kcal/day. The prescribed diet included plant foods, cereals, legumes, and fish, with olive oil as the primary source of fat and moderate to no consumption of red wine. The diet provided three main meals and three snacks, with a target macronutrient composition of 55% carbohydrates, 20% protein, and 25% fat. The dietary intervention aimed to reduce the consumption of foods with a high glycaemic index and high saturated fat content while substituting them with healthier alternatives that were based on the taste and preferences of the women. Physical intervention The physical intervention encouraged pregnant women to engage in moderate-intensity activity for at least 30 minutes, three times a week. The 'talk test' was used to monitor the intensity of the exercise. Follow-up	All women in the control group received standard physical activity recommendations. Women were asked about their adherence to the suggested lifestyle.	Maternal outcomes: · GDM · Pregnancy-induced hypertension, Preterm birth · Gestational age at delivery (days) · Induction of labour · Caesarean delivery Neonatal outcomes: · Birth-weight (g), · LGA infants (≥90th centile) · Macrosomia (>4000g) · SGA infants (≤10th centile)

			appointments were scheduled at weeks 16, 20, 28, and 36 of pregnancy with both the gynaecologist and the dietitian. At each follow-up, weight was measured, and dietary habits were assessed.		

Chao, 2017	Method of randomisation: Women were randomly allocated to the control group and the intervention group Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Women up to 16 weeks pregnant were recruited from two obstetrics clinics in Philadelphia, PA, USA. · Self-reported pre-pregnancy BMI between 25 and 50 kg/m2 · 18 and 40 years of age · Ability to read and understand English Exclusion criteria: · Diabetes mellitus · History of gestational diabetes · Twins or other multiples · HIV · Chronic steroid use Number of participants: Intervention, n= 20 Control, n=21 Type of intervention: Mixed	Participants received weekly 20-minute telephone counselling sessions with a dietician trained in behavioural weight-loss treatment. The sessions took place between weeks 16 and 36 of gestation or until delivery. A treatment manual based on Look AHEAD trial was adapted to create a program focusing on appropriate weight gain during pregnancy. The program focused on weight management through nutrition, exercise, and lifestyle changes, aiming to improve adherence to the diet and activity plan, prevent disordered eating, and reduce environmental food cues. Participants maintained food records and aimed for a calorie increase of only 300 per day above pre-pregnancy levels. Weight gain goals were 0.6 lbs/week for overweight and 0.5 lbs/week for obese women in the second and third trimesters. The program also emphasized on improving mood and reducing stress. The women were required to weigh themselves weekly with a WiFi scale. The WiFi scales sent data to	The control group received standard counselling during their obstetrics visits on nutrition, exercise, and weight gain goals. They didn't receive the telephone and WiFi weighing intervention or specific feedback on weight gain progress during pregnancy from study staff. All participants completed monthly 24-hour food recalls using an online system.	Outcomes: · GDM · GWG

			personalized weight charts accessible online for remote weight monitoring and feedback. The study dietician reviewed treatment sessions weekly and provided customized feedback based on weights, food records, and adherence issues.		

Cordero, 2014	Method of randomisation: Women were randomly allocated to the control group and the intervention group Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Pregnant women living in the health care area of Hospital Puerta de Hierro, Madrid, Spain · Age, 33.24 (+/-4.3 yr) · Women without medical obstetric contraindications · Women having medical clearance for physical exercise Exclusion criteria: · Not listed Number of participants: Intervention, n=101 Control, n=156 Type of intervention: Physical activity	Physical Activity Program The physical activity program for pregnant women in the intervention group lasted from weeks 10 to 14, with exercise sessions lasting 50-60 minutes three times a week. The sessions consisted of two on-land sessions in a gym hall and one aquatic water-based activity in small and large pool tanks. The exercise intensity was set using Borg's scale and maternal heart rate was monitored to ensure it did not exceed 60% of the calculated heart rate reserve. A fitness specialist and an obstetrician supervised all sessions to ensure patient safety and adherence to the training program. On-land session. Land sessions were divided into two parts: phase 1 included activation, physical and psychological preparation, and various exercises such as locomotive games, articular movement, and light stretches. Phase 2 consisted of low-impact aerobics, including aerobics, fitness, modern dance, Latin dance, cardio boxing, rhythm, and percussion.	The women in the control group remained inactive.	Primary outcome : · GDM (The National Diabetes Data Group criteria) Secondary outcomes: · GWG · Gestational age at delivery · Type of delivery · Birthweight · Length

			In the next phase, the body was toned through targeted muscular exercises that engaged almost all muscle groups. However, exercises that focused on the abdominal muscles were avoided. To tone different muscle groups, a program of two sets of 15 repetitions was completed. For biceps and triceps, dumbbells weighing 2 kg were used, while lunges were used for quadriceps stimulation. Gluteal work was done on all fours using the body weight. Exercises that involved extreme stretching, the Valsalva manoeuvre, ballistic movements, joint overextension and jumping were specifically avoided. Additionally, the exercises were performed supine for no longer than 2 minutes. The pelvic floor exercise block began with identifying the affected areas, then progressed to practicing slow and fast contractions in different positions. The final phase focused on improving flexibility in the affected muscle groups. The block also included relaxation and visualization exercises, self-massage, and pair massage.		

			Sessions included various exercises accompanied by music with different tempos. The exercises used materials such as foam rubber balls, elastic bands, dumbbells, Swiss balls, and mats. Aquatic activities included upper and lower body movements. The central part of the work was divided between (a) displacements while swimming (except butterfly style) and (b) strength exercises and aquatic activities (propulsion exercises). In the final part of the routine, we did flexibility exercises, relaxation, and breathing in the small pool tank. We used aquatic materials like foam rubber balls, swimming accessories, and weights for resistance. Water temperature was 28.5-29°C.Timing of sessions. Aerobic sessions on land: 10-min warm-up, 20-min choreography, 12-min resistance exercises, 10-min pelvic floor exercises, 8-min stretching. Aquatic activities: 10-minute warm-up, 30-minute core session (swimming laps, step climbs, lunges, strength exercises in water), 10-minute stretching.		

			All sessions were supervised by a qualified fitness specialist (group size: 10-12 women).		

Dekker, 2015	Method of randomisation: Randomisation was done using number allocation through an external service. Stratification of the randomisation was based on BMI (≤40 or >40 kg/m2) and parity (0 or ≥1). Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Aged 18-45 · BMI 30 kg/m2 or greater · Pregnancy care at the RBWH · Willing and able to be randomized to an exercise intervention · Able to provide informed consent Exclusion criteria: · Non-English speaking · Medical or obstetric contraindication to exercise including hemodynamically significant heart disease · Restrictive lung disease · Incompetent cervix (cerclage) · Multiple gestation · Severe anaemia · Chronic bronchitis · Type 1 diabetes · Orthopaedic limitations · Poorly controlled seizure disorder Poorly controlled hyperthyroidism, or a heavy smoker Number of participants: Intervention, n = 19 Control, n = 16 Type of	At 12-weeks' gestation, all participants attended a group education session where written information on exercise, nutrition and adequate GWG was provided. The exercise intervention consisted of an individualised exercise plan meeting the specified energy expenditure requirements based on personal preferences and ability, monthly face-to-face exercise advice by physiotherapists and paper-based diaries for self-monitoring of activity. Women not meeting the specified energy expenditure requirements were offered additional face-to-face support to identify barriers and alterations to the exercise plan.	At 12-weeks' gestation, all participants attended a group education session where written information on exercise, nutrition and adequate GWG was provided.	Maternal outcomes: · GDM · GWG (kg) · Body mass index (kg/m2) · Fasting glucose (mmol/L) Neonatal outcomes: · Gestational age delivery (days) · Five minute Apgar score · C-section (n) (% of group) · Birth weight (g) · Length (cm) · Head circumference (cm) · Abdominal circumference (cm) · Mid upper arm circumference (cm)

		intervention: Physical activity			
Dodd, 2014	Method of randomisation: Randomisation was done by telephoning the central randomisation service, using a computer-generated schedule with balanced variable blocks. Stratification occurred for parity (0 v ≥1), BMI at antenatal booking (25-29.9 v ≥30 Allocation concealment: Not reported Blinding: Outcome assessors	Inclusion criteria: · Women with a BMI of 25 kg/m2 or greater · Singleton pregnancy between 10 and 20 weeks gestation Exclusion criteria: · Women with multiple pregnancies · Type 1 or 2 diabetes diagnosed · prior to pregnancy Number of participants: Intervention, n= 1075 Control, n=1067 Type of intervention: Mixed	Pregnant women who received Lifestyle Advice underwent a comprehensive dietary and lifestyle intervention. The intervention included a range of strategies such as dietary modifications, exercise routines and behavioural changes, which were delivered by a research dietician and trained research assistants. The dietary advice provided to the women was in line with the current Australian standards, which advocated for a balanced intake of carbohydrates, fats and proteins. The women were advised to reduce their consumption of foods high in refined carbohydrates and	Women receiving standard care followed local hospital guidelines without routine advice on diet, exercise or gestational weight.	Outcome: · GDM Primary neonatal outcomes: · The incidence of infants born large for gestational age (birth weight ≥90th centile for gestational age and infant sex) and with birth weight above 4 kg Secondary neonatal outcomes: · Gestational age at birth · Apgar score of 7 or above at 5 minutes of age · Need for resuscitation at birth; birth weight above 4.5 kg or

			saturated fats, increase their intake of fibre and consume two servings of fruits, five servings of vegetables and three servings of dairy daily. To increase physical activity, the women were encouraged to increase their walking and incidental activity.		below 2.5 kg · Birth weight (and Z-scores) · Birth length (and Z-scores) Head circumference (and Z-scores) · Admission to neonatal intensive care unit · Admission to special care baby unit
Dodd, 2019	Method of randomisation: A computer-based randomisation service in the Discipline of Obstetrics and Gynaecology, The University of Adelaide was used. Allocation concealment: Not reported. Blinding: Blinding of participants was not possible given the nature of the intervention, but where possible, antenatal care-providers, outcome assessors and data analysts were blinded to treatment allocation	Inclusion criteria: · Women with a BMI of 18.5 to 24.9 kg/m2 · A singleton pregnancy between 10–20 weeks Exclusion criteria: · Women with multiple pregnancies · Women with diabetes (type 1 or type 2) diagnosed before pregnancy Number of participants: Intervention, n=319 Control, n=322 Type of intervention: Mixed	Women randomized to the Lifestyle Advice Group received an intervention consisting of six sessions throughout their pregnancy. The intervention included three face-to-face sessions with a dietitian, one shortly after trial entry, another at 28 weeks' gestation, and a third provided by a research assistant at 36 weeks' gestation. Additionally, women received three telephone calls from the research assistant at 20, 24, and 32 weeks' gestation. Dietary advice aligned with Australian guidelines. Balance carbs, fats, and proteins. Reduce energy-dense, non-core foods high in carbs and fats. Increase fiber, 2 fruit, 5 veg, 3 dairy daily.	Women who were randomised to the standard care group received their antenatal care according to hospital guidelines, which did not include information relating to dietary intake, physical activity or weight gain during pregnancy. Women in the standard care group received antenatal care without dietary, activity, or weight gain information.	Primary outcome: · Proportion of infants with birth weight > 4 kg Secondary Infant Outcomes: · Preterm birth before 37 weeks' gestation · Perinatal mortality · Infant death · LGA · SGA · Admission to neonatal intensive care unit or special care baby unit · Hyperbilirubinemia · Nerve palsy · Fracture · Birth trauma · Shoulder dystocia Maternal outcomes: · GDM · GWG Hypertension · Pre-eclampsia · Need for

			The intervention was tailored using health decision-making stage theories. Women were given written dietary and activity info, individual diet and activity plan, recipe book and menu plans in first session with a research dietitian. Women were encouraged to set realistic goals for diet and exercise, supported to make changes and monitor progress using the SMART goals approach - specific, measurable, achievable, realistic, and timely criteria to increase success. These principles were reinforced at subsequent contacts with research staff.		and length of antenatal hospital
El Beltagy, 2013	Method of randomisation:Not reported. Allocation concealment: Not reported. Blinding: Not reported.	Inclusion criteria: Obese women at risk of gestational diabetes Exclusion criteria: Not reported Number of participants: Intervention, n = 48 Control, n = 48 Type of intervention: Mixed	Mild physical activity programme and diet modification for 12 weeks	No details	Outcomes · GDM · GWG

Garmendia, 2020	Method of randomisation: The cluster units were randomly allocated to: 1) enhanced implementation of nutritional health care standards [intervention group (IG)], or 2) routine care [control group (CG)]. Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · <15 week of gestation, Between 16 and 40 y of age · Residence within catchment areas of selected PHCCs · No plans to move for the following 2 years Exclusion criteria: · High-risk pregnancies indicated by any of the following guidelines of the Chilean Ministry of Health · Prior history of abortion (>2), children with low birth weight (<2500 g) · Prematurity or perinatal death · Current multiple gestation · Uterine scar · Chronic diseases · Currently underweight (BMI <18.5 kg/m2 Number of participants: Intervention, n=2565 Control, n=2066 Type of intervention: Mixed	CHiMINCs is an intervention that helps primary healthcare centers implement evidence-based guidelines. It involves training healthcare professionals on nutrition, counseling pregnant women on diet and physical activity, providing a PA program, and referring patients to dietitians as needed. Based on gestational weight gain recommendations, the intervention aims to improve communication skills of PHCC professionals. For more information, please refer to the source. At each PHCC visit, midwives provided pregnant women with specific recommendations for their gestational weight gain (GWG), based on a computer chart following IOM 2009 guidelines. They also gave advice on healthy nutrition and physical activity, including the benefits of breastfeeding, avoiding sugary drinks, limiting bread, choosing lean meats and fish, and eating lots of vegetables and fruits. Women were invited to attend one-hour physical activity classes, supervised by trainers three times	The participants in the control group were provided with routine antenatal care and nutritional counseling in accordance with national guidelines. The nutritional status of pregnant women was evaluated based on BMI increases according to gestational age, using Atalah's chart. While the Chilean guidelines included GWG recommendations based on nutritional status, no further advice was given during each prenatal appointment to achieve adequate GWG. Dietary recommendations were provided, including an additional consumption of 350 calories per day	Primary outcomes: · GWG · Adequate birth weight · Birth length · Macrosomia · LGA Secondary outcomes: · GDM · Birth (<37 weeks) · Infants with low birth weight (birth weight <2500 g) · Infant born small for gestational age [birth weight≤10th percentile for gestational age according to Alarcón-Pittaluga curves] · Low score at 1 min and at 5 min on the Apgar score test (score below 7).

			a week, to achieve moderate-intensity activity. Midwives referred pregnant women to dietitians based on specific criteria: gaining over 3 kg in the first trimester, and over 3 kg/month for normal weight women, 2 kg/month for overweight women, and 1.5 kg/month for obese women in the second and third trimesters.	during the second and third trimesters.	
Garnaes, 2016	Method of randomisation: Women were randomly allocated to the control group and the intervention group Allocation concealment: Not reported. Blinding: Not reported.	Inclusion criteria: · Pre-pregnancy BMI ≥ 28 kg/m2 · Age≥ 18 year old · Gestational week < 18 Carrying a singleton live fetus at 11–14 week ultrasound scan. · The participants had to be able to come to St. Olavs Hospital for assessments and exercise classes Exclusion criteria: · High	The exercise group received exercise sessions at the hospital three times weekly, supervised by a physical therapist following guidelines from the American College of Obstetricians and Gynecologists. Sessions included 35 minutes of treadmill walking/jogging and 25 minutes of resistance training. Exercises were adjusted based on each woman's strength level and included pelvic floor exercises.	The control group received standard maternity care from their healthcare providers, following Norwegian guidelines for healthy pregnant women. They were encouraged to continue their regular activities, including exercise.	Primary outcome: · GWG Secondary outcomes: · GDM · BMI · Body composition · Physical activity level · Skinfold thickness · Blood pressure · Incidence of maternal hypertension in late pregnancy

		risk for preterm labor, diseases that could interfere with participation, and habitual exercise training (twice or more weekly) in the period before inclusion. Number of participants: Intervention, n=46 Control, n=45 Type of intervention: Physical activity	Participants also followed a 50-minute home exercise program once a week, including 35 minutes of endurance training and 15 minutes of strength exercises, and did daily pelvic floor muscle exercises. They were given a weight gain curve and encouraged to compare their weight gain with it. Participants attended one motivational interview session during the intervention period.		
Guelinckx, 2010	Method of randomisation: Women were randomly assigned to three different groups Allocation concealment: Not reported Blinding: None	Inclusion criteria: · Obese (BMI of > 29.0 kg/m2, IOM criteria) · White women with gestational age < 15 weeks consecutively attending the antenatal clinic Exclusion criteria: · Pre-existing Diabetes or developing GDM · Multiple pregnancy Gestational age of > 15 weeks · Premature labour (< 37 weeks) · Special nutritional needs such as metabolic disorder, allergic conditions kidney problems and Crohn's disease · Suboptimal	Lifestyle intervention based on a brochure or on active education Passive group: provided with a brochure containing information on diet, physical activity and tips to limit GWG at the first antenatal consultation. Active group: received same brochure and also actively counselled by a trained nutritionist in three group sessions at 15, 20 and 32 weeks of gestation. The sessions had up to five women and lasted 1 hour each. Counselling on balanced diet was based on the official national dietary recommendations (energy intake: 9–11%, proteins; 30–35%, fat; 50–55%, carbohydrates). Aim was to limit intake of energy-dense	No intervention	Outcomes: · GDM · PIH · PE · Chronic hypertension · GWG · Gestational age at delivery · Induction of labour · Caesarean section · Birthweight/length · Macrosomia (birthweight > 4000 g) · Total physical activity score

		knowledge of Dutch language Number of participants: Intervention (active), n = 65 Intervention (passive), n = 65 Control, n = 65 Type of intervention: Mixed	foods, replacing with healthier alternatives such as fruits, increasing wholewheat grains and low-fat dairy products, and reducing saturated fatty acids. General topics such as energy balance, body composition, food labels, and physical activity were discussed. Tips for behavioural modification to reduce emotional eating and binge eating were provided. Total energy intake was not restricted in any group but aimed to do so indirectly by limiting the intake of energy-dense foods. Nutritional data were obtained from 7-day dietary records. A physical activity score was calculated for each trimester of the pregnancy by using the Baecke questionnaire		

Harrison, 2013	Method of randomisation: Computer-generated randomisation Allocation concealment: Sealed opaque envelopes Blinding: Care providers, researchers and outcome assessors were blinded to group allocation	Inclusion criteria: · Gestational age of 12–15 weeks · Overweight [BMI of ≥ 25 or ≥ 23 kg/m2 if high-risk ethnicity (Polynesian, Asian and African populations) or obese (BMI of ≥ 30 kg/m2)] increased risk of GDM as per a validated risk prediction tool · Willing to complete an oral glucose tolerance test at 28 weeks of gestation instead of the standard glucose challenge test at GDM screening Exclusion criteria: · Multiple pregnancies · Type 1 or 2 diabetes · BMI of ≥ 45 kg/m2 · Pre-existing chronic medical conditions · Non-English-speaking Number of participants: Intervention, n = 121 Control, n = 107 Type of intervention: Mixed	Individual four sessions behaviour change lifestyle intervention in antenatal clinic setting at 14–16, 20, 24 and 28 weeks of gestation. The intervention was based on the social cognitive theory, adapted from the study group's earlier lifestyle intervention programme (HeLP-her)The sessions were delivered by a health coach (exercise physiologist). Healthy eating and physical activity were encouraged along with specific dietary advice in pregnancy. Behavioural change strategies were aimed at identifying short-term goals and promoting self-efficacy and self-monitoring. Goals included lifestyle changes such as reducing high-fat or convenience foods, increasing fruit/vegetable intake and increasing frequency of physical activity. Participants themselves set goals. Pedometers and weight-gain charts based on IOM recommendations were provided to monitor the progress. Written Australian dietary and physical activity guidelines and other resources to encourage optimal health, GWG and lifestyle were provided	A single brief education session based on Australian Dietary and Physical Activity Guidelines was provided along with written versions of guidelines. GWG was not discussed	Primary outcome: · GWG (weight was measured at baseline; 12, 16 and 28 weeks of gestation) Secondary outcome : · GDM

Hawkins, 2014	Method of randomisation: Randomisation was stratified by age (< 30 years, ≥ 30 years) and pre-pregnancy BMI (25–30 kg/m2, ≥ 30 kg/m2 with a block size of four. Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Hispanic women aged 18–40 years · Gestational age of < 18 weeks · Overweight or obese (pre-pregnancy BMI ≥ 25 kg/m2) Self-reported participating in < 30 minutes of moderate-intensity activity per week. Exclusion criteria: · History of type 2 diabetes, hypertension, heart disease or chronic renal disease · Current medications that adversely influence glucose tolerance Not planning to continue the pregnancy to term · Contraindications to participating in moderate-intensity physical activity or a low-fat/high-fibre diet · Self-reported participation in ≥ 30 min of moderate-intensity exercise on ≥ 3 days/week or ≥ 20 min of vigorous-	The lifestyle intervention involved 6-monthly in-person counselling sessions and five telephone-delivered booster sessions by bilingual educators. The tailored approach was developed from the transtheoretical Model and Social Cognitive Theory and included motivationally targeted materials, tip sheets, and strategies for overcoming barriers to physical activity. The overall goal of the exercise component was to encourage pregnant women to achieve the American College of Obstetricians and Gynecologists guidelines (ACOG) for physical activity during pregnancy (≥ 30 min of moderate-intensity activity on most days of the week) through increasing walking and developing a more active lifestyle. Personalized physical activity goals were established. Participants tracked progress using a digital pedometer and a physical activity log. The dietary component aimed to decrease intake of foods high in saturated fat and increase dietary fiber. Participants received a low-literacy pictured-based food guide. Health	Standard care	Primary outcomes: · Physical activity · Diet Secondary outcomes: · GDM · GWG Infant birth weight, g Gestational age at delivery, weeks

		intensity exercise on ≥ 1 day/week · Multiple gestation (e.g. twins) Number of participants: Intervention, n=33 Control, n=35 Type of intervention: Mixed	educators assessed the participants' readiness for change and helped them set dietary goals. They provided a low-literacy pictured-based food guide and self-monitoring logs. Booster sessions were conducted to review logs, troubleshoot challenges, introduce new materials and set new goals. Subsequent sessions included a review of logs, problem-solving, new tailored materials, and goal setting. The intervention was developed using a culturally sensitive approach to better meet the needs of the Hispanic population. Intervention fidelity Health educators received extensive training to ensure consistent delivery of the intervention. This included a three-session interviewer training course, booster training sessions, and monthly quality assurance reviews.		

Hui, 2011	Method of randomisation: Computer-generated randomisation allocation table performed by a staff member without involvement in the study design Allocation concealment: Sealed and labelled envelope Blinding: Participants and study staff were not blinded	Inclusion criteria: · No pre-existing GDM Exclusion criteria: · Medical, obstetric Skeletal or muscular disorders that could contraindicate physical exercise during pregnancy Number of participants: Intervention, n = 102 Control, n = 88 Type of intervention: Mixed	Exercise component: a community-based exercise programme – recommended exercise included walking, mild to moderate aerobic, stretching and strength exercises (3–5 times per week for 30–45 minutes/session). The programme started around 20–26 weeks of gestation and finished at 36 weeks. The group exercise sessions were held in air-conditioned gymnasia in community centres. Group floor aerobic, stretching and strength exercises were led by licensed fitness trainers. Participants were instructed to record daily physical activities in activity logs Dietary component: interviews and counselling were provided twice in pregnancy by registered dietitians (at enrolment and 2 months after enrolment). Dietitians provided personalised dietary counselling to participants based on their food choice map interview results, pregnancy week, weight gain and the Health Canada guidelines for food intake in pregnancy	Standard prenatal care recommended according to the Society of Obstetricians and Gynaecologists of Canada were given to the control group. Exercise instruction and dietary intervention were not provided to participants in the control group	Outcomes: · GDM · GWG · LGA · Birthweight

Hui, 2014	Method of randomisation: Randomization was performed using a computer-generated randomisation allocation table. Allocation concealment: Participants received a sealed envelope labelled with the assigned randomisation number, which contained instructions for participants Blinding: The nature of the study meant that participants and study staff were not blinded to the types of interventions.	Inclusion criteria: · Women with less than 20 weeks of pregnancy · No existing diabetes during pregnancy and signed consent form. Exclusion criteria: · Not listed Number of participants: Intervention, n=57 Control, n=56 Type of intervention: Mixed	Intervention program Instructed exercise Participants in the intervention group received a weekly community-based exercise program, including aerobic exercise, stretching, and strength exercises. The program was delivered in weekly group exercise classes or via a DVD format for home use. Participants exercised for 30-45 minutes, 3-5 times a week, from 20-26 gestational weeks to 36 gestational weeks. They recorded their exercise activities in a logbook. Attendance less than 3 times in group exercise, no interest in exercising at home, or no record in the logbook were considered as withdrawal from the study. Dietary intervention Intervention group participants received two individualized dietary consultations using the Food Choice Map (FCM) software, a proven tool for assessing dietary intake. During the consultation, participants and dietitians marked food stickers on a magnetic board to recall food intake. Nutritional information on	Control group participants did not receive exercise or dietary interventions. They received standard prenatal care and a package of information on healthy habits during pregnancy from Health Canada.	Outcomes: · GDM · GWG · Birth weight (g) · Large-for-gestational-age · Caesarean section

			the stickers was scanned into a computer, and daily calorie intake and macronutrients were analyzed instantly. Nutritional recommendations were based on the dietary intake analysis and Health Canada guidelines for food intake during pregnancy, while considering personal food preferences, beliefs, and budgeting. The FCM software helped identify factors relevant to participants' food choices and intake, providing a complete weekly intake and reasons behind food choices. Our unique approach involves creating a personalized, achievable dietary plan that considers participants' food choices. We provide them with a copy of the FCM as their diet plan, and reinforce recommendations at a follow-up consultation two months later.		

Jeffries, 2009	Method of randomisation: A computer random number generator was used to randomly assign women to the intervention and control group. Allocation concealment: number cards allocating women to the two groups were placed in opaque, sequentially numbered envelopes Blinding: Patients	Inclusion criteria: · Pregnant women with gestational age of ≤ 14 weeks Exclusion criteria: · Aged < 18 or > 45 years · Non-English speaking · Multiple pregnancy · Type 1 or 2 diabetes Number of participants: Intervention, n = 148 Control, n = 138 Type of intervention: Diet	Women allocated to the intervention group were given personalised weight measurement card including information on optimal GWG (based on their BMI at the time of recruitment and the US IOM guidelines) and were asked to record their weight at 16, 20, 24, 28, 30, 32 and 34 weeks of gestation. The patient was allowed to choose to measure weight at hospital or at home	No intervention	Outcomes: · GDM · GWG · Birthweight SGA and LGA (weight < 10 centile and > 90 centile) · Preterm delivery · Instrumental delivery · Caesarean delivery · PE · PIH · Apgar score at 5 minutes of < 7 · Hypoglycaemia · Shoulder dystocia · Gestational age at delivery
Kennelly, 2018	Method of randomisation: Randomization was performed using a computer-generated sequence in a ratio of one to one. Allocation concealment: The biostatistician prepared sequentially numbered, sealed opaque envelopes, which were opened at the first study visit. Blinding: As a result of the nature of the intervention, neither participants nor researchers were blinded to the intervention or outcomes.	Inclusion criteria: · Singleton pregnant women between 10 and 15 weeks of gestation · BMIs between 25.0 and 39.9 In possession of a smartphone Exclusion criteria: · Not listed Number of participants: Intervention, n=278 Control, n=287 Type of intervention: Mixed	Participants allocated to the intervention group received standard antenatal care plus a “Healthy Lifestyle Package.” The “Healthy Lifestyle Package” began with a single face-to-face education session conducted individually or in pairs. The information provided during the education session is reinforced through various delivery channels, such as a smartphone application, emails sent every two weeks by the research team, and two follow-up hospital visits at 28 and 34 weeks of gestation. The emails are standardized to cover a specific theme every two weeks, with some discourse between	Women in the control group received standard antenatal care, which in Ireland does not include uniform advice on diet, exercise, or weight gain during pregnancy.	Primary outcome: · GDM Secondary outcome: · GWG · PE or PIH · Onset of labor · Caesarean delivery as primary procedure · Duration of labor (min) · Epidural · 3rd-degree tear · Mode of delivery (Spontaneous vaginal, instrumental, elective caesarean, emergency caesarean)

			researchers and participants when individuals have specific inquiries.		

Khaledan, 2010	Method of randomisation: Not reported Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: Singleton pregnant women with intact fetal membrane were recruited. Exclusion criteria: Exclusion criteria included heart disease associated with significant Hemodynamic changes, chronic pulmonary disease, or cervical insufficiency or correction of cervical insufficiency, multiple pregnancy, permanent vaginal bleeding at second and third trimester of pregnancy, placenta previa after twenty weeks and six of pregnancy, the risk of preterm delivery in the current pregnancy, rupture of fetal membranes, presence of hypertension during pregnancy, severe anemia, unchecked arrhythmia on mother, chronic inflammation of airways, type 1 diabetes	Pregnant women in the experimental group were encouraged to do exercise three times a week for 2 months. This study based on a modified Clapp program includes three sessions per week for eight weeks and the duration of each session was half an hour up to forty five minutes. The first 15 minutes stretching and flexibility was done to make muscles and joints soft and flexible. Then the aerobic stage rally was performed to continue with the rhythm so that the person takes a walk so slowly in a second leg on the ground, and heart rate is maintained within 60 percent of maximum heart rate. This step was started by five minutes in the first session and then in each session one minute added to the time and in eighteenth session the time was reached to 15 minutes and then it remained constant up to the end of meeting. The intensity of exercise was based on 60 percent of maximal heart rate for each person that was calculated through relation 220- age × 60/100 (17). Each time the rate was recorded about three times	Standard care	Outcomes: mode of delivery cause of cesarean section increased maternal and fetal weight neonatal birth weight gestational age.

		with poor control, extreme morbid obesity, very low maternal weight, history of completely sedentary lifestyle, fetal growth restriction in current pregnancy, uncontrolled hypertension, skeletal and structural limitations, seizure disorders, uncontrolled hyperthyroidism and were heavy smokers. Number of participants: Intervention: 20 Control: 24 Type of intervention: Physical activity	(beginning, middle and end of rally) during aerobic exercise by subjects' carotid pulse. After the aerobic phase, all participants used of fluids like water or juice. Then cooling stage for 10 to 15 minutes with light stretching was done in sitting position.		

Khoury, 2005	Method of randomisation: The randomisation list was generated from a table of random numbers drawn up by the investigator who had no contact with the participants Allocation concealment: Consecutively numbered, sealed, opaque envelopes provided to dietitian delivering intervention Blinding: investigators/clinicians and outcomes assessors	Inclusion criteria: Aged 21–38 years · BMI of 19 to 32 kg/m2 · Non-smokers or ex-smokers (quit ≥ 5 years ago) · Not immigrants to Norway from non-Western countries · Single healthy foetus at 17–20 weeks' gestation on ultrasound · No previous pregnancy complications first, second or third pregnancy · Not vegetarian or following a Mediterranean-type diet. Exclusion criteria: · High-risk pregnancies caused by diabetes · Endocrine disease · Hypertension · Drug abuse · Thromboembolic disease or significant cardiac · Gastrointestinal · Pulmonary or haematological disease History of neonatal death, stillbirth · Preterm delivery or recurrent abortion (3+ previous spontaneous abortions) · Ongoing hyperemesis gravidarum or bleeding after gestational age of 12 weeks in the current pregnancy Number of participants: Intervention, n = 141 Control, n = 149 Type of intervention: Diet	Diet/dietary advice: Cholesterol-lowering diet from gestational week 17–20 to birth. Dietitian visits were arranged at inclusion, and at 24, 30 and 36 weeks of gestation. Aims of dietary intervention were to: limit dietary cholesterol to 150 mg/day reduce the intake of saturated fat to 8% of dietary energy target total fat 32% of total energy intake (including 8–9% of energy from polyunsaturated fat and 16–17% from monounsaturated fat), protein 16–17% of energy, and carbohydrates 50–51% of energy tailor energy intake for target at a weight gain of 8 to 14 kg from pre-pregnancy levels encourage the intake of fatty fish, vegetable oils, mainly olive oil and rapeseed oil, nuts, nut butters, margarine based on olive oil or rapeseed oil at least six-a-day of fresh fruits and vegetables was advised prefer low-fat dairy products Subjects were advised to have meat for a main meal twice a week and use legumes, fatty fish, poultry, etc. on other days. Cooking lessons were arranged for special foods. Coffee was limited to two cups/day.	The control group was advised to consume their usual diet, not to introduce more oils, low-fat meat and dairy products than usual. Target weight gain was 8–14 kg and energy intake breakdown of fats, carbohydrate and proteins was same as intervention group.	Outcomes: · GDM · GWG · Gestational age at delivery · Preterm delivery · Preterm stillbirth · Intrauterine growth restriction · Hypertensive complications (PIH/PE) · Fetal distress · Birthweight · Maternal and neonatal lipid profile

Kunath, 2019	Method of randomisation: Women were randomly assigned to the intervention and to the control group. Allocation concealment: Not reported. Blinding: Not reported.	Inclusion criteria: Women with a pre-pregnancy BMI of between ≥ 18.5 kg/m2 and ≤ 40.0 kg/m2 · A singleton pregnancy, ≤12th week of gestation, · Aged between 18 and 43 years · Sufficient German language skills Exclusion criteria: · Women with a multiple or complicated pregnancy · Women with severe pre-existing illnesses Number of participants: Intervention, n=1139 Control, n=1122 Type of intervention: Mixed	Pregnant women in the intervention group had 3 face-to-face counselling sessions during pregnancy and one after delivery. These sessions, led by trained midwives, gynaecologists, or medical assistants, coincided with routine prenatal and postnatal visits for consistency. Each 30-45 minute session promoted a balanced diet, physical activity, and weight monitoring. Women received weight-gain charts tailored to their BMI and were encouraged to follow a diet, be active for 150 minutes weekly, and monitor their progress using a pedometer. Lifestyle counsellors used presentation materials and checklists to ensure consistent guidance. Medical and midwifery practices were supervised for adherence to the program, and lifestyle counselling sessions were reviewed for quality control. Further details can be found in the published study protocol.	Participants in the control group received information leaflets on healthy pregnancy lifestyle and attended routine prenatal care.	Maternal outcomes: · GDM · Hypertension · Preeclampsia/HELLP syndrome · Bleeding · Preterm labour Obstetric outcomes: · Birth mode · Spontaneous birth · Elective caesarean section · Emergency caesarean section · Instrumental vaginal delivery · Induction of labour · Anaesthesia · Weight retention, kg (6–8 weeks postpartum) Neonatal outcomes: · Birth weight, g · Birth length, cm · Head circumference, cm · Large for gestational age (> 90th percentile) · Small for gestational age (< 10th percentile) · Macrosomia (weight > 4500 g) · Preterm birth · Neonatal complications at birth

Luoto, 2011	Method of randomisation: Cluster randomisation of paired municipalities based on number of births, population size, socioeconomic status and type (rural/urban). The municipalities, not participants, were randomised into intervention and study groups Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: At least one of the following risk factors: · BMI of ≥ 25 kg/m2 · GDM · Any signs of glucose intolerance · Macrosomic baby (≥ 4500 g) in any prior pregnancy · Family history of type 1 or 2 diabetes in first- or second-degree relatives · Aged ≥ 40 years Exclusion criteria: at least one of the following: · Abnormal baseline oral glucose tolerance test at 8–12 weeks' gestation (fasting glucose > 5.3 mmol/l, 1-hour glucose > 10.0 mmol/l or 2-hour > 8.6 mmol/l · Pre-existing type 1 or 2 diabetes · Could not speak Finnish aged < 18 years · Twin pregnancy contraindications to physical activity substance abuse, treatment psychiatric illness Number of	Five counselling sessions at 8–12 weeks, 16–18 weeks, 22–24 weeks, 32–34 weeks and 36–37 weeks. One primary session each for physical activity and diet followed by booster sessions. The primary session was 20- to 30-minutes long, but the booster sessions lasted for 10–15 minutes. The interventions were based on PRECEDE–PROCEED and stages of change models. GWG: IOM recommendations were discussed. A BMI-specific weight-gain chart was included. Physical activity: the aim was to increase leisure time physical activity to meet recommendations or maintain it if they had already reached it. The weekly action plan was agreed with each participant and the recommended minimum weekly leisure time physical activity dose was 800 MET minutes. Monthly 2-hour thematic meetings including group exercises were offered and these were led by physiotherapists Diet: advised as per Finnish dietary recommendations – saturated fat ≤ 10%, polyunsaturated fat 5–10% and total fat 25–30% (includes	Routine care including usual dietary and physical activity counselling	Outcomes: · GDM · Weight of the newborn infant adjusted for gestational age

		participants: Intervention, seven municipalities, n = 196 Control, seven municipalities, n = 246 Type of intervention: Mixed	saturated, monounsaturated, polyunsaturated, and trans-fatty acids) of total energy intake and fibre 25 to 35 g/day. They were encouraged to include high-fibre bread, five portions of fruits/vegetables, low-fat dairy products, fish twice weekly, only moderate amounts of spread/oil and restrict sugar containing snacks/drink. The nurse checked if the written objectives were met at each booster visit		

McCarthy, 2016	Method of randomisation: A computer-generated random number table with balanced variable blocks of 4, 6 or 8 was used to randomise treatment allocation. Allocation concealment: Opaque, sequentially numbered sealed envelopes were filled with allocation to standard care or serial self-weighing (intervention). Blinding: Researchers assessing these outcomes were blinded to treatment allocation.	Inclusion criteria: · Overweight or obese (booking or early pregnancy BMI of ≥25.0) · Gestation <20 weeks · Aged at least 18 years · Singleton pregnancy · English-speaking Exclusion criteria: · Women with pre-existing diabetes · Known major fetal abnormality Number of participants: Intervention, n=190 Control, n=192 Type of intervention: Diet	Women were randomly assigned to receive serial self-weighing and basic dietary advice as an intervention. They were given a card that listed their booking BMI and provided guidance on their target gestational weight gain according to the IOM GWG guidelines. The card also had space to chart their serial weights. There were seven general points of weight management advice based on The Australian Guide to Healthy Eating. The research midwife then provided an individual session of approximately 30 minutes to offer simple dietary advice, encourage serial weighing, and discuss weight gain with doctors and/or midwives at subsequent antenatal appointments. Reminder messages were placed in antenatal progress notes of overweight women stating, "I'm in the current study aiming to gain 7-11 kg. Please talk to me about my weight." Obese women were given a similar reminder note recommending a target weight gain of 5-9 kg in their progress notes.	Women randomized to standard care were given a card that listed their booking BMI and advised their target gestational weight gain, while no other changes were made to routine care. Regular weighing was not included.	Primary outcomes: · GDM · Pregnancy-induced hypertension (PIH) · Preeclampsia · Mode of birth other than spontaneous vertex [including elective and emergency caesarean section (CS), vacuum and forceps delivery] · Postpartum haemorrhage (PPH) · Perineal trauma of 3rd or 4th degree · Admission to adult intensive care High dependency unit · Postnatal stay on birth suite of greater than 6 hours · Maternal death. Secondary outcomes: · GWG · CRP · Leptin · Adiponectin · Quality of life (as assessed by the WHOQOL-BREF)

Nascimento, 2011	Method of randomisation: List of random numbers generated by SAS version 9.1 statistical program (SAS Institute Inc., Cary, NC, USA) Allocation concealment: Sealed sequentially numbered opaque envelopes Blinding: Not blinded	Inclusion criteria: · Pre-pregnancy overweight (BMI of 26.0–29.9 kg/m2) or obesity (BMI of ≥ 30.0 kg/m2) · Aged ≥ 18 years · Gestational age of 14 to 24 weeks Exclusion criteria: · Multiple pregnancy Exercising regularly · Contraindications for exercise, such as cervical incompetence · Severe hypertension · Diabetes · Vascular complications and risk of abortion Number of participants: Intervention, n = 39 Control, n = 41 Type of intervention: Physical activity	Exercise protocol: women performed exercise weekly under the guidance of a trained physical therapist. The exercises were light to moderate intensity exercises, with heart rates not exceeding 140 beats per minute. (ACOG recommendations). Standardised research protocol consisting of a 22-exercise sequence was followed. Group or individual exercises lasted 40 minutes with 10 minutes of general stretching, 22 minutes of exercises to strengthen the limb muscles, and 10 minutes of guided relaxation. Home exercise counselling. Women were counselled on home exercise to be done five times/week, with exercises from the protocol or walking. They were required to note the details of daily exercise in a monthly exercise book	Routine antenatal advice and standard nutritional counselling. They were not provided physical activity counselling	Primary outcomes: · GDM · GWG Secondary outcome: · Increased blood pressure Perinatal outcomes: · Caesarean section · Newborn infant weight, · Gestational age at delivery · Preterm birth · Apgar scores at 1 and 5 minutes · LGA · SGA Quality of life (World Health Organization Quality of Life – BREF questionnaire)

Olson, 2018	Method of randomisation: Women were randomly assigned to the intervention and the control group. Allocation concealment: Not reported Blinding: Not reported.	Inclusion criteria: · Age 18-35 years · Gestational age ≤20 weeks at time of enrolment. Exclusion criteria: · BMI < 18.5 and ≥ 35 kg/m2, Multiple gestation · Weight-affecting medical or psychiatric conditions · No e-mail addresses Number of participants: Control group, n=563 (Received treatment, n=500) Pregnancy intervention & postpartum control, n=563 (Received treatment, n= 497) Pregnancy and postpartum intervention, n =563 (received treatment, n=495) Type of intervention: Mixed	Participants who were assigned to the intervention group were granted access to a password-protected intervention website. This self-directed intervention was designed using the Integrative Model of Behaviour Prediction and the Behaviour Model for Persuasive Design and was based on formative research undertaken with the target population. The intervention was developed on the basis of a successful non-electronic pregnancy lifestyle intervention for low-income women. Women in the intervention group had access to three behaviour change tools, including a weight gain tracker, a goal-setting and self-monitoring tool for diet and physical activity, as well as health information such as tips, articles, information about local pregnancy and parenting-related resources, a blogging tool, and an event and appointment reminder.	Women in the placebo control group had access to a password-protected control website. They didn't have access to weight gain tracker and diet/physical activity tools as these were believed to be active intervention components.	Primary outcome: · GWG Secondary outcomes: · GDM · Adherence to the treatment protocol

Ong, 2008	Method of randomisation: Not reported Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Singleton pregnancy · Normal 18-week anatomy scan · No evidence of cardiovascular disease · No pre-existing diabetes Exclusion criteria: · Not listed Number of participants: Intervention, n = 6 Control, n = 6 Type of intervention: Physical activity	Physical activity: home-based exercise programme beginning at week 18 of gestation; three sessions per week of stationary cycling (home-based) supervised exercise. Exercise training was performed at home on an upright stationary cycle ergometer provided to each participant for the study period. Each session consisted of a 10-minute warm-up followed by one or two 15-minute bouts of cycling (with rest periods if necessary). Exercise intensity was controlled by heart rate initially aimed at 50–60% of maximum heart rate and later increased to 60–70% of maximum heart rate. The duration was later increased to 40–45 minutes. Sessions ended with a 10-minute cool-down period of slow pedalling	No intervention	Outcomes: · GDM · GWG · Post-intervention glucose · Insulin levels on oral glucose tolerance test

Oostdam, 2012	Method of randomisation: Computer-generated randomised allocation schedule stratified to the centre where the participants will be followed up. Within each centre, participants were randomly allocated to the study or control group. Block randomisation in blocks of four performed Allocation concealment: Only the programmer of central database knew key of coding related to group assignment Blinding: Independent examiners assessing outcomes blinded but participants and researchers could not be blinded	Inclusion criteria: · Obese (BMI of ≥ 30 kg/m2) or overweight (BMI of ≥ 25 kg/m2) with at least one of the following: · History of macrosomia (birthweight > 97th percentile of gestational age) · History of abnormal glucose tolerance during previous pregnancy · Family history of type 2 diabetes in first-degree relative · Gestational age of 14–20 weeks · Aged > 18 years · Sufficiently fluent in Dutch · Capable of moderately physical activity · Willing to give consent Exclusion criteria: · GDM diagnosis before randomisation · Hypertension (systolic > 160 mmHg and/or diastolic > 100 mmHg) alcohol abuse (i.e. two glasses of alcohol or more per day) · Drug abuse (except for incidental analgesic agents) · Use of	Exercise programme of aerobic and strength training twice weekly under supervision of a trained physiotherapist from recruitment through to remainder of pregnancy. Each session lasted for 60 minutes. Aerobic training provided using cycle ergometers, treadmills, cross-trainers and rowing machines. Strength and aerobic training tailored to individual participants, taking into consideration predicted maximum muscle strength, aerobic capacity and target heart rate. ACOG recommendations were used as a guidance	Usual care by midwives and obstetricians	Primary outcomes: · Fasting plasma glucose · Relative increase in insulin resistance in mother · Neonatal birthweight Secondary outcomes: · GDM · GWG · Maternal serum triglycerides · High-density lipoprotein, · Cholesterol · HbA_{1c} · Maternal physical activity level · Fetal growth · Changes in health-care and non-health-care costs

		medication affecting insulin secretion/sensitivity (antiviral, corticosteroids, antihypertensive drugs) · Sserious pulmonary (chronic obstructive pulmonary disease, exercise-induced asthma) · Cardiac, hepatic or renal (serum creatinine level of < 150 µmol/l) · Impairment malignant disease serious mental or physical impairment impacting on ability to participate in the study Number of participants: Intervention, n = 62 Control, n = 59 Type of intervention: Physical activity			

Pelaez, 2019	Method of randomisation: A statistical randomization computer was used to perform a simple randomization to allocate women to each group. Allocation concealment: Not reported. Blinding: Not reported.	Inclusion criteria: · Healthy women with singleton and uncomplicated gestation · Not participating in other exercise program · Spanish communication skills Exclusion criteria: · Women not planning to give birth at Hospital Universitario de Fuenlabrada · Having any contraindications according to the American College of Obstetricians and Gynecologists' guidelines Number of participants: Intervention, n=115 Control, n=230 Type of intervention: Physical activity	Each session began with an 8-minute warm-up involving walking, movement games, light dancing, and gentle stretching. The 35-minute core section featured low-impact aerobics like dance and adapted cardio-boxing, followed by 10 minutes of resistance training for major muscles, including the core, gluteus, and back. Exercises utilized barbells, elastic bands, and body weight exercises like squats and push-ups. The 15-minute cooldown included pelvic floor exercises, stretching, and relaxation. High-impact exercises and supine positions were avoided. Group activities and social networks fostered motivation, while open communication was encouraged. The program was led by a PhD student in physical activity and sports sciences.	Women in the standard care group received basic care, including monitoring by midwives and obstetricians, along with general nutrition and physical activity counseling. They were advised to increase their intake of milk, fiber, and dairy products while reducing fats and sugars. Moderate-intensity exercises like walking or swimming were recommended, while activities that could cause harm or falls were discouraged. Exercising independently was not discouraged.	Primary outcome: · GWG Secondary outcomes: · GDM · Fetal macrosomia · Type of delivery · Macrosomia (birth weight >4000 g)

Perales, 2014	Method of randomisation: Computer-generated list of random numbers was used Allocation concealment: Not reported Blinding: Researchers and outcome assessors were blinded. Randomisation procedure including sequence generation, allocation concealment, and implementation was made for three different authors to facilitate blinding. Blinding of participants was not possible	Inclusion criteria: · Pregnant women living in Madrid, Spain, who underwent ultrasound examination within 12 weeks of gestation Exclusion criteria: · Absolute obstetrical contraindication to exercise [as per ACOG (2002)] · Plans to deliver baby elsewhere · Not receiving antenatal care throughout the pregnancy · Participating in another physical activity programme regular exercise before pregnancy (four or more times per week) Number of participants: Intervention, n = 101 Control, n = 83 Type of intervention: Physical activity	The program consisted of three 55- to 60-minute sessions per week from early pregnancy (9-12 weeks) until the end (39-40 weeks). Each session included a 5-8 minute warm-up, 25 minutes of aerobic dance and resistance exercises targeting leg, buttock, and abdominal muscles, 10 minutes of balance exercises, 10 minutes of pelvic floor muscle training, and a 5-8 minute cooldown. Exercises in the supine position were limited to two minutes, while extreme stretching, jumping, ballistic movements, joint overextension, and the Valsalva maneuver were avoided. Intensity was kept light to moderate, guided by heart rate (55-60% of maximum) and adjusted via the Borg scale. Sessions of 10-12 women were supervised by a fitness specialist with obstetrician assistance. The hospital venue was spacious and well-lit, maintained at 19-21°C with 50-60% humidity, and accompanied by music. Proper nutrition was ensured before each session.	Standard Care	Outcomes: · GDM · GWG · Percentage of women with excessive weight gain (as per IOM guidelines) · Percentage of women with adequate weight gain (as per IOM guidelines) · Gestation age at delivery · Mode of delivery (normal, instrumental, Caesarean section) · Birthweight · Length of the baby at birth · Head circumference · Apgar score at 1 minute · Apgar score at 5 minutes

Petrella, 2013	Method of randomisation: Computer program that generated random allocation in blocks of three Allocation concealment: Sealed numbered white envelopes Blinding: Both the gynaecologist and dietitian delivering the interventions knew the allocation of the patient.	Inclusion criteria: · Women with singleton pregnancies · Pre-pregnancy BMI of ≥ 25 kg/m2 · Aged > 18 years were recruited during 12th week of gestation from antenatal clinics Exclusion criteria: · Twin pregnancy · Chronic conditions (diabetes, hypertension and untreated thyroid diseases other medical conditions) known to affect bodyweight · Previous GDM · Smoking during pregnancy · Previous bariatric surgery · Women who just started regular physical activity, or used herbal products or dietary supplements known to affect bodyweight · Not intending to deliver at the study centre Number of participants: Intervention, n = 33 Control, n = 30 Type of intervention: Mixed	Diet intervention was initiated by a gynaecologist and a dietitian who gave 1-hour counselling on recommended weight gain in pregnancy. The calorie allowance was 1500 kcal/day with an extra 200 kcal/day (if obese) and 300 kcal/day (if overweight) to account for physical activity programme. The target diet composition was 55% carbohydrate (80% complex low glycaemic index), 20% protein (50% animal and 50% vegetable) and 25% fat (12% monounsaturated, 7% polyunsaturated and 6% saturated fat). The last snack was 2 hours after dinner to prevent overnight hypoglycaemia. The minimum recommended intake of carbohydrates was 225g/day. Exercise intervention was in line with recommendations for general population. Women were advised 30 minutes of moderate intensity activity for a minimum of 3 days a week. Adherence was checked by a pedometer. Women were advised that the exercise intensity should allow them to maintain a conversation (‘talk test’)	The control group received a simple nutritional booklet based on Italian guidelines for a healthy diet during pregnancy.	Primary outcome: · GWG Secondary outcomes: · GDM · Gestational hypertension · Preterm delivery

Phelan, 2011	Method of randomisation: Computerised, randomly changing block sizes, stratified as per clinic and BMI category Allocation concealment: Opaque envelopes Blinding: No blinding	Inclusion criteria: · Aged > 18 years · Singleton pregnancy Gestational age of between 10 and 16 weeks · BMI of between 19.8 and 40 kg/m2 · Non-smoker · Fluent in English · Access to a telephone Exclusion criteria: · Self-reported major health or psychiatric diseases · Weight loss during pregnancy · ≥ three miscarriages Number of participants: Intervention, n = 201 Control, n = 200 Type of intervention: Mixed	Standard care plus a behavioural lifestyle intervention ('Fit for Delivery') to avoid excessive weight gain during pregnancy. The intervention was based on the 1990 IOM guidelines for weight and nutrition during pregnancy and used established principles of learning theory to encourage changes in eating and physical activity. The intervention included a face-to-face interview with an interventionist at the start of treatment. Discussion focused on appropriate GWG targets, physical activity (30 minutes of walking, most days), and calorie intake (20 kcal/kg). Daily self-monitoring of weight, diet and physical activity was recommended along with emphasis on limiting high-fat foods. Weight scales, food diaries and pedometers were given to facilitate self-monitoring. Postcards promoting healthy lifestyle were mailed weekly. Personalised weight gain graphs with feedback were provided following each visit	Standard scheduled visits, monthly until 28 weeks of gestation, fortnightly between 28 and 36 weeks of gestation, weekly until delivery and at 6 weeks after delivery. Participants were provided standard nutrition counselling by physicians, nutritionists, nurses, and counsellors. A brief (15-minute) face-to-face visit with the study interventionist was arranged at recruitment. Women were provided with study newsletters containing general information related to pregnancy such as vitamins, at 2-monthly intervals and post-partum. Women were	Primary outcome: · GWG Secondary outcomes: · GDM · Maternal hypertension · PE · Gestational age at delivery · Preterm delivery · Caesarean section · Infant birthweight · Low birthweight · Macrosomia

Phelan, 2018	Method of randomisation: The randomisation was computer-generated by the study statistician, and women were randomly assigned within the site and by ethnicity (Hispanic or non-Hispanic) to the control and intervention group. Allocation concealment: Not reported. Blinding: Not reported.	Inclusion criteria: · Gestational age between 9 and 16 wk, as assessed by ultrasound · BMI (in kg/m2) ≥25 · English or Spanish speaking · Age ≥18 yrs · Singleton pregnancy Exclusion criteria: · Participants with glycated hemoglobin ≥6.5 · Participants with self-reported major health diseases (e.g., heart disease, cancer, renal disease, and diabetes) · Current substance abuse · Current treatment for a serious psychological disorder (schizophrenia, bipolar disorder), · Contraindications to aerobic exercises · Participant with repeated no-shows or loss of contact during initial screening and other less frequent criteria Number of participants: Intervention, n=132 Control, n=132 Type of intervention: Diet	Telephone support of dietitian was offered thrice during intervention to all women in intervention group. Women failing to meet targets received up to two additional telephone calls/month with personalised advice including structured meal plans until targets were met	Participants in the enhanced-usual care group received the typical prenatal care offered by their providers, including physicians, nurses, nutritionists, and counsellors from the Women, Infants, and Children's Special Supplemental Nutrition Program (WIC).	Outcomes: · GDM · GWG · Preterm delivery (<36 wk) · Caesarean delivery · Preeclampsia · Maternal hypertension · Low birth weight (<2500 g) · Macrosomia (>4000 g)

Poston, 2013	Method of randomisation: Randomisation was performed online. Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · BMI ≥30 kg/m2 · Singleton pregnancy · Gestational age >15+0 weeks and <17+6 weeks' gestation Exclusion criteria: · Unable or unwilling to give written informed consent · Gestation <15+0 weeks and >17+6 weeks · Pre-existing diabetes · Pre-existing essential Hypertension(treated) · Pre-existing renal disease Multiple pregnancy · Systemic lupus erythematosus (SLE) · Antiphospholipid syndrome · Sickle cell disease; Thalassemia · Celiac disease · Currently prescribed metformin · Thyroid disease · Current psychosis Number of participants: Control, n=75 women, n=84 neonates) Intervention, n=79 women and neonates n=85 Type of intervention: Mixed	The intervention used psychological models like control theory and social cognitive theory. We set SMART goals (Specific, Measurable, Achievable, Relevant, and Time-Specific), logged behaviors, and fostered social support through group sessions, offering phone or email sessions for those unable to attend. Dietary Advice: The study assessed the impact of a specific diet on glycemic index (GI), glycemic load, and saturated fat intake. The intervention group was advised to consume low GI foods, replace sugary drinks with low GI alternatives, and reduce saturated fats. Physical Activity Advice: Women in the test group were encouraged to gradually increase their daily physical activity, monitored with a pedometer. They set step goals and maintained these levels post-intervention. The guidelines emphasized moderate-intensity walking. Program Delivery: UK health trainers (HTs) delivered the program, equipped with a manual	Women in the control group attended data collection appointments with the study midwife at 27+0-28+6 and 34+0-36+6 weeks, coinciding with routine antenatal visits.	Maternal outcomes: · GDM · GWG · Pre-eclampsia · Mode of delivery · Blood loss at delivery · Inpatient nights Neonatal outcomes: · Gestational age at delivery · Birthweight · Anthropometry · Inpatient nights

			and training in behavior modification. Women received a handbook, pedometer, logbook, and DVD at their first appointment. Group sessions addressed diet and physical activity, setting weekly goals and discussing barriers and solutions.		

Poston, 2015	Method of randomisation: Randomisation was done online using a computer-generated program. The randomisation schedule was minimised according to ethnicity, parity, age, BMI and centre Allocation concealment: sequential study numbers allocated, irrespective of allocation to the intervention or control group Blinding: Not reported	Inclusion criteria: · Women with a singleton pregnancy between 15 and 18+6 weeks' gestation · BMI of ≥ 30 kg/m2 at first antenatal appointment Exclusion criteria: · No informed consent outside 15 to 18+6 weeks' gestation · Multiple pregnancy · Medical disorders · Hypertension requiring treatment · Pre-existing renal disease · Systemic lupus erythematosus · Sickle cell disease · Antiphospholipid syndrome · Thalassaemia · Celiac disease · Thyroid disease · Current psychosis · On metformin Number of participants: Intervention, n = 783 Control, n = 772 Type of intervention: Mixed	1:1 interview at baseline with a health trainer specifically trained for the study, followed by 8 weekly sessions of 1/1.5hrs each, were strongly recommended to attend a minimum of 5 sessions with other sessions covered by telephone or e-mail. Health trainers cover specific goal-setting, self-monitoring and feedback on performance, problem-solving and use of social support. Women were provided with handbook, DVD of recommended exercise regime, pedometer, logbook for recording weekly goals and steps achieved through pedometer. Exercise advice: to increase pedometer steps and daily activity incrementally; moderate activity in the form of walking encouraged in line with UK RCOG recommendations, with more options depending on baseline activity Diet: to promote healthier eating with no restriction of calories, substitute low glycaemic index for medium/high glycaemic index food, restrict sugar-sweetened beverages but not fruits and reduce saturated fatty acid intake.	Routine antenatal care, explaining the risks of obesity, advising on a healthy diet and safe levels of physical activity	Primary outcomes: · GDM (According to International Association of the Diabetes and Pregnancy Study Groups criteria) · LGA baby (> 90th weight centile) Secondary outcomes: · GWG · PE · Mode of delivery · Induction of labour · Blood loss at delivery · Inpatient nights · Birthweight of baby · Gestational age at delivery · Neonatal death · Neonatal complications

Rauh, 2013	Method of randomisation: Computer-generated cluster randomisation of gynaecological practices into intervention or control groups Allocation concealment: Randomisation performed by a researcher not involved in study design Blinding: Study design did not permit blinding	Inclusion criteria: · Aged > 18 years · Singleton pregnancy · Gestational age of < 18 weeks · BMI of ≥ 18.5 kg/m2 · Language skills: 'sufficient' German Exclusion criteria: · Contraindication to physical activity, such as cervical incompetence, placenta praevia, or persistent bleeding · Pre-pregnancy diabetes · Uncontrolled chronic diseases affecting weight such as thyroid dysfunction or psychiatric diseases Number of participants: Intervention, four practices, n = 167 Control, four practices, n = 83 Type of intervention: Mixed	The intervention group had two counseling sessions at 20 and 30 weeks of pregnancy, lasting 60 and 30 minutes respectively. These sessions offered general lifestyle guidance, focusing on nutrition, physical activity, and appropriate gestational weight gain (GWG). Dietary goals included reducing high-fat, high-calorie foods while increasing low-fat foods, fruits, vegetables, whole grains, and fish. Advice on fats, cooking oils, and spreads was also provided. Physical activity recommendations encouraged 30 minutes of moderate-intensity exercise most days, emphasizing walking, swimming, cycling, and aquatic activities. Participants were given information on local prenatal exercise programs. Weight charts tailored to BMI and following IOM guidelines were provided, and women were asked to monitor their weight weekly. Personalized feedback on diet and exercise was based on their 7-day dietary and physical activity records.	Routine antenatal care including an information leaflet consisting of 10 general statements on a healthy lifestyle during pregnancy not including advice on diet or gaining weight.37	Primary outcome: · GWG Secondary outcomes: · GDM · Birthweight · Length of the baby at birth · Impaired glucose tolerance · Mode of delivery (spontaneous, Caesarean, vacuum) · Induction of labour · Preterm delivery · LGA · SGA

Renault, 2013	Method of randomisation: Randomisation was stratified by parity to ensure equal distribution of primiparous women in all groups Allocation concealment: A web allocation by an independent agency allowed allocation concealment Blinding: Not reported	Inclusion criteria: · BMI of ≥ 30 kg/m2 · Aged > 18 years · Singleton pregnancy · Normal scan at 11–14 weeks' gestation · Gestational age of < 16 weeks at inclusion · Ability to read and speak Danish Exclusion criteria: · Multiple pregnancy · Pre-pregnancy diabetes · Conditions limiting level of physical activity · History of bariatric surgery Alcohol or drug abuse Number of participants: Intervention 1 (exercise), n = 142 Intervention 2 (diet and exercise), n = 142 Control, n = 141 Type of intervention: Mixed	All participants had a consultation with a dietitian after their initial ultrasound at 11-14 weeks of pregnancy. They were advised to follow a low-fat, low-calorie Mediterranean diet (1200-1675 kcal/day), emphasizing fish and oils, in line with Danish guidelines. Women were instructed to aim for less than 5 kg of gestational weight gain (GWG) through diet alone. For physical activity, the dietitian recommended a daily step count of 11,000, and participants were given pedometers. They tracked their steps over seven consecutive days every four weeks. Reminders were sent via text messages to encourage compliance. If 11,000 steps wasn't achievable, they set personalized goals. Participants logged their step count and weight on a chart. Women in the physical activity plus diet group had biweekly consultations (11-13 sessions) with a dietitian, either in person or by phone. They received feedback, encouragement, and tailored advice on diet and weight targets.	Standard care including one consultation with a dietitian after the initial ultrasound scan at 11–14 weeks' gestation. Dietary advice was as per Danish national guidelines for healthy eating. Only oral advice was given and women were asked to aim for a GWG of < 5 kg.	Primary outcome: · GWG Secondary outcomes: · GDM · Gestational hypertension · PE · Induction of labour · Caesarean section (emergency/planned) · Gestational age at delivery · Preterm delivery (28–34 weeks and 34–37 weeks) · Fetal birthweight · Relative birthweight · SGA · LGA · Macrosomia · pH of umbilical cord blood · Placental weight

Rono, 2018	Method of randomisation: Computer-generated randomly permuted blocks. Allocation concealment: An independent statistician outside the study group created the randomisation sequence and prepared the opaque randomisation envelopes. Blinding: Not reported	Inclusion criteria: · Women aged 18 years or older Planning pregnancy within 1 year · BMI ≥30 kg/m2 · Previous history of GDM · With no overt diabetes at inclusion Exclusion criteria: · Women on medications that influence glucose metabolism (such as continuous oral corticosteroids or metformin), Multiple pregnancies · Physical disability · Current substance abuse · Severe psychiatric disorder, Significant difficulty cooperating (such as insufficient Finnish language skill) · Women who did not become pregnant within 1 year from their first visit Number of participants: Intervention: n=65 Control: n=63 Type of intervention: Mixed	Participants in the study received personalized advice on diet and physical activity from trained nurses. They visited a nurse every 3 months before pregnancy and once each trimester during pregnancy and attended local antenatal clinic visits. The intervention group was recommended to engage in physical activity for a minimum of 150 minutes per week at moderate-intensity and adopt an overall active lifestyle. They were also advised to consume healthy foods and reduce the intake of sugar-rich foods. Women with a BMI ≥25 kg/m² were recommended to achieve a 5%-10% weight loss before pregnancy. For women with a pre-pregnancy BMI ≥30 kg/m², it was recommended to avoid weight gain during the first two trimesters.	Participants in both intervention and control groups received the same number of visits to the study nurse, completed the same questionnaires and measurements. They were given information leaflets on healthy diet and exercise and received the usual antenatal care provided to all Finnish pregnant women by public primary healthcare centers, including 10-15 visits to a nurse and 2-3 visits to a physician during pregnancy.	Outcomes: · GDM · Pre-eclampsia · Pregnancy-induced hypertension · Hepatogestosis · Birth weight (g) · Birth weight z-score (SD) Respiratory distress or transient tachypnea of newborn · Congenital malformation.

Ruiz, 2013	Method of randomisation: Computer generated Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Sedentary (not exercising > 20 minutes on > 3 days a week) · Singleton pregnancy · Uncomplicated pregnancy · Not at high risk of preterm delivery (≤ 1 previous preterm delivery) · No participation in any other trial Exclusion criteria: · Contraindication to exercise Number of participants: Intervention, n = 481 Control, n = 481 Type of intervention: Physical activity	The program involved supervised 50- to 55-minute physical activity sessions 3/week from week 9 to 38-39 of pregnancy, averaging 85 sessions per participant. Groups of 10-12 women exercised at a light to moderate intensity, targeting a heart rate ≤60% of the maximum predicted for age. They used heart rate monitors, guided by the Borg scale with a perceived exertion range of 10-12. It included 10min warm-up, a 25-30min core session, and 10min cooldown. Warm-up and cooldown involved walking and light stretching for the limbs, neck, and trunk, plus pelvic floor exercises and relaxation in the cooldown. The core session featured moderate-intensity aerobics weekly and resistance training twice/week. Aerobic dance lasted 3-4min with 1min breaks. Resistance exercises using barbells or elastic bands targeted various muscle groups to improve posture, strengthen labour muscles, and prevent back pain. They avoided jumping, ballistics, extreme stretching, and joint overextension, while supine exercises were limited to 2 min.	Usual care with regular scheduled visits to obstetricians and midwives. Information health-care professionals provided nutrition and physical activity counselling and they were not discouraged from exercising.	Primary outcome: · GWG Secondary outcomes: · GDM · Hypertension · Gestational age at delivery · Type of delivery (natural, instrumental or Caesarean) · Time of dilatation · Expulsion childbirth · Low birthweight · Macrosomia

Sagedal, 2016	Method of randomisation: Computer-generated randomisation list with groups of 20 women. Consecutive randomisation based on the time of completion of consent form, questionnaires and blood tests required prior to enrolment Allocation concealment: Staff providing intervention and checking outcomes were not involved in randomisation Blinding: Not reported.	Inclusion criteria: · Aged ≥ 18 years · BMI of ≥ 19 kg/m2 · Singleton pregnancy · Gestational age of < 20 weeks · Fluency in Norwegian or English Exclusion criteria: · Pre-existing diabetes · Physical disabilities preventing participation in a physical activity programme (as per recommendations of the ACOG) · Current substance abuse · No plans to deliver in the study centres (planned relocation) A total of 606 women were randomised. Of these, 591 were analysed, with 296 in the intervention group and 295 in the control group. Type of intervention: Mixed	Diet: Participants had an initial phone consultation with a physician, nutritionist, or public health graduate student, followed by a follow-up session 4-6 weeks later. Recommendations, based on Norwegian health guidelines, emphasized ten key points, such as increased fruit and vegetable intake, drinking water instead of energy drinks, regular meals, and reducing sugary snacks. The intervention group received pamphlets and password-protected website access to information on healthy eating and exercise during pregnancy. They also attended two evening meetings that included trial details and a cooking class. Physical Activity: Participants attended two weekly supervised exercise sessions at local fitness centers, overseen by physiotherapists or sports science graduates. Sessions included 40 minutes of strength and moderate cardiovascular exercises and 20 minutes of warm-up and stretching, including pelvic floor exercises. Women were encouraged to add an unsupervised weekly session	Standard prenatal care	Outcomes: · GDM · GWG · Infant birthweight and the per cent of LGA (> 90th percentile) infants · Maternal glucose values hormones related to glucose metabolism · Incidence of operative deliveries · Delivery complications

			to achieve 30 minutes of moderate activity, five days a week. Pamphlets and website resources provided guidance on safe pregnancy exercises.		
Stafne, 2012	Method of randomisation: Concealed randomisation in blocks of 30 by web-based computerised procedure Allocation concealment: staff involved with training/assessment not involved in randomisation Blinding: unblinded except glucose and insulin measurements blinded to group allocation	Inclusion criteria: · White women · Aged ≥ 18 years · Singleton live fetus Exclusion criteria: · High-risk pregnancies diseases that could interfere with participation · Women who lived too far (more than 30-minute drive) from the hospitals Number of participants: Intervention, n = 375 Control, n = 327 Type of intervention: Physical activity	Standardised exercise programme including aerobic activity, strength training and balance exercises supervised by a physiotherapist. Training sessions in groups of 8–15 women offered once weekly for 12 weeks (between 20 and 36 weeks of gestation). Each session lasted 60 minutesA written 45-minute home exercise programme (30 minutes of endurance training and 15 minutes of strength/balance exercises) was recommended twice weekly and women were asked to record the exercise activities in personal training diaries. Physical activity was also assessed by questionnaires	Usual care, not discouraged from exercising. Written recommendations on diet, pelvic floor exercises and pregnancy-related lumbopelvic pain	Primary outcome: · GDM Secondary outcomes: · GWG · BMI at follow-up · PE · Gestational hypertension · Caesarean delivery · Operative vaginal delivery · Gestational age at delivery · Birthweight ≥ 4000 g · Apgar score · Admission to the NICU

Vinter, 2011	Method of randomisation: Computerised 1 : 1 randomisation with stratification by smoking status Allocation concealment: Closed envelopes were used Blinding: Not reported	Inclusion criteria: · Aged 18–40 years · Gestational age of 10–14 weeks · BMI of 30–45 kg/m2 (pregestational or first measured weight in pregnancy) Exclusion criteria: · Prior major obstetric complications · Chronic diseases (e.g. diabetes and hypertension) · Positive oral glucose tolerance test in pregnancy · Alcohol/drug abuse · Unable to speak Danish Multiple pregnancy Number of participants: Intervention, n = 180 Control, n = 180 Type of intervention: Mixed	Intervention type: dietary counselling and exercise Diet: trained dietitians provided counselling based on official Danish recommendations at 15, 20, 28 and 35 weeks' gestation. The goal was to limit GWG in pregnancy to 5 kg. Individualised calorie goals based on weight and activity level were provided Physical activity: moderate physical activity lasting 30–60 minutes was encouraged and a pedometer was provided to motivate and improve physical activity. A free full-time membership to local fitness centre was provided for 6 months. This included a 1-hour weekly closed training session with a physiotherapist. The exercises included aerobic activities with elastic bands and light weights, and balance exercises. The women were grouped 4–6 times with the physiotherapist after physical training	Information on purpose and content of the study. Access to a website with advice on diet and physical activity in pregnancy	Outcomes: · GDM · GWG (weight at 35 weeks minus weight at inclusion) · PE · PIH · Caesarean section · Macrosomia/LGA · Admission to the NICU

Vitolo, 2011	Method of randomisation: Not reported Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Pregnant women between 10 and 29 weeks' gestation Exclusion criteria: · Positive human immunodeficiency virus test · Previous diagnosis of GDM · Hypertension · Anaemia · Any conditions preventing women from undertaking exercise in pregnancy · Aged > 35 years Number of participants: Intervention, n = 159 Control, n = 162 Type of intervention: Diet	Dietary counselling according to nutritional status. For pregnant women with low birthweight, this was adopted as a priority to increase the energy density of the diet with the addition of a tablespoon of oil in the main meals, eat two snacks per day of high energy (with sample portions) 100 g once a week and fruit daily. Well-nourished pregnant women received vegetables, legumes, fruits and water six times per day and restricted the consumption of foods rich in fat and cooking oils. For pregnant women with excess weight, between meals (3–4 hours) were prioritised; not repeat the food portions of meals and snacks; restrict daily consumption of soft drinks and sweets, processed foods high in fat and also oil preparations. They were determined daily servings of vegetables, vegetables and fruit. All guidance provided values and portion sizes	The control group did not receive the dietary guidelines but were informed about their nutritional status and were asked to carry on with their prenatal care	Outcomes: · GDM · GWG · PE · Infant birthweight · Prematurity

Walsh, 2012	Method of randomisation: Not reported Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Secundigravid women with previous macrosomic infant (birthweight > 4 kg) Exclusion criteria: · Women with medical disorders including history of GDM, those on any drugs · Unable to give full informed consent · Aged < 18 years · Gestational age > 18 weeks · Multiple pregnancy Number of participants: Intervention, n = 394 Control, n = 406 Type of intervention: Diet	One 2-hour dietary education session with the research dietitian in groups of two to six women. The diet was in line with current recommendations for pregnant women. General advice on healthy eating in pregnancy and following the food pyramid was provided. Women were taught about the rationale for having low glycaemic index food and encouraged to replace high glycaemic index carbohydrates with low glycaemic index alternatives. Written resources were provided after the education session. Women were not advised to reduce their total caloric intake. The research dietitian met women again at 28 and 34 weeks of gestation to reinforce the advice and clarify any doubts. All women completed three food diaries of 3 days each: before dietary intervention and in the second and third trimesters of pregnancy	Routine antenatal care with no specific dietary recommendation or advice about GWG	Outcomes: · GDM · GWG Birthweight · Maternal glucose intolerance

Willcox, 2017	Method of randomisation: Computer-generated random numbers. Allocation concealment: Numbered cards allocating women to either the intervention or control groups were placed in opaque, sequentially numbered envelopes. Blinding: Given the nature of the intervention, participants could not be blinded to group assignment.	Inclusion criteria: · Women with a singleton · Live gestation between 10+-0 and 17+-6 weeks · Self-reported pre-pregnancy BMI >25 kg/m2 · Able to speak, read and write English · Owning a mobile phone Exclusion criteria: · <18 years of age · Multiple pregnancy · Comorbidities requiring significant medical and/or dietary management · Discontinuation of hospital care Number of participants: Intervention, n = 50 Control, n = 50 Type of intervention: Mixed	A trained researcher conducted the initial interview, providing participants with a booklet explaining the txt4two program, weight tracking, and goal setting. They discussed appropriate gestational weight gain (GWG) targets and monitoring, and helped women set nutrition or physical activity goals aligned with evidence-based recommendations. Following interview, participants got 4/5 tailored, interactive text messages weekly, with custom info for their gestational week, encouraging healthy behaviors, and tracking individual goals and GWG. Messages were mapped to behaviour change techniques and allowed women to choose text frequency (weekly or fortnightly) for weight and goal reviews. They included a study-specific website with details and short videos featuring health professionals explaining the benefits and components. A private Facebook chat page allowed participants to interact with each other and health professionals. Both the website and chat page were promoted via text messages.	As part of usual care, participants in both intervention and standard care groups were mailed brief information brochures containing advice regarding diet and physical activity prior to the first hospital visit and were also encouraged to weigh at first visit.	Outcomes: · GDM · GWG · Diet and physical activity were assessed at baseline and the 36-week visit.

Wolff, 2008	Method of randomisation: Computerised randomisation Allocation concealment: Not reported Blinding: investigators/clinicians	Inclusion criteria: · Caucasian women · BMI of ≥ 30 kg/m2 early pregnancy (15 ± 3 weeks of gestation) · Non-diabetic at inclusion Exclusion criteria: · Smoking · Aged < 18 or > 45 years · Multiple pregnancy · Medical complications known to affect fetal growth · Adversely contraindication for limiting weight gain Number of participants: Intervention, n = 28 Control, n = 38 Type of intervention: Diet	Ten 1-hour dietary consultations (healthy diet, restriction of energy intake): the intervention group received 10 consultations of 1 hour each with a trained dietitian during the pregnancy. Women were asked to eat a healthy diet according to the official Danish dietary recommendations (fat intake, maximum 30 energy per cent; protein intake, 15–20 energy per cent; carbohydrate intake, 50–55 energy per cent). Energy intake was restricted on the basis of individually estimated energy requirements and estimated energy requirements of fetal growth [energy requirement = basal metabolic rate × 1.4 (physical activity level factor of 1.2 + 0.2 added to cover energetic cost of fetal growth)]	No intervention	Outcomes: · GDM · GWG · Gestational age at delivery · PIH · PE · Prolonged pregnancy · Caesarean delivery · Birthweight · Placental weight · Infant length · Head circumference · Abdominal circumference

Appendix 6: Detailed clinical characteristics of the randomised controlled trials (non-IPD)

Abdel-Aziz, 2018	Method of randomisation: A computer-generated randomisation using an allocation table. Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: Women between 20 and 30 years in the first trimester (<12 weeks of gestation) of pregnancy. Women attending the ANC clinic. Without a history of any chronic medical problems Exclusion criteria: Women under 18 years of age. With a previous history of abortion, stillbirth and any chronic disease. Women on any medications that might interfere with their body weight (steroids, diuretics, and thyroid hormones). Number of participants: Intervention, n=75 Control group, n=72 Type of intervention: Diet	Women in the intervention group received standard care delivered at the centre group and attended six extra counselling sessions with the nutrition counsellor, with face-to-face appointments every 2 weeks during the implementation phase. The nutrition counsellor assessed participants' compliance with the intervention sessions by registering the number of counselling sessions attended by the participants and illustrated the response rate of attendance. All women in the intervention group received three brief (i.e., 10–15 minutes) supportive phone calls from the nutrition counsellor during the intervention. Nutrition counselling message The nutrition counsellor who was a member of the research team discussed with the participants how to	Participants of the control group received standard maternity care. Women in standard care attended their regularly scheduled visits with their prenatal care providers, which typically occurred monthly until 28 weeks of gestation, biweekly for 28–36 weeks of gestation, and weekly until delivery. Women received standard nutrition counselling provided by the physicians and nurses based on the Maternal and child Health Program components.	Maternal outcomes: • Gestational weight gain • Anaemia • Gestational diabetes • Pregnancy-induced hypertension • Caesarean section Fetal outcomes: • Macrosomia • Preterm

			control weight gain during pregnancy and how to maintain or optimise a healthy lifestyle in a period of physical and mental changes. Each counselling session took about 20 minutes, except for the first session, which took approximately half an hour; the counsellor explained the aim of the study and the intervention again. The counsellor provided nutritional guidance to pregnant women based on dietary guidelines. They aimed to improve eating habits, educate participants on healthier food choices, and prevent EGWG. Participants were taught to choose whole grains, fruits and vegetables, healthy fats and protein sources, limit intake of unhealthy foods and drinks, and avoid unhealthy habits. Walking for 30 minutes three times per week was encouraged.		
Barakat, 2012	Method of randomisation Not reported	Inclusion criteria: Women with singleton pregnancies. Women	Exercise: Participants followed a physical conditioning program	Standard care	Maternal outcomes: • 50 g maternal

	Allocation concealment Not reported Blinding: Not reported	with uncomplicated pregnancies and healthy. Exclusion criteria: Women with the following obstetric contraindications: Active illness of the myocardium. Heart insufficiency. Rheumatic heart illness (type II or above). Thrombophlebitis. Recent pulmonary embolism (last 5 years). Acquired infectious disease. Cervical incompetence. Multiple pregnancy. Genital haemorrhage. Premature breakage of the ovular membranes. Retarded intrauterine. Development. Fetal macrosomia. Serious blood disease. Serious hypertension. Absence of prenatal control. Suspects of fetal suffering. Risk of premature labour. Prepregnant type 1 or 2 diabetes. Number of participants:	consisting of three 35-45 minute sessions per week (on Mondays, Wednesdays, and Fridays). Two of these sessions were land-based aerobic exercises, while the third session involved aquatic activities. The program started at weeks 6-9 of the pregnancy and continued until the end of the third trimester (weeks 38-39). The original plan was for each participant to complete an average of 85 training sessions, with exercise intensity monitored using a heart rate (HR) monitor (Accurex Plus; Polar Electro OY, Kempele, Finland). Participants were instructed to maintain light to moderate exercise intensity, keeping their HR consistently under 70% of their age-predicted maximum HR value (220 minus age). Land exercise: Each workout session consisted of a 7-8 minute warm-up and cool-down period, including walking and light stretching		glucose screen (MGS) • GWG • GDM Pregnancy outcomes : Type of delivery: • Instrumental delivery • Caesarean section • Systolic blood pressure (mm Hg) • Diastolic blood pressure (mm Hg) Fetal outcomes: • Birth weigh • Apgar score 1 min • Apgar score 5 min • Size of newborn

		Intervention, n= 40 Control, n= 43 Type of intervention: Physical activity	exercises targeting most muscle groups. The 25-minute core session featured toning and light resistance exercises, targeting major muscle groups like the pectoral, dorsal, and shoulder muscles. Participants completed one set of 10-12 repetitions of abdominal curls and exercises using either barbells (3 kg/exercise) or low-to-medium resistance bands (Therabands). Exercises that involved extreme stretching, joint overextension, ballistic movements, or jumps were avoided. Lying on their back was limited to a maximum of 2 minutes. The exercise program included workouts that target major muscle groups such as the arms and abdomen. These exercises help improve your posture, prevent low back pain, and strengthen the muscles that are important for labor and the pelvic floor during the third trimester. Additionally,		

			the program includes an aerobic dance routine every two weeks. Aquatic activities: Exercising in water minimizes joint impact. Aquatic sessions include swimming, jogging, walking, stretching, lunges, step climbs, skiing, and strength exercises. Tools like noodles, floats, and gloves are used for muscle conditioning. Water was kept at 28-29°C and precautions were taken to prevent infections.		
Barakat, 2013	Method of Randomisation: Women were randomly assigned to control or intervention groups. Allocation Concealment: The researcher responsible for random assignments did not know the next participant's	Inclusion criteria: Being sedentary (not exercising >20 min on >3 days/week) Singleton, uncomplicated gestation Not at high risk for preterm delivery (ie, ≤1 previous preterm delivery). Exclusion criteria: Women not planning to give birth in the same obstetrics hospital department (Hospital Severo Ochoa, Madrid, Spain) and not under	Exercise: The exercise intervention group trained for 50-55 minutes, three days a week (Mon, Wed, Fri) from week 10 to 12 of pregnancy until the end of the third trimester (weeks 38-39). The intervention included aerobic, strength, and flexibility exercises, met the standards of the American College of Obstetricians and Gynaecologists, and used a heart rate monitor to maintain moderate exercise intensity. The participants'	The control group received general advice on physical activity from their midwife and had the same prenatal care and visits with healthcare providers (midwives, obstetricians and family doctors) as the exercise group. They were not discouraged from exercising on their own.	Primary outcomes: • GWG • GDM-WHO criteria • GDM IADPSG criteria Secondary outcomes: • Birth weight gestational age • Caesarean delivery • Apgar score 1 min Apgar score 5 min

	treatment and was not involved in assessments. Blinding: Assessment staff remained blinded to the participants' group assignments.	medical follow-up throughout the entire pregnancy period. Women with medical conditions preventing them from exercising. Number of participants: Intervention, n= 210 Control, n= 218 Type of intervention: Physical activity	heart rate was consistently below 70% of their age-predicted maximum, and the rate of perceived exertion (RPE) was between 10 to 12, corresponding to 'fairly light' and 'somewhat hard' exertion. The participants began with a 10-12 minute gradual warm-up and followed it with a similar cool-down period. They engaged in walking and stretched almost all the muscle groups of their body. The session lasted 25-30 minutes and included moderate-intensity resistance exercises that toned the muscles and mobilized the joints. They avoided extreme stretching, joint overextension, ballistic movements, and jumps. They also included one session per week of aerobic dance, involving the upper and lower body limbs of very low impact, designed in sections of 3-4 minutes with 1-minute breaks, which		

			included stretching and relaxation activities.		
Barakat, 2014	Method of randomisation: A computer-generated list of random numbers was used. Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: • Pregnant women who underwent their first ultrasound examination in Hospital Universitario de Fuenlabrada at 10 to 12 weeks of pregnancy Women with singleton pregnancies Exclusion criteria: Pregnant women with the following contraindications for exercise: Hemodynamically significant heart disease. Restrictive lung disease Incompetent cervix Multiple gestation. Ruptured membranes Preeclampsia/pregnancy-induced hypertension Number of participants: Intervention, n=107 Control, n=93 Type of intervention: Physical activity	Exercise: The program had three 55-60 minute sessions per week, starting between 9-13 weeks of pregnancy till the end of the third trimester (weeks 39–40). The exercise routine included a 5-minute walk and static stretching, toning and joint mobilization exercises, aerobic dance, and specific exercises targeting major muscle groups in the legs, buttocks, and abdomen to stabilize the lower back. Balancing exercises were included for 10 minutes, followed by pelvic floor muscle training exercises for 10 minutes, and a 5-minute cool-down period. Exercises involving Valsalva manoeuvre, extreme stretching, joint overextension, ballistic movements, and jumping were avoided. The workout prescribed light to moderate-intensity aerobic activity to achieve a 55% to 60% maximal heart rate.	During this period, women in the CG did not engage in physical activity and solely relied on information from their midwives or healthcare providers.	Maternal outcomes: •GDM • GDM Fetal outcomes: • Gestational age • Preterm delivery • Apgar score • Head circumference, • Birth size and weight • Gender • pH of umbilical cord

			Participants were shown their heart rate on a poster to determine the appropriate intensity for their aerobic exercise. Heart rate was calculated using the Karvonen formula based on trimester, physical condition, and age. Exercise intensity was adjusted based on Borg Scale ratings, with the aim of a level of 12-13. All subjects wore heart rate monitors during training to maintain light to moderate intensity. To ensure patient safety and adherence, a qualified fitness specialist supervised group sessions of 10-12 subjects with the assistance of an obstetrician. Sessions were held in a spacious, well-lit room at the University Hospital of Fuenlabrada with favourable environmental conditions and accompanied by music. Participants were provided with adequate nutrition before each session.		
Barakat, 2019	Method of randomisation:	Inclusion criteria: Women with singleton	Exercise: Pregnant women in the intervention group	Pregnant women in the standard care group attended regular visits with	Primary outcomes: • GDM

	Computer-generated list of random numbers Allocation concealment: Not reported. Blinding: The randomization blinding process was performed by three different researchers	and uncomplicated pregnancies (no type 1, 2 or GMD at baseline). No history/risk of preterm delivery. Not participating in any other trial Exclusion criteria: Women not planning to give birth in the same obstetric hospital, or with no medical follow-up throughout pregnancy. Women having any serious medical conditions (contraindications) that prevented them from exercising safely. No. of participants: Intervention, n=234 Control, n=222 Type of intervention: Physical activity	received standard care and a supervised moderate exercise program, three days a week (55-60 min per session) from the 8-10th week of pregnancy until the end of the third trimester. The exercise protocol was supervised by a qualified of physical activity and sport science professional (ten years of experience). The program included 83-85 group training sessions adhering to American College of Obstetricians and Gynecologists guidelines. It consisted of gradual warm-up, aerobic exercises, muscle strengthening, coordination, stretching, pelvic floor strengthening, relaxation, and a final talk. Women wore a heart rate monitor (Accurex Plus, Finland) during training to keep HR under 70% of the age-predicted maximum. Perceived exertion was rated 12-14 (Somewhat Hard). The exercise session began with a 10-minute light warm-up consisting of walking and	obstetricians and midwives, (according to Hospital protocol), usually every 4–5 weeks until the 36–38th week of gestation and then weekly until delivery. They received counselling on nutrition and physical activity and were asked about their exercise habits once each trimester using a “Decision Algorithm” by telephone.	• GWG Secondary outcomes: • Maternal gestational age at delivery • Type of delivery • Birth weight

			static stretching to avoid muscle pain. Similarly, the session ended with a 10-minute cool-down, including relaxation and pelvic floor muscle training. The main section was 30-35 minutes long and included moderate-intensity aerobic and resistance exercises. All sessions were supervised by a qualified fitness specialist and an obstetrician and performed in a well-lit spacious room with music and favourable environmental conditions. The program involved group sessions with 12-15 participants, and adherence was measured using a checklist.		
Barquiel, 2023	Method of randomisation: The randomization was automatically generated by an Excel program that assigned a random	Inclusion criteria: singleton pregnancy, gestational age less than 17 weeks' gestation, maternal age >=18 years, pregestational BMI>=30 kg/m, and absence of physical or mental diseases that caused disability to participate	The intervention type was behavioral. The intervention group had an educational session about an adequate diet and physical activity given by nurses with expertise in obesity and diabetes. The educational session was based on the educational model received by women with gestational	The intervention and control group received information about diet quality, physical activity and were informed about the concept of an adequate gestational weight gain based on the 2009 Institute of Medicine (IOM) recommendations. The control group received a leaflet and verbal explanations given by the doctors and midwives.	Primary outcome: GWG Secondary outcomes: Gestational hypertension GDM Preterm birth Cesarean section

	number to consecutive patients. Allocation concealment: Not reported Blinding: Not reported	Exclusion criteria: Not reported Number of participants: Intervention: 85 Control: 84 Type of intervention: Mixed	diabetes. The session was scheduled at the first prenatal visit and lasted 3 h. Diet for each woman was calculated for the pregestational BMI, physical activity, and pregnancy specific necessities. The recommended caloric intake was calculated as 24-30 kcal/kg/d. The distribution of macronutrients was 50% of complex carbohydrate, 20% of protein and 30% of fat. Diet quality followed the Mediterranean pattern, based on the preferent intake of vegetables, legumes, fruit, white meat, fish and olive oil, and limited consumption of sweets and saturated and trans fats as contained in spread fats, commercial sauces, and other processed foods. Grilled, baked, stewed, meals cooked with sofrito and not fried meals were advised. One hour of daily physical activity adapted to pregnancy was recommended.		rate LGA SGA

Brownfoot, 2016	Method of randomisation: sequence was generated by an independent organisation (Australian Research Centre for Health of Women and Babies, UoA) Allocation concealment: the randomisation sequence was properly concealed in consecutively numbered opaque, sealed envelopes Blinding: Not reported	Inclusion criteria: Women with a singleton pregnancy who attended their first antenatal booking visit prior to 21 weeks and were planning to have their pregnancy care through hospital clinics. Women between 18-45 years of age Exclusion criteria: Women younger than 18 or older than 45 years of age. Women who had medical comorbidities. Women with substance abuse. Women unable to understand English. Number of participants: Intervention, n= 386 Control, n= 396 Type of intervention: Mixed	As part of the intervention, women were weighed at each antenatal clinic appointment, followed by counselling from their treating clinician according to the IOM gestational weight gain guidelines. In the intervention group, the weight of the women was recorded in the antenatal clinic notes at every visit. All antenatal clinic rooms had a prominently displayed sign with suggested weight gains according to the IOM guidelines. According to these guidelines, the clinicians were encouraged to discuss appropriate weight gain with the women, but their responses were not scripted. The recorded weight was intended to trigger a discussion about weight gain guided by the IOM information, as would be the situation in normal clinical practice. Furthermore, the scales were removed from the general antenatal clinic	The control group had standard antenatal care comprising recording weight at booking and then at 36 weeks.	Primary outcome: GWG Secondary outcomes Maternal outcomes: GDM, PIH, PE, Macrosomia, IUGR, Delivery, gestation, Induction, 3rd/4th-degree tear Shoulder dystocia, Mode of delivery, NVD, Instrumental. Caesarean Elective · Caesarean delivery, Emergency · PPH · Wound infection Perinatal outcome: Mean birthweight (g) Hypoglycaemia Respiratory distress syndrome Jaundice Infection Birth trauma. Perinatal death Low Apgar (<7 at 5 minutes). Admission to SCN · NICU

			waiting area to prevent the control women from weighing themselves during their antenatal visit.		
Buckingham, 2019	Method of randomisation: Women were randomly assigned to the intervention group and the control group Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Exercising <3/wk for 30 min/session for the 6 months Before conception · BMI between 18.5 and 45.5 kg/m2 · Receiving regular prenatal care. Willing, if asked, to walk 10,000 steps/d · Meet with a Registered Dietitian Nutritionist (RDN) every month, and follow nutrition recommendations provided by the RDN. Exclusion criteria: · H/O chronic disease (e.g., T1D, cardiovascular disease, thyroid disease) Previous GDM or pre-eclampsia. No. of participants: Intervention, n=23 Control, n=24 Type of intervention: Mixed	Participants in the intervention received a behavioural lifestyle intervention that included counselling and a wearable fitness tracker including dietary software (Fitbit Flex Activity Monitor; Fitbit Inc.). The intervention was targeted towards increasing physical activity (PA) and modifying carbohydrate intake, with the primary goal of increasing the proportion of women who met the 2009 IOM GWG weight-gain guidelines. Participants in this group took part in a minimum of six 15- to 30-minute one-on-one visits with an RDN/Licensed Dietitian from no later than gestation week 14 to childbirth. Participants were weighed by the RDN at each face-to-face session. Weight gain was plotted on an IOM weight-gain chart and feedback on weight gain was	Participants in the UC group attended routine prenatal visits with their healthcare providers. Nurses recorded their weight, which was plotted on an IOM weight-gain chart specific to each participant's pre-pregnancy BMI. The chart was emailed to the participant within a week of the appointment. Appropriate weight gain was determined based on pre-pregnancy BMI calculated from self-reported weight and height measured at enrollment. Weight gain was calculated as weight measured at each prenatal appointment minus self-reported pre-pregnancy weight. No additional lifestyle counseling was provided to this group.	Primary outcomes: · GDM · GWG · Physical activity · Dietary intake Secondary outcomes: · Birth weight · Birth length · Gestational age at delivery · APGAR Score 1 and 5 min, Preterm delivery · Low birth weight · Macrosomia · Caesarean delivery (planned and unplanned) · Pre-eclampsia · Pregnancy-induced hypertension

			provided. The counselling sessions focused on appropriate weight gain during pregnancy using an individualized meal plan, PA goals, and behavioural modification using motivational interviewing. Participants were able to view steps taken per day and log food intake on the wearable fitness tracker website. Additionally, participants had weekly email contact with the RDN to discuss nutrition and PA goals and weight gain and to address any questions or concerns.		
Cahill, 2018	Method of randomisation: The randomisation sequence was determined by using a random number generator and a fixed allocation block strategy Allocation	Inclusion criteria: African American ancestry. Age 18 to 45 years. Body mass index (BMI) of 25.0 to 45.0 kg/m2 measured at the initial visit during the 1st trimester. Singleton viable gestation at or before 15 0/7 weeks (established by date of last menstrual period if it was within 5 days of the 1st trimester	PAT participants received the standard curriculum plus a cognitive-behavioural lifestyle program. This included goal-setting for appropriate GWG, regular self-assessment, education, observational learning through role-play, and home environment changes. The lifestyle program addressed barriers and facilitators for healthy GWG identified by	Participants assigned to the standard PAT curriculum had home visits focused on development-centered parenting support and education and parent-child interaction using a family strength-based approach.	Maternal outcomes · GWG. Body fat and fat-free masses. Indices of glycemic control. Plasma lipid profile. BP. Obstetric outcomes: GDM. Hypertensive disease of pregnancy. Preterm birth.

	concealment: Not reported Blinding: Investigators and study staff were blind to group assignment	ultrasound dating or by ultrasound itself). Disadvantaged socioeconomic status (Medicaid recipient or home zip code associated with a median Household income below the poverty level). Exclusion criteria: Diabetes, h/o GDM or macrosomia. Glycosylated hemoglobin ≥ 6.5. Any contraindication to exercise during pregnancy. Substance abuse. Non-English speaker Number of participants: Intervention, n= 119 Control, n= 121 Type of intervention: Mixed	African-American women. Parent educators audiotaped visits and completed checklists, reviewed by study staff. Study staff also randomly observed two home visits per year per educator, as per PAT standards. During the study, participants visited the Washington University Clinical Research Unit twice; once at 15 weeks and again at 35 weeks of gestation. During these visits, various measurements were taken, including body weight, body composition, plasma glucose, insulin and lipid concentrations, and the plasma glucose and insulin response to an oral glucose load. Blood samples were collected before and at 30, 60, 90, and 120 minutes after ingesting a 75-g glucose drink. Additionally, infant plasma glucose and insulin concentrations were assessed from cord blood obtained at the time of delivery. After delivery,		Caesarean delivery · Fetal death (after 20 0/7 weeks Neonatal secondary outcomes: · Birth weight and length · Body composition (fat-free mass and percent body fat) · Percent who were large for gestational age · Percent who were small for gestational age · Umbilical cord plasma glucose · Insulin concentrations Medical complications: · Neonatal intensive care unit admission within 24 hours of life · Respiratory distress syndrome · hypoglycemia [plasma glucose < 30 mg/dL at any time) · Neonatal death

			infant length, weight, and body composition were determined before hospital discharge. All research and clinical visits were conducted by staff who were blinded to the participant's treatment assignment.		within the first 28 days of life).
Chan, 2018	Method of randomisation: A computer-generated list of random numbers in blocks of 6 was used by a study coordinator Allocation concealment: Treatment assignments were concealed in consecutively-numbered sealed envelopes, which were opened sequentially upon subject enrollment Blinding: All	Inclusion criteria: · Maternal age >35 years old at the expected date of confinement · Prior history of GDM or birth of child >=4 kg; · Pre-pregnant body mass index (BMI) or BMI at the 1st trimester >25 kg/m2 · Family history of diabetes at the first degree relatives Exclusion criteria: · Those who were participating in any clinical trial · Women with pre-existing diabetes · Multiple pregnancies · Substance abuse · Renal, liver and thyroid dysfunction · Cognitive impairment · Any other indication of major medical or psychological illnesses ·	In addition to regular antenatal care, the intervention group received a dietitian-led lifestyle program based on a clinically proven LMP from the first antenatal booking (up to 12 weeks of gestation) until 24 weeks of gestation. They had bi-weekly face-to-face/phone consultations in the first 2 months and monthly face-to-face sessions until the end of the program. During the first face-to-face session, the dietitian reviewed the participant's lifestyle habits, medical and pregnancy history, fetal growth status, and weight gain progress and discussed specific dietary and lifestyle advice to achieve a desirable weight status. In follow-up	The control group received routine antenatal care. During each antenatal visit, nurses monitored the body weight of pregnant women. They were also given an educational booklet with dietary and exercise recommendations for pregnancy. Optional antenatal classes were offered, subject to availability.	Outcomes: · GDM · GWG · SGA (<10th percentile) · LGA (>90th percentile) · Macrosomia (birth weight >=4 kg) · Preeclampsia · Gestational hypertension · Caesarean section · Preterm delivery · Gestation age at birth(week) · Birthweight(g) · Birthweight<2500 g · Apgar score at 5 min<7 · Shoulder dystocia

	investigators, outcome assessors, clinicians and nurses of routine antenatal and postnatal care were blinded to the treatment assignment	Physical restriction that led to exercise avoidance Number of participants: Intervention, n=110 Control, n=110 Type of intervention: Mixed	consultations, the dietitian reviewed the participant's dietary and lifestyle practices and provided recommendations. Each participant was given an individualised menu plan and healthy lifestyle booklets to achieve a varied, balanced diet emphasising fruit and vegetable consumption, moderate-carbohydrate, low-fat, low-glycemic index (GI), and low-caloric products in appropriate portions. The diet plan was designed to achieve desirable fetal growth and maternal weight throughout pregnancy. The dietitian also offered advice on using dietary supplements and managing pregnancy discomforts. Participants met the exercise instructor once during the LMP. The instructor reviewed their medical history, fitness level, and musculoskeletal problems. Based on international guidelines, the instructor designed a		

			suitable exercise regime - 30 min of low-impact aerobic exercise 3 times a week.		
Da Silva, 2017	Method of randomisation: A computerised RNG. Block randomisation with 9 pregnant women in each block. Each block resulted in allocation of 3 women for intervention and 6 women as controls, ensuring a recruitment balance of 1:2 throughout the study. Allocation concealment: Not specified Blinding: Principal researcher was not involved in the exercise training and	Inclusion criteria: · Women whose pregnancy exercise levels did not include self-reported participation in an exercise program (LTPA > 150 min/week) · ss18 years or older · Living in the urban area of the city of Pelotas, Rio Grande do Sul State, Brazil Exclusion criteria: · Self-reported hypertension · Cardiovascular disease · Diabetes diagnosed before pregnancy · History of miscarriage or preterm birth · IVF in the current pregnancy · Twin pregnancy · Persistent bleeding in the current pregnancy · Body Mass Index (BMI) > 35 kg/m2 · Heavy smoker (> 20 cigarettes a day) Number of participants: Intervention, n=213 Control, n=426 Type of	A structured exercise training program was initiated between 16 and 20 weeks of gestation and continued for at least 16 weeks. Women in the intervention group were provided with moderate-intensity exercise sessions three times a week for an hour, planned according to the ACOG recommendations and supervised individually. Each session consisted of warm-up exercises, aerobic activities (treadmill or stationary bike), strength training (dumbbells, machines, or elastic bands), and stretching exercises. The intensity of the exercises was measured based on individual perceived effort, which was kept between 12 to 14 on the Borg Scale. A total of 48 training sessions were planned for each participant and were divided into three stages. The first stage (week 1 to 4)	Women in the control group received standard antenatal care and were encouraged to continue their normal daily activities.	Primary outcomes: · Preterm birth · Pre-eclampsia · Gestational age · Birth weight · Length and head circumference Secondary outcomes: · GWG · GDM · SGA · LGA

	analyses were performed blinded for group allocation. Staff involved with exercise or outcome assessments had no influence.	intervention: Physical activity	began with a 5-minute warm-up period, followed by 15 minutes of aerobic exercise, 35 minutes of strength training/floor exercises (3 sets of 12 repetitions each), and a 5-minute stretching session. The second stage (week 5 to 10) started with a 5-minute warm-up period, followed by 20 minutes of aerobic exercise, 30 minutes of strength training/floor exercises (3 sets of 10 repetitions each), and a 5-minute stretching session. Lastly, the third stage (11 to 16) began with a 5-minute warm-up period, followed by 25 minutes of aerobic exercise, 25 minutes of strength training/floor exercises (3 sets of 8 repetitions each), and a 5-minute stretching session. Each session was led by a team of five trained physical education professionals, and two physical education professionals were present during each shift, supervising a maximum of six pregnant		

			women per hour to provide personalized attention. The intervention program was conducted at the gym of the Physical Education School in the Federal University of Pelotas.		
Deng, 2022	Method of randomisation: Random allocation sequence generated electronically using simple random number table, with an equal allocation ratio. Allocation concealment: Not reported Blinding: Blinding of participants after assignment was not feasible and researchers who performed outcome assessment	Inclusion criteria: · <13weeks of gestation; Resident in Beijing · Single pregnancy At least one risk factor for GDM · Age ≥35 years · Pre-pregnancy overweight or obesity · Fasting blood glucose ≥5.1mmol/L in early pregnancy · Family history of first-degree relatives with diabetes · History of or current abnormal lipid metabolism · History of macrosomia · History of GDM; or polycystic ovary syndrome Exclusion criteria: · Diagnosis of diabetes Vaginal bleeding · Severe medical conditions preventing physical exercise · Psychiatric illness Number of participants:	Diet and exercise: Diet and exercise interventions were provided for the intervention group from 14 weeks of gestation, until the 75-g OGTT was measured at 24 to 28 weeks of gestation, with a total of seven interventions. Researchers included nurses, nutritionist, and exercise experts. The diet and exercise program was tailored for every pregnant woman. The nurses managed the program during the whole intervention, including follow-up, recording, and WeChat group contact. The study involved pregnant women receiving guidance from nutritionists and exercise experts. The intervention included a one-hour clinic visit with two steps: filling out a	The control group only received routine health management until the birth of the baby. Body weight measurement and the pregnancy outcomes of all women were recorded.	Primary outcome: · GDM Secondary outcomes: · GWG · Delivery mode (caesarean section, natural delivery) · Gestational hypertension · Premature infants · Macrosomia

	and data analysis were not blinded	Intervention, n= 41 Control n=43 Type of intervention: Mixed	questionnaire to determine their prior diet and exercise habits and receiving a personalized diet and exercise program. The program included educational manuals and recording of a diet and exercise diary. Nurses established WeChat contact to remind participants to adhere to the program. The intervention group uploaded their diary, measured their body weight, and controlled their weight gain every two weeks at the clinic. WeChat intervention was offered to those who could not attend the clinic due to work. Researchers adjusted the program according to the diaries and biochemical indicators. The women attended routine antenatal visits from 29 weeks of gestation until delivery.		
Ding, 2021	Method of randomisation: A computer-generated algorithm was used.	Inclusion criteria: BMI≥24 kg/m2 at onset of pregnancy · Age below 35 years · <12 weeks of gestation, Active on WeChat every day	Dieticians send weekly dietary guideline messages to pregnant women in a WeChat group. The intervention group receives monthly personalized	There were no requirements for the control group.	Primary outcome: · GDM Secondary outcomes: · GWG · Preterm delivery · Gestational hypertension ·

	Allocation concealment: Not reported Blinding:Not reported	Exclusion criteria: Women with a history of GDM and macrosomia in previous pregnancies Women who had a history of diagnosis with diabetes. Polycystic ovary syndrome. Hyperthyroidism. Hypothyroidism. Previous abortion No of participants: Intervention, n=104 Control group, n=111 Type of intervention: Mixed	nutrition care until receiving an oral glucose tolerance test. Personalized guidelines are based on "the guide of diagnosis and treatment of gestational diabetes mellitus (2014)." The group follows Beijing Friendship Hospital Pregnancy Education's WeChat account for detailed guidance. Participants walk at least 6000 steps a day, with walking data obtained from smartphones.		Preeclampsia · Postpartum haemorrhage (PPH), Caesarean delivery · Macrosomia · Low birth weight (LBW) · Fetal distress · Amniotic fluid contamination
Eslami, 2018	Method of randomisation: Using randomized blocks with block sizes of 4 and 6, an allocation ratio of 1:1, and stratification by health centres Allocation concealment: Intervention given was written on pieces of	Inclusion criteria: · Age>18. GA of 16-20wks. Min secondary school education. Singleton pregnancy without complications. Pregnancy being the female's 1st 2nd or 3rd BMI>25 at prenatal care records or according to 1st trimester's weighing. Willingness to participate. Owning a cell phone Exclusion criteria: Diagnosis of physical or mental illness. GDM.	The intervention group received relevant education on various topics related to their health, including nutrition and physical activity. The education was delivered in the form of a 60- to 90-minute group session followed by a half-hour question-and-answer session. The participants were provided with two phone numbers to contact in case they had any questions and given an educational booklet which was developed based on the	The control group did not receive any educational booklet (standard care)	Outcomes: · GDM · GWG

	paper, placed in opaque envelopes, and numbered consecutively Blinding: Was not possible, and only the data analyser was blinded	Following a specific dietary regiment. H/o hospitalisation in the current pregnancy. Change of residence over the course of the study. Separation from the spouse. Risk of preterm childbirth. Addiction or use of drugs and alcohol. H/o infertility. Use of assisted reproduction techniques. Death of close relatives. Divorce. Other acute emotional problems over the past month Number of participants: Intervention, n=70 Control, n=70 Type of intervention: Mixed	World Health Organization (WHO) recommendations and the Ministry of Health advice. The content of the booklet was based on a review of the literature on nutrition and physical activity in overweight and obese females. After the training session, the mothers in the intervention group received educational text messages every other day for four weeks. Eight weeks after the start of the intervention, all participants were contacted by phone and their weight was measured again. Finally, their diabetes status was determined by interpreting the results of fasting blood sugar (FBS) and glucose tolerance test (GTT), which were conducted in all participants at 24 to 28 weeks of gestation. The educational booklet was later also given to the control group after the intervention was over and		

			the results had been assessed.		
Ferrara, 2020	Method of randomisation: Women were randomly assigned to the intervention group and the control group. Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Pre-pregnancy BMI between 25-40. Aged >=18 years. Singleton pregnancy Exclusion criteria: Fertility-assisted pregnancy. On bed rest. Diabetes. GDM. Current uncontrolled hypertension. Thyroid disease diagnosed in last 30 days. H/o CVD, cancer, Lung or serious gastrointestinal disease. H/o of eating disorder or bariatric surgery. SMI. Recent H/o mood or anxiety disorder. Drug or alcohol use disorder. More than 13 weeks' gestation. Number of participants: Intervention, n=199 Control, n=195 Type of intervention: Mixed	In addition to regular prenatal care, a group of women were randomly selected to receive a lifestyle intervention program that was adapted from the Diabetes Prevention Program (DPP) and mainly delivered through telehealth. The program was designed to be practical for pregnant women and easy to implement by healthcare facilities. The core of the lifestyle intervention program included two in-person sessions and 11 telephone sessions aimed at teaching behavioral strategies to improve weight, diet, physical activity, and stress management. The goal of the program was for women to gain weight within the Institute of Medicine (IOM) guidelines range, with a target of 7 kg for women with overweight and 5 kg for women with obesity.	Women in the control group received standard Kaiser Permanente Northern California (KPNC) antenatal medical care, which included an antenatal visit at 7–10 weeks' gestation, an additional seven antenatal visits on average, and periodic health education newsletters, including the Institute of Medicine GWG guidelines and information on healthy eating and physical activity in pregnancy.	Outcomes: · GDM · Gestational hypertension · Pre-eclampsia · Primary caesarean section · Preterm delivery at 25-37 weeks · SGA · LGA

Gonzalez-Plaza, 2022	Method of randomisation: Randomisation was computer-based in which two random number lists Allocation concealment: Opaque numbered envelopes were prepared to mask the group assignment Blinding: Not reported	Inclusion criteria: BMI ≥30 based on WHO classification) At GA 12-18wks who attended hospital obstetric clinics during prenatal care. Singleton pregnancy. Aged ≥18 years. Use Android or iPhone with an internet connection Exclusion criteria: Already used an app for monitoring physical activity and weight. H/o psychiatric disorders, endocrine–metabolic disorders, or chronic hypertension. contraindication for performing exercise or mobility problems that do not allow moderate walking; Women with language difficulties in understanding Spanish. No. of participants: Intervention, n=72 Control, n=78	A digital intervention was used to improve self-control, self-efficacy, and outcome expectations. The intervention aimed to overcome barriers to using a smart band and a supportive app for receiving information and assistance from a midwife. The smart band used was the Mi Band 2, and the accompanying app was the Mi Fit app. Pregnant women were advised to take 10,000 steps a day equivalent to 30 minutes per day of moderate physical activity, over the week (≥5 days) as recommended by the American College of Obstetricians and Gynaecologists. Participants were trained to set step and weight goals, and the Mi Fit app sent notifications and alerts to help them achieve these goals. The Hangouts app was used to receive personalised information through SMS text messages or videos sent by the research team twice a week. The messages contained	Pregnant women in the control group received oral and written support material. They were advised to perform moderate physical activity for 30 minutes a day, at least 5 days a week, and aim for a GWG between 5-9 kg, according to the IOM. Midwives provided instructions to achieve the physical activity goal gradually and recommended a balanced (Mediterranean) diet of 1800 kcal.	Outcomes: · GWG · GDM · Pre-eclampsia · Pregnancy-induced hypertensive disorder · Prematurity · Type of delivery (unplanned caesarean section) · Macrosomia · Admissions to the neonatal intensive care unit

			information regarding physiological changes in the mother and fetus, and healthy habits related to pregnancy, labour, and postpartum. The information sent was extracted from a specialized webpage, and the videos were from the Health Department of Catalonia and the Catalan Midwives Association. Pregnant women were encouraged to use the Hangouts app at least once a week to ask questions to the midwife, and queries were resolved with an immediate response.		
Hajian, 2020	Method of randomisation: Randomisation was conducted by using a randomizer software. Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Singleton pregnancy with 16-20 weeks of gestational age · BMI 25–29.9 kg/m2 · Age range 18–40 years · No underlying chronic diseases Exclusion criteria: · Pregnant women taking any type of chemical or herbal drug (other than dietary supplements recommended during	Intervention group received personalised nutritional counselling and physical activity training. Researcher provided training on physical activity and nutrition during pregnancy for 30-45mins, depending on the mother's awareness and needs. Nutritionist provided dietary consultation. The group received educational material and advised to attend follow-up and weight	The control group was evaluated solely for energy intake and level of physical activity and did not receive any further advice or intervention from the researcher.	Outcomes: · GWG · GDM · Neonatal weight · Neonatal height · Head circumference · Variable caesarean (cause of caesarean– elective, bradycardia and progress failure) · Jaundice

		pregnancy) · Unwillingness of the mother to continue the study or to participate simultaneously Number of participants: Intervention, n=33 Control n=33 Type of intervention: Mixed	control sessions. Researcher provided their contact number for self-care questions during the 6-month intervention period. Attempts were made to coordinate primary interventions with prenatal care visits to avoid additional costs. During first visit (16–20 weeks pregnant), researcher measured the weight, height, and BMI of both groups. A food frequency questionnaire and a physical activity questionnaire were used to evaluate energy intake and macronutrients. After completing the questionnaire, the intervention group received guidance on healthy eating and exercise during pregnancy, and the nutritionist provided individual counselling on their daily diet. At the second visit (26-28 weeks pregnant), the participant's compliance with recommended diets, weight gain, and physical activity		

			levels were tracked. Participants completed the IPAQ questionnaire 2nd time and were advised to engage in proper physical activities(aerobic exercise, walking 20-30 minutes daily in the afternoon). Stretch training was taught to the participants, and nutrition counselling was provided if needed. FBS and 2-hour oral glucose tolerance test (OGTT) were recorded based on mother's files in reference centers in each health complex in accordance with the screening instructions and diagnosis of gestational diabetes. At the 3rd visit (35-37 weeks pregnant), compliance with recommended diets regarding weight gain and physical activity levels based on IPAQ were tracked.		
Herring, 2016	Method of randomisation: Randomisation was computer-based Allocation	Inclusion criteria: · Age ≥ 18 years · Self-identification as African American · Gestational age < 20 weeks; First trimester · BMI 25–45	The intervention aimed to help low-income African-American mothers build motivation, support, and self-efficacy for weight-related behaviour change	Women receiving usual care at Temple University received standard obstetrical care, including an initial visit during the first trimester, monthly follow-ups until week 24, and every 2 to 3 weeks until week 36.	Outcomes: · GDM · GWG · Birth weight · SGA · LGA · Mode of delivery

	concealment: The randomisation status was concealed in opaque envelopes prepared by the statistician Blinding: Providers and clinic staff were blinded to subject randomisation to prevent contamination	kg/m2 · Medicaid recipient (income proxy) · Cell phone ownership with unlimited text messaging · Facebook member Exclusion criteria: · Pregnant women with conditions requiring specialised nutritional care (e.g., history of bariatric surgery) · Current tobacco use · Multiple pregnancies Number of participants: Intervention, n=27 Control, n=29 Type of intervention: Mixed	while being responsive to their social context. To achieve this, we used Social Cognitive Theory and the Social Ecological Model. The intervention provided skills training and support: 1) participants received personalised daily texts to build self-efficacy and skills. Messages like “Snacking at night will just give me heartburn. But if it’s yoghurt, then I’ll be good. I don’t eat any junk late at night.” were sent. 2)They received self-monitoring texts 3-4 times weekly and automatic feedback. 3) Incentives like raffle entries were provided for responding to self-monitoring texts. We identified 3 evidence-based weight control targets - energy intake, physical activity, and self-weighing - and created behaviour change goals around them. We recommended limiting sugar-sweetened beverages and high-fat/junk food, sticking to one plate of food at each meal, walking 5,000	Weekly visits were conducted from week 36 until delivery. Providers assessed patient weight, blood pressure, urine protein, and fetal heart rate, and the American College of Obstetricians and Gynecologists provided information about optimal weight gain during pregnancy.	

			steps daily, gradually increasing walking by 500 steps weekly, and weighing themselves weekly at home. Provided Pedometers and a walking DVD to promote activity. They were invited to a private Facebook group ("Pregnant Moms Temple") for additional support and training via links to websites and videos. Only invited members were allowed access to maintain confidentiality. A health coach with a bachelor's degree provided behavioural weight control counselling to participants. Weekly calls in the first two weeks were followed by 2-3 calls (15-20 minutes calls). The scripted calls were recorded for quality control purposes, and a web application was used for notetaking and storing process data. Intervention was created to support clinical care but was not fully integrated into it. Healthcare providers often prioritize other clinical needs overweight control. To make		

			the intervention more widely available, it was designed to use technology for content delivery.		
Horn, 2018	Method of randomisation: Women were randomized at a 1:1 allocation in random blocks of four and six Allocation concealment: Not reported Blinding: Randomization was sequentially blinded, with statistician-provided allocation stored in a Microsoft Access database	Inclusion criteria: · Women aged between 18 and 45 years · Singleton pregnancy Fluency in English · Access to the Internet and smartphone · BMI between 25 and 40 Gestational age<16 weeks (verified by ultrasonography) · Willingness to participate in the study Exclusion criteria: · Diagnosis of diabetes or HbA1c >6.5% measured before enrolment · Invitro fertilisation · Weight difference >15 lb relative to self-reported pre-pregnancy weight · Substance abuse · Smoking · Plans to terminate pregnancy · Plans to move out of the area Number of participants: Intervention, n=140	An RDN (Registered Dietitian Nutritionist) greeted intervention participants and provided coaching on healthier diets, increased activity, and better sleep. Participants received weekly email resources aligned with MAMA-DASH goals. The DASH diet, modified for pregnant women, emphasized nutrient-dense foods like low-fat dairy, fish, lean meats, fruits, vegetables, whole grains, and legumes, while discouraging sugary drinks and unhealthy snacks. The RDN used the LOSE IT! app to monitor dietary adherence, offering feedback through weekly coaching calls and generating reports comparing participants' data with MAMA-DASH goals. Reports were emailed and discussed during calls.	Usual-care participants received access to the MOMFIT website, which included dietary guidelines and pregnancy recommendations the American College of Obstetrics and Gynecology. They also received biweekly newsletters on pregnancy and infant care.	Outcomes: · GWG · GDM · Activity/sleep (35 weeks) · Diet (35 weeks) · Caesarean section · SGA · LGA

		Control, n=141 Type of intervention: Mixed	Participants were encouraged to exercise for 30+ minutes or walk 10,000+ steps daily and sleep for 7-9 hours. Both groups accessed secure websites with guidelines, but the intervention group also received individualized emails, texts, and calls from the RDN, along with electronic handouts and LOSE IT!. Group sessions were recorded for those who couldn't attend. Calls included Motivational Interviewing techniques, weekly nutrition report reviews, and goal setting. The study featured six 30-minute group sessions and an in-person prenatal lactation session for intervention participants and their significant others.		
Jing, 2015	Method of randomisation: According to the sequence of time and randomized	Inclusion criteria: Eligible women were aged at least 18 years, could understand the written Chinese language, and did not have pre-existing	The key points of education included the harm of GWG and GDM, the benefit of encouraged behaviors, the difficulty to change habits, and the importance of belief	Pregnant women in the control group received only conventional interventions, such as standard health education manuals produced by the hospital.	Dietary intake Time spent (h/day) on different intensities and categories of

	numbers produced by SAS version 11.0. Allocation concealment: Participants and data analysts were masked to group assignment. Investigators were not masked to implement the personalized intervention for intervention group Blinding: Not reported	diabetes. Exclusion criteria: Women with any pregnancy-related complications or general medical disorders not associated with pregnancy were excluded. Number of participants: Intervention: 131 Control: 131 Type of intervention: Mixed	in the efficacy of the interventions. In addition to standard health education manuals, women in the intervention group received an education manual on diet and physical activity (written by the research team) after randomization, and one-to-one counseling for at least 20 minutes in a private room with a trained graduate student (W.J.) after group assignment and at 16–20 and 20–24 weeks. The same graduate student was also available to answer questions and provide feedback on diet and physical activity behavior until 20–24 weeks either over the phone or via a group established on Tecent instant messenger (generally known as QQ in China) specifically for the present study .		physical activity GWG GDM
Ko, 2014	Method of randomisation: Randomisation was computer-based in a list of random	Inclusion criteria: · Women aged 18-45 years attending prenatal clinics at Madigan Army Medical Center Exclusion criteria: · Women who	The intervention comprised of a moderate to vigorous exercise program. It began with 30-minute sessions thrice a week and aimed to increase the frequency to 4-	The women in the control group did not participate in any instructional sessions with the exercise interventionist and did not receive any motivational mailings. They were advised to maintain their usual levels	Primary outcome: · The presence of gallbladder sludge or stone Secondary outcomes: · GDM · Cholesterol ·

	numbers Allocation concealment: Not reported Blinding: Instigators and the subjects' obstetricians were blinded to the intervention assignment, but participants were not	did not have a gallbladder · Over 20 weeks pregnant when first presenting for prenatal care · Not expecting to deliver at Madigan · Women who were medically unable to participate in an exercise program according to the criteria of the American College of Obstetricians and Gynecologists Number of participants: Intervention, n= 591 Control, n=605 Type of intervention: Physical activity	5 times per week, with each session lasting for 45 to 60 minutes. Participants were provided with supervised sessions to learn the exercise techniques and were encouraged to meet with the exercise interventionist monthly to learn techniques for self-motivation and adherence to behaviour change. The participants gradually increased their sessions to three times per week at the gym and one to two sessions at home, each lasting for 30 minutes. From the second to the sixth month, the participants performed aerobic training at the gym three times a week, with one or two sessions at home. Women participated in the intervention program from enrolment until 36 weeks of gestation and received regular mailings at home with information about setting goals for physical activity, reflecting on the reasons for exercising, and additional behavioural tip	of physical activity, but were not instructed to stop or avoid exercising.	Insulin · Leptin · Adiponectin

			sheets developed for the APPEAL study.		
Kong, 2014	Method of randomisation: Women were randomly assigned to the intervention or control group using a computer-based random number generator (Microsoft Excel 2010, WA) Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Age 18-45years Singleton pregnancy · Non-smoker· Self-reported BMI >=25 before pregnancy · No H/o chronic diseases (T1DM, CVD, thyroid, or lung disorder) · No prior history of GDM Women who engaged in less than three 30-min bouts of leisure PA (physical activity) for 6 months preceding enrolment Exclusion criteria: · Not listed Number of participants: Intervention, n= 18 Control group, n=19 Type of intervention: Physical activity	The study involved an unsupervised walking program for pregnant women. The intervention group attended a training session where they were given instructions on using a treadmill safely and advised to follow the 2008 U.S. physical activity guidelines. Treadmills were provided to eliminate barriers pregnant women faced when engaging in physical activity. Participants were given logs to report the location and duration of their walks, but the intensity of the walks was not reported. The unsupervised walking program started between week 12 and week 15 of gestation and continued until at least week 35. Depending on the duration of each participant's pregnancy, all intervention participants could complete a minimum of 20 weeks. The first two weeks of the program were an	Both groups were given PA logs, but the control group's self-reported leisure-time PA was not analysed due to inconsistencies. The unsupervised walking program began between weeks 12-15 and lasted until week 35. Participants had at least 20 weeks to complete the program, reaching 150 min of MPA per week. The first 2 wk of the intervention program served as an acclimation period whereby participants were asked to walk for 50 min in week 1, followed by 100 min in week 2. By the third week, all participants were encouraged to be at their walking goal of 30 min most days of the week for an overall total of at least 150 min of weekly. Women in the control group were not given PA recommendations but were not restricted from participating in PA during pregnancy.	Outcomes: · GDM · GWG · Gestational length at delivery · Birth weight z-score · Low birth weight · Macrosomia · Apgar score 1 min and 5 min. Preterm delivery · Caesarean delivery · Preeclampsia · Maternal hypertension

			acclimation period where participants were required to walk for 50 minutes in week one, followed by 100 minutes in week two. By the third week, all participants were encouraged to walk for at least 30 minutes most days of the week, for a total of at least 150 minutes of moderate physical activity per week.		
Korpi-Hyovalti, 2012	Method of randomisation: Randomisation was computer-based. Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Pregnant women (weeks 8–12) · With one or more risk factors: · BMI > 25 kg/m2 · Previous history of GDM or birth of child >4·5 kg · Age >40 years · Family history of diabetes Exclusion criteria: · Women who were diagnosed as having GDM already during gestational weeks 8–12 Number of participants: Intervention, n=27 Control, n =27 Type of intervention: Diet	The study involved a clinical nutritionist providing personalized dietary advice to the lifestyle intervention group. The dietary goals were carbohydrates at 50-55% of energy, fat at 30%, saturated fat less than 10%, and protein at 15-20%, with at least 15g of dietary fiber per 4184 kJ. The women were advised to consume a diet rich in vegetables, fruits, and berries, and to use low-fat dairy products, meats, and vegetable oils. The recommended energy intake was 126 kJ/kg per day for normal-weight women and 105 kJ/kg per day for overweight women. The	Diet Counseling: In the follow-up group, participants received general diet and physical activity guidance to reduce GDM risk in a single session with a nurse. Advice was provided verbally and in writing. Women completed the Three-Factor Eating Questionnaire and a 4-day food record at the beginning of pregnancy, again at weeks 26-28, and finally at weeks 36-40. Prenatal clinic follow-ups occurred monthly per Finland's standard care. Dietary Assessment: Nutrient intake was assessed using Nutricaw software, which analyzes Finnish and international food composition data. The intervention group submitted 26 initial food records, 22 at weeks 26-28, and 17 at pregnancy's end, while the follow-up group provided 25 initial	Outcomes: · GDM · GWG · Birthweight

			nutritionist provided information about the goals of eating, demands of pregnancy, meals and snacks, fiber intake, and quality of fats. The Three Factor Eating Questionnaire was used in the beginning of pregnancy and at weeks 36–40, and the women completed a baseline 4-day food record before the first appointment and repeated it before the fifth at weeks 26–28 and sixth appointments weeks 36–40.	records, and 18 at weeks 26-28 and the end. Analysis included data from 17 intervention group women and 18 follow-up group women who returned all three records.	
Liu, 2022	Method of randomisation: A randomization list was generated by the statistician Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: Age 18-44. GA ≤ 16 wks. Self-reported White or Black/African American. English-speaking. Pre-pregnancy BMI≥25 and weight ≤ 370 lb (max weight assessed by scale) Exclusion criteria: Multiple gestations · Contraindications to aerobic exercise during pregnancy Hospitalization for a mental health · Substance abuse disorder in the past 6	Intervention participants were advised to attend clinic visits with their prenatal care providers and follow guidelines for healthy gestational weight gain, physical activity, and dietary intake for pregnant women. They were encouraged to accumulate 150 minutes per week of moderate-intensity PA and follow a diet high in fruits, vegetables, and whole grains while low in saturated and trans fats. The “MyPlate Daily Checklist for Moms” was used to help participants	The participants of this group were advised to attend their prenatal care provider's clinic visits. To ensure their engagement and retention throughout the program, the group was provided with 6 monthly mailings and 10 weekly podcasts, which were publicly available online. These podcasts mainly focused on healthy pregnancy and fetal development, and were similar in duration and frequency to the ones provided to the intervention group. It's worth noting that the mailings and podcasts did not discuss any topics related to weight, physical activity, or diet.	Outcomes: · GWG · GDM · Gestational hypertension · Pre-eclampsia · Caesarean section · Long hospital stay (>4 days for caesarean deliveries and >2 days for vaginal deliveries) · Preterm delivery · Low birth weight · Macrosomia · Low 1-minute Apgar score (<7) · Gestational

		months. A physical disability that prevents exercise. Doctor's advice not to exercise during pregnancy · Current or previous eating disorder · Participants were withdrawn from the study if they had a miscarriage, stillbirth, or discovery of multiple gestation after randomization No. of participants: Intervention n=112 Control n=105 Type of intervention: Mixed	select a balanced diet, and customised calorie goals were provided. Social Cognitive Theory guided the intervention components. The intervention began with a detailed counselling session before the 18th week of pregnancy. The participant's dietary intake and physical activity report were shared, and a weight-gain-tracking graph was provided. Participants set a goal for PA and diet. They received a binder of study handouts, a pedometer, and a bathroom scale. The initial 10 weekly group sessions were replaced with 10 individual phone counselling calls due to recruitment challenges and low attendance. Only one intervention group was conducted before the protocol change, with 6 participants. Participants were analyzed after an in-depth counseling session. They received 10 weekly phone calls and 10 podcasts, discussing diet,		hypertension · Pre-eclampsia · Preterm birth · SGA

			physical activity, and behavioral strategies. They plotted their weight and discussed progress towards goals during each call. After 10 calls, they received shorter weekly or biweekly counseling calls throughout pregnancy. A private Facebook group was created for participants to support each other.		
McDonald, 2021	Method of randomisation: Randomization was done via computerized sequencing (GraphPad software) Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Singleton pregnancy (<16 wks of GA) Age 18-40. Pre-pregnancy BMI 18.5-34.99. Physician clearance to participate in an exercise program · Fluent in English and be contacted via phone or e-mail Exclusion criteria: · Preexisting DM. Comorbidities known to affect fetal development (e.g., lupus). On meds known to affect fetal development or pregnancy outcome Using tobacco, alcohol, or other recreational drugs No. of participants:	The exercise sessions included a 5-minute warm-up at the start, and a 5-minute cool-down at the end, during which the treadmill speed was reduced to 3.0 mph or lower. The aerobic exercise group underwent individual supervised sessions of moderate-intensity exercise (40-59% VO2peak) for 50 minutes, three times a week. The intensity of the exercise was monitored using a previously validated Target Heart Rate (THR) for pregnant women. Aerobic exercises such as treadmill running, elliptical training, stationary cycling, rowing,	Participants in the control group were given the option to participate in low-intensity stretching sessions with a focus on major muscle groups. These sessions involved standing or sitting stretches and included breathing techniques. Both exercise and stretching/breathing sessions were supervised and held at one of two university-affiliated gyms.	Outcomes: · GWG · GDM · Neonatal weight (kg) · Length (cm) · Pre-pregnancy weight

		Intervention, n=42 Control, n=32 Type of intervention: Physical activity	and stair stepping were performed during the sessions.		
Michalopoulou, 2023	Method of randomisation: An independent researcher generated the randomization list with 2:1 allocation to intervention: control, using random permuted blocks of 3 and 6. Allocation concealment: Allocation was only revealed to the recruiter after a participant had enrolled, using online software (Study Randomizer) to ensure allocation	Inclusion criteria: GA <20 wks. Aged ≥18 years. BMI ≥30 at booking Planned antenatal care and delivery at the study setting. Exclusion criteria: Severe congenital fetal anomaly (confirmed by ultrasound). Planned termination of pregnancy or ectopic pregnancy. Pre-pregnancy DM or taking metformin. Renal disease. Severe liver disease. Organ transplant. Cardiac failure (grade II NYHA or severe). Severe neurological disorder (including epilepsy). Severe psychiatric disease requiring in-patient admission. GDM NICE diagnosis at baseline. Eating disorder. Hyperemesis	The dietary advice aimed at providing 130–150 g total carbohydrate/day, with no specific advice to change protein or fat intake, for approximately 6 months (<20 weeks' gestation until delivery). It focused on three main principles (3Rs): Refrain from sugary foods and drinks; Reduce portions of starchy carbohydrates; and Replace refined starchy carbohydrates with unrefined varieties, and sugary foods/drinks with low/no-sugar alternatives. A research dietitian delivered a 30-min one-off consultation, explaining the diet principles, and providing support and motivation, including advice on goal setting, self-monitoring, and problem solving. The consultation was combined with a structured self-help booklet detailing how to apply the 3Rs, and providing	Standard care	Primary Outcomes: (i) adoption of the diet by the intervention group: mean carbohydrate consumption at 24–28 weeks' gestation, (ii) retention rate: proportion of all participants who complete a second OGTT at 24–28 weeks' gestation. Secondary Outcomes: GDM Gestational hypertension Preeclampsia Mode of delivery Induction of labour Birth weight Macrosomia LGA SGA

	concealment. Blinding: Not blinded	gravidarum. Not fluent in English. H/o bariatric surgery. Participating in other intervention trial. Any other significant disease or disorder which prevent participation, or influence outcome. No of participants: Intervention: 34 Control: 17 Type of intervention: Diet	general healthy eating advice, meal and snack ideas, and guidance on food labels. Participants also received recipes and materials to help with behavioural control (diet-related goal setting, and diet- and weightrelated self-monitoring booklet and charts). Throughout pregnancy until delivery, the dietitian offered up to six 10–15-min telephone sessions, and participants were instructed to weigh themselves once a week.		NICU admission Shoulder dystocia Neonatal hypoglycaemia Neonatal hyperbilirubinemia Requiring phototherapy
Okesene-Gafa, 2019	Method of randomisation: Eligible women were allocated randomly by the research midwife using a web-based randomization program using random permuted blocks of 4-8 participants Allocation concealment:	Inclusion criteria: Singleton pregnancy. GA12-17wks. BMI>30 Exclusion criteria: pre-existing diabetes or HbA1C >50 mmol/mol, Known congenital abnormality. On probiotics. H/o bariatric surgery Severe hyperemesis. Medications or medical conditions that alter glucose metabolism. No of participants: Dietary intervention, n=	Intervention group received a handbook with information on healthy foods, recipes, managing cravings, and staying active. They also received home-based education sessions from a community health worker trained in SMARTER goal setting and behaviour change techniques. During subsequent visits, the community health worker plotted the woman's weight on a pregnancy weight-gain chart and provided	As part of their routine dietary advice, women were given daily capsules containing either Lactobacillus rhamnosus GG and Bifidobacterium lactis BB12 (at a minimum dose of 6.5 x 10-9 colony forming units; www.chr-hansen.com) or identical capsules containing microcrystalline cellulose and dextrose anhydrate as a placebo. The former group, which received probiotics, was instructed to take one capsule daily until birth alongside their routine antenatal care, while the latter group was given the same instructions for the placebo capsules.	Outcomes: · GWG · GDM · SGA · Admission to neonatal intensive care unit (NICU)

	Not reported Blinding: Participants, researchers, and data analysts were blinded to probiotic and placebo allocation.	116 routine dietary advice N = 114 Type of intervention: Diet	feedback. Women in this group also received motivational text messages three times a week. Messages were created to supplement dietary education and were written in a way that mimicked communication from a baby to their mother. For instance, one message said, "Mum, remember to read food labels." The service was completely voluntary, allowing women to opt-out of the messaging program at any time. Women who were placed in the routine dietary advice group received Ministry of Health pamphlets titled "Eating for Healthy Pregnant Women" and "Healthy Weight-Gain in Pregnancy," without any dietary guidance from community health workers or text messages. Women in this group also had intervention visits before the 26-28 week HUMBA study glucose test (75-g oral glucose tolerance test, OGTT). Women in the		

			routine dietary advice group received NZ Health Ministry pamphlets with no additional support.		
Parat, 2019	Method of randomisation: Randomization was performed using a computer-generated sequence Allocation concealment: Sealed opaque envelopes containing the random allocation were numbered consecutively and delivered to each study center Blinding: Not reported	Inclusion criteria: · Pregnant women with a maximum of 21 gestational weeks (GWs) · Aged ≥18 years · Pre-pregnancy BMI > 25 kg/m2 · Women who agreed to participate, · Women covered by the French medical insurance system · Singleton pregnancy · Able to understand (written and spoken) French Exclusion criteria: · Any maternal condition that could possibly impact the fetus or fetal conditions in early pregnancy · Psychological disorders (including eating disorders) · Pre-existing diabetes · Newly diagnosed gestational dysglycemia · History of bariatric surgery Number of participants: Intervention, n=102	As part of the intervention, an individualized plan was created for each participant based on their educational diagnosis and in consultation with them. This plan included strategies to achieve realistic goals for lifestyle changes. Each participant was scheduled for at least two face-to-face visits with a dietician (at 26 and 30 GW) and four group education sessions (at 21, 28, 35 GW, and 2 months postpartum). During these sessions, participants discussed their behaviours, successes, and difficulties in achieving their goals. The individualized plan was then adapted based on these discussions. The first group education session at 21 GW focused on improving participants' knowledge of healthy diets and the benefits of physical activity during pregnancy. The	The women in the control group received general information about diet and exercise during a face-to-face meeting with a dietician at 26 weeks' gestation. They were provided with the national booklet on nutrition during pregnancy (www.mangerbouger.fr/PNNS/Guides-et-documents/Guides-nutrition). If the participant requested it, or if gestational diabetes mellitus (GDM) was diagnosed, an additional dietician visit was arranged.	Outcomes: · GDM · GWG · Hypertension during pregnancy requiring anti-hypertensive treatment, · Pre-eclampsia · Delivery mode including caesarean section and need for instrumental delive

		Control, n=104 Type of intervention: Mixed	second session at 28 GW focused on the psychosocial aspects of pregnancy, weight gain, balanced diet, and physical activity. The third session at 35 GW was dedicated to the baby's needs and how to feed the baby. The last session, held 2 months after birth, focused on baby's health, weaning, and nutrition. Each session ended with physical activity and relaxation. Between sessions, participants could have face-to-face visits with dieticians and/or a diabetologist at 26 and 30 GW to discuss maintaining a healthy diet and motivation. The intervention aimed to promote healthy lifestyle changes without focusing specifically on weight objectives. More details about the intervention can be found in the supplementary information.		
Perales, 2016	Method of randomisation: A computer-generated list of random	Inclusion criteria: · Pregnant women living in the Health Care Area of Hospital Puerta de Hierro and Hospital Severo	Women who were randomly assigned to the IG/EG (intervention/experimental group) were invited to participate in a supervised	During this period, women in the CG did not engage in physical activity. Instead, they relied on information provided by their midwives or healthcare professionals.	Outcomes: · GDM · GWG · Gestational age · Birthweight · Type of labor (Normal and

	numbers was used Allocation concealment: Not reported Blinding: Not reported	Ochoa, Madrid Spain · Women who underwent ultrasound examination at 9 to 11 weeks of pregnancy Exclusion criteria: · Not listed Number of participants: Intervention, n=83 Control group, n=83 Type of intervention: Physical activity	physical conditioning program. The program consisted of three, 55- to 60-minute sessions per week, which began between 9 and 11 weeks of gestation and continued until the end of the third trimester (weeks 39–40). Each session started with a warm-up that lasted for 5 to 8 minutes, consisting of walking and static stretching of most muscle groups. This was followed by an aerobic dance and specific exercises that targeted the specialist. The specialist worked with groups of 10–12 subjects, while an obstetrician provided assistance. The exercises were accompanied by music and were performed at the Centro de Salud Leganes Norte and Centro de Salud de Torrelodones. The exercises were performed in a spacious, well-lit room under favourable environmental conditions (altitude 600 meters, temperature 19-21.8°C, humidity 50%–60%).		Instrumental) · Birth size (cm) · Head circumference (cm) · Agpar score 1 min and 5 min · pH of umbilical cord

			Before the start of the exercise session, each participant's intake of calories and nutrients was ensured to be adequate.		
Perales, 2016a	Method of randomisation: Randomisation was computer-based Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Healthy pregnant women having no obstetric complications · No serious medical condition preventing them from exercising safely · Time of pregnancy 16 weeks · Not exercising regularly for more than 30 min on 3 days a week · Able to communicate in Spanish · Giving birth and being followed throughout pregnancy at the Hospital Universitario de Fuenlabrada Exclusion criteria: · Not listed Number of participants: Intervention, n=120 Control, n= 121 Type of intervention: Physical activity	The exercise program followed ACOG guidelines and involved three 60-minute supervised sessions per week. Women wore Heart Rate monitors to maintain a target HR intensity zone during aerobic activities which included different exercises and music choreographies. The sessions included a 5-7min warm-up, aerobic activities for 25-30mins, strength training, and 5-10in cool-down periods. Exercises were performed using light weights (0.5-1kg) or body weight to improve muscle strength and prevent muscle imbalances. The strength part of the session (using 3-kg dumbbells or bodyweight) engaged major muscle groups, such as upper/lower limb muscles, back, shoulders, and abdominal muscles, with the aim of	Standard care	Outcomes: · GWG · GDM · Hypertension · Type of delivery · Duration of labour · Gestational age · Birth weight · Height · APGAR(1 and 5 min) · pH of umbilical cord

			improving general muscle strength and preventing common muscle imbalances during pregnancy. The program also involved exercises aimed at improving balance, pelvis mobility, and body awareness, as well as pelvic floor muscle exercises for the prevention of urinary incontinence. The program avoided exercises involving extreme stretching, joint overextension, ballistic movements, or jumps. The aerobic and strength training components lasted the same duration throughout the program. The exercises were modified based on the trimester to improve body awareness, balance, and pelvis mobility to ease delivery.		
Polley, 2002	Method of randomisation: Women were randomly assigned to the control group or to the intervention	Inclusion criteria: GA 20wks. Exclusion criteria: Age<18y. First prenatal visit >12 weeks gestation, and those with a high-risk pregnancy (ie drug abuse, chronic health problems,	Professionals with a master's or doctoral degree in nutrition or clinical psychology provided intervention during regularly scheduled clinic visits for pregnant women. Women were given information on healthy weight gain, exercise	Participants in the standard prenatal care group only received the nutrition counseling provided by the doctors, nurses, nutritionists, and WIC counselors at Magee-Womens Hospital. The focus of this counseling was to promote a well-balanced diet and encourage the use of multivitamin/iron supplements. The	Outcomes: · GDM · Pre-pregnancy BMI (kg/m2) · Pre-pregnancy weight (kg) · Infant birth weight · Low birth weight (4000 g) · Gestation at delivery, preterm

	group Allocation concealment: Not reported Blinding: Not reported	previous complications during pregnancy, or current multiple gestation). Underweight women (BMI< 19.8 based on self-reported weight at height at the last menstrual period). Number of participants: Intervention, n=57 (30 normal weight, 27 overweight) Control, n= 53 (31 normal weight, 22 overweight) Type of intervention: Mixed	during pregnancy, and healthy eating during pregnancy. Newsletters were sent biweekly to promote healthy habits. Personalized graphs of weight gain were sent after each visit. Women exceeding recommended weight gain received individualized nutrition and behavioural counselling. A stepped-care approach was used, with increasingly structured behavioural goals set for women exceeding recommended weight gain. The main objective was to reduce the consumption of high-fat foods, particularly fast-food items, and replace them with healthier options such as fruits and vegetables. If these changes were insufficient to help the woman attain, the IOM-recommended weight, a more structured meal plan with customized calorie goals was devised. The exercise intervention focused on encouraging more physical activity, such as walking, and making	research staff did not provide any additional information or counselling to this group.	delivery (<36 weeks) · Caesarean delivery · Pre-eclampsia · Maternal hypertension

			lifestyle changes, like walking instead of driving short distances. Women were also contacted by phone in between clinic visits to monitor their progress towards achieving the goals set at their previous appointments.		
Price, 2012	Method of randomisation: Women were randomly assigned to the control group or to the intervention. Allocation concealment: Opaque envelopes containing and equal number of group assignments were prepared by the study statistician Blinding: Not reported	Inclusion criteria: · No aerobic exercise more than once per week for at least the past 6 months; Viable singleton pregnancy at 12–14 week BMI < 39 kg/m2 · No chronic heart or lung disease · No poorly controlled diabetes, hypertension, epilepsy, or hyperthyroidism · No severe anaemia · No orthopaedic limitations · No history of premature delivery, infant delivered for SGA, or unexplained fetal death Exclusion criteria: · Not listed Number of participants: Intervention n=31, control n=31 Type of intervention: Physical activity	The intervention involved a supervised aerobic training program lasting 45-60 min, 4 times/week at a moderate intensity level (12-14 on the Borg Scale of perceived exertion) in line with guidelines of the ACOG. Day 1 and 2 - group walks over hilly terrain, and circuit training on the 3rd day. The circuit training included 1-10 minutes of aerobic exercise on treadmills, elliptical trainers or stationary bicycles, alternating with an equal time interval of weight training, mostly using weight machines with a weight that allowed for one set of 20 repetitions. Upper extremity exercises involved overhead press, seated bench press, seated rowing, pectoral	Control group didn't exercise, only exerted as needed for work/household chores. Told not to exercise to keep group distinction. Tested every 6 weeks after randomization. Dietary advice followed, no calorie estimation.	Outcomes: · GDM · Length of pregnancy · Newborn birth weight · Gestational hypertension Length of first · Second stages of labor · Frequency of caesarean section · Frequency of assisted delivery · Newborn Apgar scores Placenta weight

			flexion, triceps extension, and bicep curls. Lower extremity exercises included leg extension and hip adduction/abduction. Core muscle exercises included back extension and loaded torso rotation on weight machines, followed by crunches as well as prone and supine bridges on 55-cm exercise balls. The circuit session ended with 5 minutes of hamstring, quadriceps, and calf stretching. To ensure four exercise sessions per week, each woman completed a brisk 30–60min/week. The author recorded exercise activities and attendance. Active subjects continued to exercise with the group until 36 weeks gestation or until delivery if they wished to do so.		
Quinlivan, 2011	Method of randomisation: Randomisation was conducted using computer-generated	Inclusion criteria: · Pregnant with a fetus with no known anomalies · Spoke English · Did not intend to relinquish their infant · Did not have a multiple	Women who were part of the intervention group during the study attended a specialized antenatal clinic that differed from routine care only in four ways: (i) they received continuous	Women in the control group were allocated to routine public antenatal care. This consisted of midwifery, obstetrician and general practitioner antenatal clinics, with access to high-risk antenatal clinics if indicated on medical grounds. Women in the	Outcomes: · GDM · GWG · Birthweight

	numbers Allocation concealment: Sealed opaque envelopes were used Blinding: Not reported	gestation · Able to attend hospital for antenatal care Overweight (BMI 25–29.9 kg/m2) · Obese (BMI > 29.9 kg/m2) Exclusion criteria: · Not listed Number of participants: Intervention, n=63 Control, n=61 Type of intervention: Diet	care from the same provider, (ii) they were weighed upon arrival, (iii) they were given brief dietary interventions by a food technologist at each antenatal visit, and (iv) they received psychological assessments and interventions if required. If any of these women were diagnosed with gestational diabetes, they continued to receive care at the obesity clinic but were treated using the same clinical care guidelines as the women in the general obstetric diabetes clinic.	control group who were subsequently diagnosed with gestational diabetes were referred to a public obstetric diabetes clinic for ongoing care.	
Rakhshani, 2012	Method of randomisation: An online RNG Allocation concealment: Allocations were written on paper and placed in sealed, opaque envelopes, which were kept in a locked cabinet. Blinding: Single	Inclusion criteria: · GA <12wks. H/o poor obstetrical outcome. Had complications in previous pregnancies Twin pregnancies. Age <=20 or >=35 Obesity at time of recruitment. A H/o poor obstetrical outcomes among blood relatives, i.e. sister, mother or grandmother Exclusion criteria: Severe renal, hepatic or gallbladder, or heart	The yoga group underwent a 1hr yoga session 3 times a week from the 13th week to the 28th week of gestation. This amounted to a total of 28 sessions. Gestational periods for interventions were chosen since most women detect pregnancy by 12th week of gestation, and those at high risk are likely to deliver preterm. Moreover, organ developments are usually complete by the 28th week of gestation. Certified	The control group, on the other hand, was offered standard care alongside walking for half an hour in the morning and evening, which was the usual antenatal exercise provided by the hospital during the same period.	Outcomes: · GDM · Pregnancy induced-hypertension · Pre-eclampsia, · Eclampsia · Preterm deliveries, Emergency c-section · SGA · LGA · Low 1 min APGAR score · Low 5 min APGAR score

	blind study, physicians, lab techs, and hospital staff were blinded on the group selection	disease Structural abnormalities in the reproductive system Hereditary anaemia Seizure disorders. STDs. Any medical conditions that prevented from participation. No of participants: Intervention, n= 30 Control, n= 38 Type of intervention: Mixed	yoga therapists conducted the yoga classes using an instruction manual in a designated room. The interventions offered to the study group were classified into 3 categories, including breathing exercises, yogic postures, and meditative exercises which consisted visualization, guided imagery, and sound resonance techniques. Women were asked to visualize the fetus in the uterus, the umbilical cord, and the placenta. They were guided to imagine the blood flowing from their bodies, into the placenta, through the umbilical cord, and nourishing their fetuses. Both groups received standard care, including pamphlets about diet and nutrition during pregnancy, regular check-ups by the obstetrician, and bi-weekly follow-ups by the research staff. Follow-ups ensured that study participants were adhering to their		

			intervention practices and routine hospital check-ups.		
Roland, 2023	Method of randomisation: Randomisation is performed via a numbered randomisation list administered through the database Research Electronic Data Capture (REDCap) Allocation concealment: Not reported Blinding: None	Inclusion criteria: Written informed consent, age >=18, GA max 15 weeks, ultrasonic-confirmed viable intrauterine pregnancy, BMI 18.5–45 and weight <150 kg, ability to wear a wrist-worn activity tracker 24/7 until one year postpartum and having a smartphone. Exclusion criteria: were in a structured exercise at moderate-to-vigorous intensity for >1hr/week during early pregnancy, previous preterm delivery, obstetric or medical complications, multiple pregnancies, inability to speak Danish, or alcohol or drug abuse. Number of participants: Intervention: 174 Control: 45 Type of intervention: Physical Activity	Two diferent exercise interventions (EXE and MOT) on moderate-to-vigorous-intensity physical activity during pregnancy compared to standard care (CON). Participants in the EXE intervention were ofered one-hour supervised exercise training at moderate intensity three times per week, including two exercise sessions in a gym and one in a swimming pool. The gym sessions consisted of a combination of aerobic and resistance training with 30 min stationary bike training and 30 min of other exercise, for example, using elastic bands. In the swimming pool, participants did 15 min of swimming and 45 min of water exercises with plates, balls etc. Te MOT intervention consisted of four individual and three group physical activity motivational counselling sessions of 1–2 h duration	Standard care. Also, wear an activity tracker to determine their activity level. The face of the tracker looks like a normal watch showing only time and battery life.	Primary outcome: min/week of moderate-to-vigorous intensity physical activity Secondary outcome: GWG GDM Gestational hypertensive disorders Induction of labour Mode of delivery Gestational age delivery Premature delivery Birth weight Birth length SGA LGA 5 min apgar score

			during pregnancy and a personalized text message once weekly to motivate to increased physical activity. EXE and MOT sessions were conducted by instructors with a bachelor's or master's degree in physiotherapy, exercise physiology or similar. During the COVID-19 pandemic, starting from March 11th, 2020, and throughout the intervention period, most exercise training sessions, motivational counselling sessions and periodically test visits (except delivery) were conducted online from home using Zoom Cloud Meetings or telephone. EXE could access to the swimming pool for three months during this period.		
Sadiya, 2022	Method of randomisation: Not reported Allocation concealment: Not reported Blinding: Not blinded	Inclusion criteria: Aged 18 to 45, GA ≤12wks, singleton pregnancy, having ≥2 risk factors for GDM (high-risk ethnicity (Middle Eastern, Southern Asian) 1st degree relative with T2D, pre-pregnancy	The intervention included two face-to-face individualized dietary consultations and two telephonic counseling sessions by a licensed dietitian. At recruitment, the frst face-to-face consultation occurred and the second was	Standard care	Primary Outcome: GDM Secondary Outcome: GWG fetal birth weight mode of delivery

		BMI≥30, previous macrosomia weight >4.5kg, H/o GDM or PCOS Exclusion criteria: Pre-existing diabetes, fasting blood glucose ≥126mg/dl or Hba1c≥5.8% at 1st prenatal visit, on medications interfering with glucose metabolism (corticosteroids, metformin), psychiatric disorders, hypertension or medical conditions preventing physical exercise, unable to comprehend/cope with requirements, or give consent, or with ≥2 consecutive 1st trimester abortions who conceived spontaneously. No of participants: Intervention: 30 Control: 33 Type of intervention: Mixed	12weeks later, while telephone follow-ups were conducted between the two face-to-face. We have suggested a target weight gain in the second and third trimesters based upon recommendations from the Institute of Medicine (IOM); normal weight (1 lb./week), overweight (0.6 lb./week), and obese (includes all classes) (0.5 lb./week). The dietitians were skilled at providing intervention based on American Diabetes Association (ADA) recommendations using standardized teaching material and followup tools. The dietary counseling focused on optimizing participants' consumption of whole grains, vegetables, fruits, portion control, lowering intake of ultra-processed food, and simple sugars. A macronutrient composition of 50-55% carbohydrates, 25-30% fat, and 20% protein was targeted for the diet.		

			The women were encouraged to increase physical activity to 150minutes of moderate-intensity activity a week or to monitor a minimum of ten thousand steps per day (1hour 40minutes daily activity). In order to achieve behavior change, motivational interviewing, SMART (specifc, measurable, attainable, relevant and time-bound) goal setting, self-monitoring (pedometer, food log), and problem-solving skills were employed in the intervention.		
Seneviratne, 2016	Method of randomisation: Women were randomly assigned to the intervention and the control group Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Women aged 18–40 years · BMI ≥25 kg/m2 · Singleton pregnancy <20 weeks of gestation. Exclusion criteria: · Ongoing smoking Multiple pregnancy · Pre-existing Contraindications to antenatal exercise · Living outside the Auckland Region Number of participants:	The intervention group participated in a home-based antenatal exercise program using magnetic stationary bicycles (Sportop NB600/ NB800) from 20 to 35 weeks of gestation. Participants were provided with a written program prescribing frequency and duration of weekly exercises. They were given heart rate monitors (Polar S625/Polar RS800; Polar Electro Oy,	The control group was not prescribed an exercise intervention or provided with heart rate monitors.	Outcomes: · GDM · GWG · Length of hospital stay (hours) · Gestational hypertension · Pre-eclampsia · Preterm birth · Induction of labour · Augmentation of labour · Caesarean section

		Intervention, n=37 Control, n=37 Type of intervention: Physical activity	Kempele, Finland) to wear during all cycling sessions. Each exercise session comprised of a 5-minute warm-up and cool-down period at low intensity. A total of 67 sessions were prescribed, with the frequency varying from 3 to 5 sessions per week and duration of moderate-intensity exercise between 15 and 30 minutes per session. Each participant was visited at home by an exercise physiologist for assistance. The data was obtained by downloading heart rate monitor data (using POLAR PROTRAINER 5 software; Polar Electro Oy).		
Simmons, 2016	Method of randomisation: Randomisation was conducted using a computerized electronic random number generator Allocation concealment:	Inclusion criteria: · Pregnant women with a pre-pregnancy · BMI of >29 kg/m2 · < 19 +/-6 days of gestation · A singleton pregnancy · Aged over 18 years Exclusion criteria: · A diagnosis of GDM (using the OGTT by the IADPSG) · Preexisting diabetes · Chronic medical	Women were assigned a lifestyle coach who discussed 7 Health Eating (HE) and/or 5 PA “messages” according to previous work. The HE intervention promoted a food-based, lower simple and complex carbohydrate, lower fat, higher fiber, higher protein diet, including a focus on portion size and, therefore, a more limited	Not specified	Primary outcomes: · GDM · GWG Secondary outcomes: · Physical activity · Nutrition · Birthweight · Gestational age · SGA · LGA

	Not reported Blinding: The staff involved with measurements, but not the participants, were kept unaware of the intervention. Statistical analyses were performed blinded for allocation	conditions (local investigator defined; e.g., valvular heart disease) · A psychiatric disorder, Inability to walk >100 m safely · Requirement for a complex diet · Not fluent in the major language of the country of recruitment or unable to have a conversation with the lifestyle coach in another language for which the intervention materials were available. Number of participants: n= 94 usual care; n= 93 HE&PA; n=103 HE and n=98 PA. Type of intervention: Mixed	intake of total calories. The PA intervention promoted both aerobic and resistance physical activity. All interventions recommended a limitation in GWG to 5 kg. The messages were supported by a “toolkit” for each participant, including educational materials, pedometers, and flexible elastic Dyna-Bands. The coaching included 5 face-to-face sessions of approximately 30 to 45 minutes duration, and 4 telephone calls of >/_20 minutes or contacts using electronic mail. At least 4 face-to-face coaching sessions were expected to occur before the second measurement session (24 to 28 weeks), and the intervention was completed by 35 weeks of gestation. Standardization of the lifestyle intervention was achieved through a coach training program, which included an observed session with an actor, provision of a desk-file with all materials		

			and methods, and the use of a personal digital assistant (PDA) with made-to-order software to provide a framework for the session. A key component was for women to strive to achieve a maximum GWG of 5 kg. The coaches had scales available to help women with their weight management if weight scales were not available in the home.		
Thornton, 2009	Method of randomisation: A randomization system to determine the group assignment Allocation concealment: Envelopes prepared and sequentially numbered. A card indicating the assigned group was placed in the envelope, and the envelope	Inclusion criteria: · Pregnant with a single fetus between 12 and 28 weeks of gestation · BMI greater than or equal to 30 kg/m2 Exclusion criteria: · Patients with preexisting diabetes, hypertension, or chronic renal disease Number of participants: Intervention, n=116 Control, n=116 Type of intervention: Mixed	Both groups received counseling on conventional prenatal nutrition guidelines from a registered dietician. However, the study group received a more detailed dietary intake protocol, following guidelines like those used for GDM. The monitored patients were placed on an 18-24 kcal/kg balanced nutritional regimen. 6 weeks after delivery, all women in the study group were asked to record all foods and beverages consumed daily, which were reviewed at each prenatal visit by a physician. Patients were weighed every	Standard care	Outcomes: · GDM · GWG · Preeclampsia, · Gestational hypertension, · Preterm delivery (< 37 weeks) · Post-term delivery (>41 weeks) · Labor induction, Cesarean delivery · Adherence with prescribed nutritional regimen · Gestational age at birth · Infant birthweight · Macrosomia · Apgar score (<7 at 5 minutes)

	was sealed Blinding: Not reported		prenatal visit and encouraged to walk for 30mins/day. BP readings and urine samples for glucose, protein, and ketones were taken from both groups. The weight of all participants was recorded at the time of entry into the study, before delivery, and at 6 weeks postpartum, and the newborn was weighed by the delivery room nurse immediately after delivery. Neonatal outcome was assessed using Apgar scoring, which is routine for all deliveries. Antepartum and intrapartum complications including gestational diabetes, preeclampsia, and shoulder dystocia were identified from medical records. The type of delivery, macrosomia, anesthesia, and complications such as wound dehiscence/infection and postpartum hemorrhage were recorded.		
Tomic, 2013	Method of randomisation: Not reported	Inclusion criteria: · Good general health. Age 18-35. Viable fetus at the	Pregnant women in the study group performed regular aerobic exercise	The women in the control group were instructed not to engage in any kind of	Outcomes: · GDM · Pre-eclampsia · Pregnancy-induced

	Allocation concealment: Not reported Blinding: Not reported	regular ultrasound scan, and normal pregnancy confirmed by a clinician Exclusion criteria: · Chronic or acute medical conditions (cancer; renal, endocrinologic, psychiatric, neurological, infectious, and CVD) Multiple gestations · Persistent 2nd or 3rd trimester bleeding, placenta previa after the 26th week of gestation · Poorly controlled hypertension, DM or thyroid gland disease Incompetent cervix H/o recurrent miscarriages. Heavy smoker. Conditions that interfere with ACOG guidelines No of participants: Intervention, n=166 Control, n=168 Type of intervention: Physical activity	three times per week during pregnancy under expert supervision. The exercise routine consisted of a warm-up period of 5 minutes, 30 minutes of aerobic activity, 10 minutes of stretching, and a cool-down period of 5 minutes. The intensity of aerobic activities was in accordance with ACOG and ACSM guidelines and was measured using the Rated Perceived Exertion Scale and a heart rate monitor. The control group consisted of healthy pregnant women who didn't perform any organized regular physical exercise during pregnancy. All control participants were engaged in everyday physical activities, which included all activities performed in everyday life, household and/or at the workplace, which were also performed by participants from the experimental group. All participants visited an obstetrician four times,	exercise except daily routine activities and received standard antenatal care.	hypertension · Mode of delivery

			where their health, pregnancy details, and fetal vital signs were assessed. The obstetrician also noted complications and recorded the obstetric outcome, including pregnancy length, mode of delivery, and neonatal birth weight.		
Trak-Fellermeier, 2020	Method of randomisation: Women were randomly assigned to the intervention and the control group Allocation concealment: Not reported Blinding: Study staff other than a designated statistician and intervention staff remained blinded until the trial concluded	Inclusion criteria: · Women 18 years of age BMI >25 kg/m2 · Between 8 up and 16 weeks of gestation · Willing to deliver at University Hospital Exclusion criteria: · History of health conditions that would affect the woman's capacity to comply with the intervention (i.e., contraindication to aerobic exercise) or have a direct impact on fetal growth (i.e, diabetes or multiple pregnancy) Number of participants: Intervention, n= 15 Control, n=16 Type of intervention: Mixed	Intervention delivered by Registered Dietitians. Participants were encouraged to meet appropriate GWG recommendations by monitoring their diet, physical activity, and weight trajectory. The dietary intervention focused primarily on total calorie intake, improving carbohydrate and fat quality, reducing salt intake, and replacing red meat with low-mercury fish, nuts, and beans. Participants were encouraged to take prenatal multivitamin supplements as prescribed by obstetrician. The PA component aimed to increase movement and reduce sedentary time. Participants were	Women assigned to the control group participated in informative group sessions imparted by study staff, receiving health advice about dental care and child safety.	Outcomes: · GDM · Pre-eclampsia, · Eclampsia · Primary C-section · NICU admission · Prematurity neonatal

			encouraged to set goals for a daily physical activity/exercise routine that was considered safe during pregnancy, according to the American Congress of Obstetrics and Gynaecology. The intervention also motivated participants to increase non-exercise activity thermogenesis by promoting regular movement and encouraging specific behaviours such as standing, walking, and taking the stairs. To reduce sedentary periods, we recommended interrupting periods of sitting time with short 2-5 minute activities such as standing or walking. More details about the intervention can be found in published literature. Additional details regarding the intervention have been published elsewhere.		
Uria-Minguito, 2022	Method of randomisation: A computer-generated list of random numbers was	Inclusion criteria: Singleton, uncomplicated pregnancies (no type 1 or 2 diabetes at baseline), with no risk of preterm delivery and	Women assigned to the intervention group received standard obstetric attention and a structured and supervised online moderate exercise intervention	Standard care. Additionally, these women received physical activity and nutritional recommendations throughout pregnancy.	Primary Outcome: GDM Secondary Outcome: GWG

	used in order to ensure a blinded randomization sequence, and the access to the REDCap software for randomization was performed by one health professional from each hospital. Allocation concealment: Not reported Blinding: Not reported	with no serious medical contraindications that prevented them from exercising Exclusion criteria: Women who were simultaneously participating in another trial or exercise program, planning to give birth in a different hospital, or had no medical surveillance throughout pregnancy No of participants: Intervention: 130 Control: 130 Type of intervention: Physical activity	program three days a week (50–60 min/session) from the 8–10th week of pregnancy to the end of the third trimester, at the 38–39th week. Of the 3 sessions, two were carried out via Zoom and the last session was carried out following YouTube videos, which had been previously filmed by the physical activity professionals in our research group. The content of the videos on YouTube were adapted to the weeks of pregnancy. The exercise sessions were supervised by a qualified physical activity and sport science professional. Exercise program consisted of complementary and interrelated activities following a methodological model divided into 7 components adapted to each trimester of pregnancy, previously established by our research group: • physical and emotional activation (gradual warm-up); • aerobic		maternal gestational age birth weight mode of delivery birth length head circumference Apgar Scores 1 and 5 min

			exercises; • light muscle strengthening; • coordination and balance; • stretching and relaxation exercises; • pelvic floor muscle strengthening; • final talk. During the exercise sessions women used a heart rate (HR) monitor. HR was kept under 65–70% of the age-predicted maximum and rate of perceived exertion scale ranged from 12 to 14 (somewhat hard).		
Vesco, 2014	Method of randomisation: Women were randomly assigned to the intervention and the control group Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Pregnant women up to 21 weeks gestational age Exclusion criteria: · Diabetes mellitus or other medical conditions requiring specialized nutritional care (for example, a history of bariatric surgery), · Has plans to leave the area during the expected follow up period (through 1 year postpartum) Number of participants: Intervention, n=56 Control, n=58 Type of intervention: Mixed	The intervention program aimed to help participants maintain their weight during pregnancy and improve their pregnancy outcomes. It combined dietary and exercise recommendations with behavioral self-management techniques. The intervention diet recommended an energy-reduced eating plan based on the DASH dietary pattern without sodium restriction. Participants were encouraged to accumulate at least 30 minutes of moderate physical activity per day.	Control participants in our study received a one-time advice session from the study dietician. They were given general information about healthy eating during pregnancy, without specific focus on the DASH dietary pattern or weight management. The dietician provided feedback on their food diaries and advised them to follow their obstetrical care providers' recommendations. It's important to note that our study did not provide routine prenatal care to either group of participants. The information provided through the study was given in addition to their regular medical care.	Maternal Outcomes: · GDM · Gestational hypertension · Pre-eclampsia · Caesarean delivery Neonatal outcomes: · LGA · Macrosomia · SGA · Preterm birth (<37 weeks) · Preterm birth (<34 weeks) · NICU admission

			Intervention participants attended two individual counseling sessions and started attending weekly group sessions. The group sessions were designed to help participants set reasonable short-term goals, formulate action plans, and develop sources of reinforcement and social support to support behavior change. Each 90-minute group session included a nutrition and/or exercise topic, a behavior change topic, and a goal-setting activity for the next week.		
Wang, 2016	Method of randomisation: Women were randomly allocated to either the intervention group or the control group in a 1:1 ratio Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: · Pregnant women with a mean pre-pregnancy BMI of 26 kg/m2 and above · Before 12-16 gestational week Exclusion criteria: · Not listed Number of participants: Intervention, n=132 Control, n=133 Type of intervention: Physical activity	Participants randomized to the intervention group engaged in a supervised cycling program (3 times/week).	Participants allocated to the control group continued with their usual daily activities (not detailed).	Outcomes: · GDM · 75-g OGTT blood glucose levels

Wang, 2023	Method of randomisation: Not reported Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: Women in 1st trimester who were at high risk of GDM by a prediction model. Exclusion criteria: Not reported No of participants: Intervention: 261 Control: 258 Type of intervention: Diet	The intervention consisted of three dietary consultations offered monthly by dieticians based on 3-day food records before the oral glucose tolerance test (OGTT) at 24-28 gestational weeks.	Standard control	Primary outcome: GDM Secondary outcomes: GWG metabolic profile perinatal and pregnancy outcomes
Xu, 2021	Method of randomisation: Each participant was randomly placed into the intervention group or the control group according to the group result produced by a statistician using a computer in the clinic room Allocation concealment: Not reported Blinding: No	Inclusion criteria: · Pregnant women with excessive gestational weight gain according to the IOM guidelines, singleton pregnancy, no complications before pregnancy (i.e., type 2 diabetes mellitus, pre-pregnancy hypertension, and renal, immunologic, or hepatic diseases) Exclusion criteria: · Pregnancy outcome data were not available Number of participants: Intervention, n=203 Control, n=145 Type of intervention: Diet	Participants were educated on the importance of weight management during pregnancy and adverse outcomes of excessive GWG. The education was provided by obstetricians. The nutritionists assessed the participants' dietary habits. Intervention groups were given dietary habit questionnaire and a 3-day 24-hour dietary survey. Based on their answers, they were instructed to adjust their dietary structure and guide their lifestyle adjustment on eating speed, drinking frequency, and work and rest time. Individual meal plans were	Standard obstetrical care	Outcomes: · GDM · GWG · Premature rupture of membrane · Postpartum hemorrhage · Pre-eclampsia · Gestational hypertension · Thyroid diseases · Anaemia · Uterine inertia · Abnormal amniotic fluid

	blinding method used		given by nutritionists. Basal metabolic rate was analysed to determine their initial target energy, (basal metabolism plus 300–500 kcal). The daily target energy and food amount were fine-tuned according to the patient's body fat rate, weight, exercise, dietary habits, and so on, based on the 2016 Dietary Guidelines for Pregnant Women in China. They were prescribed physical activity according to the American College of Obstetricians and Gynecologists (ACOG) recommendations for at least 150 min per week of moderate-intensity aerobic activity or at least walking 5000 steps daily until delivery. They were asked to record the number of daily exercise steps for 5–7 days every month to evaluate their daily exercise status. Self-weighing weekly with the goal of meeting target IOM weight in the 2nd & 3rd trimesters. During check-ups, all dietary and exercise		

			plans were assessed and readjusted based on the participants' progress. The nutritionist was also available for counseling during the entire study. Intervention start at the time of inclusion. Both groups received standard dietary advice from the doctors in the Department of Obstetrics and Gynecology.		
Xu, 2023	Method of randomisation: Not reported Allocation concealment: Not reported Blinding: Not reported	Inclusion criteria: Aged ≥ 20, GA <=20wks, with >1 risk factors for GDM, such as age ≥ 35 years , pre-pregnancy BMI≥ 25 kg/m2, GDM, family history of 1st degree DM, H/o PCOS and macrosomia, miscarriage, and preterm birth (PTB) Exclusion criteria: T2DM, hypertension, hypothyroidism, multiple pregnancies, severely limited food choices, failure to guarantee the number of prenatal check-ups, presence of severe mental disorders, communication	A medical team established a WeChat group consisting of doctors, nurses, psychologists, and nutritionists. Intervention group invited join the group and provided them with health education, answered their questions in the group, and regularly share knowledge about healthy pregnancy, such as food choices and weight management, pregnancy precautions, helped them eliminate negative emotions, maintain a positive attitude, and cultivate a healthy lifestyle. Additionally provided a series of lectures for pregnant women,	Standard care	GDM, PIH, PTB, macrosomia, CS

		disorders, H/o antipsychotic use, and smoking, alcohol consumption, and drug use (past 3 months. No. of participants: Intervention: 128 Control: 123 Type of intervention: Diet	including “Pregnancy weight management,” “Nutrition and dietary recommendations for pregnant women,” “Prenatal nutrition intervention,” “Blood sugar management during pregnancy diabetes,” and “1000 Days for Health and Nutrition in Early Life.” They were encouraged to keep a food diary and share their experiences in the group. At the time of enrolment, (24-28 weeks and 38-42 weeks), the dietitian performed 3 nutritional assessments using the 24-hour dietary review method to evaluate the dietary intake status of the pregnant women. Nutritional recommendations were individualized and could be given through the food exchange method, taking into account the preferences and dietary needs of the pregnant women without exceeding the total energy intake. They were		

			encouraged to eat a balanced diet with vegetables, fruits, high-fiber whole grain products, low-fat dairy products, increased legumes, nuts and other plant proteins, and other plant proteins while avoiding foods rich in sugar and saturated fatty acids. Reminded women with excessive or insufficient GWG based on the range of GWG recommended by the 2009 Institute of Medicine (IOM) guidelines. The recommended GWG amounts in the IOM guidelines were 12.5-18.0 kg, 11.5-16.0 kg, 7.0-11.5 kg, and 5.0- 9.0 kg for pre-pregnancy BMI classification of underweight (BMI < 18.5 kg/m2), normal weight (18.5 kg/m2 ≤ BMI ≤ 24.9 kg/m2), overweight (25.0 kg/m2 ≤ BMI ≤ 29.9 kg/m2), and obese (BMI ≥ 30.0 kg/m2) in women.		

Appendix 7: Risk of Bias assessment for IPD studies

Study	Randomisation	Allocation concealment	Blinding of participants	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Overall risk of bias*
Al Wattar 2019	Low	Low	High	Low	Low	Low	Low/Medium
Arthur 2020	Low	Low	High	High	Low	Unclear	High
Assaf-Balut 2017	Low	High	High	Low	Low	Unclear	High
Baciuk 2008	Low	Low	High	Low	Low	Low	Low/Medium
Barakat 2008	Unclear	Unclear	Unclear	Low	Low	Low	Low/Medium
Barakat 2011	Low	Unclear	Unclear	Unclear	Low	Low	Low/Medium
Barakat 2012a	Low	Unclear	Unclear	Unclear	High	Low	High
Barakat 2015	Low	Low	Unclear	Low	Low	Low	Low/Medium
Barakat 2018	Low	Low	Unclear	Unclear	Low	Unclear	Low/Medium
Bisson 2015	Low	Low	High	Low	Low	Low	Low/Medium
Bogaerts 2012	Low	Unclear	High	High	Low	Low	High
Bruno 2016	Low	Unclear	High	Low	High	Low	High
Chao 2017	Unclear	Unclear	Unclear	Unclear	Low	Unclear	High
Cordero 2014	Unclear	Unclear	High	Unclear	High	Low	High
Dekker 2015	Low	Low	Unclear	Unclear	Low	Low	Low/Medium
Dodd 2014	Low	Low	Unclear	Low	Low	Low	Low/Medium
Dodd 2019	Low	Low	High	Low	Low	Low	Low/Medium
El Beltagy 2013	Low	Low	Unclear	Low	Low	Unclear	Low/Medium
Garmendia 2020	Low	Low	High	Unclear	Low	Low	Low/Medium
Garnaes 2016	Low	Low	High	Low	Low	Low	Low/Medium
Guelinckx 2010	Low	Unclear	Unclear	High	High	High	High
Harrison 2013	Low	Low	Unclear	Low	Low	Low	Low/Medium
Hawkins 2015	Unclear	Unclear	Unclear	Low	Low	Low	Low/Medium
Hui 2011	Low	Unclear	High	Unclear	Low	Low	Low/Medium

Hui 2014	Low	Unclear	High	Low	Low	High	Low/Medium
Jeffries 2009	Low	Low	Unclear	Low	Low	Low	Low/Medium
Kennelly 2018	Low	Low	High	Unclear	Low	Unclear	Low/Medium
Khaledan 2010	Low	Unclear	High	High	Low	Low	High
Khoury 2005	Low	Low	Unclear	Low	Low	Low	Low/Medium
Kunath 2019	Unclear	Unclear	Unclear	Unclear	Low	Unclear	High
Luoto 2011	Low	Low	High	High	Low	Low	High
McCarthy 2016	Low	Low	High	Low	Low	Low	Low/Medium
Nascimento 2011	Low	Low	High	High	Low	Low	High
Olson 2018	Low	Unclear	Low	Unclear	Low	Unclear	Low/Medium
Ong 2009	Low	Unclear	High	High	Low	Low	High
Oostdam 2012	Low	Low	High	Low	High	Low	High
Peleaz 2019	Low	Unclear	High	Unclear	Low	Unclear	Low/Medium
Perales 2014	Low	Low	High	Low	Low	Low	Low/Medium
Petrella 2013	Low	High	High	High	Low	High	High
Phelan 2011	Low	Low	Unclear	Low	Low	Low	Low/Medium
Phelan 2018	Low	Unclear	High	Unclear	Low	Unclear	Low/Medium
Poston 2013	Low	Low	High	Unclear	Low	Low	Low/Medium
Poston 2015	Low	Low	High	High	Low	Low	High
Rauh 2013	Low	Low	High	High	Low	Unclear	High
Renault 2013	Low	Low	High	High	Low	High	High
Rono 2018	Low	Low	High	Unclear	Low	Unclear	Low/Medium
Ruiz 2013	Low	Unclear	Unclear	Unclear	Low	Unclear	Low/Medium
Sagedal 2016	Low	Low	Unclear	Low	Low	High	Low/Medium
Stafne 2012	Low	Low	High	High	Low	Low	High
Vinter 2011	Low	Low	High	High	Low	High	High
Vitolo 2011	Low	High	High	Low	Low	High	Low/Medium
Walsh 2013	Low	Low	High	Unclear	Low	High	Low/Medium
Willcox 2017	Low	Low	High	Unclear	Low	Low	Low/Medium

Wolff 2008	Low	Low	Unclear	High	High	Low	High

* Ignoring ‘Blinding of outcome assessment’ and ‘Selective reporting’.

Appendix 8: Risk of Bias assessment for non-IPD studies

Study	Randomisation	Allocation concealment	Blinding of participants	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Overall risk of bias*
Abdel-Aziz 2018	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Low/Medium
Barakat 2012	Unclear	Unclear	Unclear	Unclear	Low	Low	High
Barakat 2013	Unclear	Unclear	Unclear	Low	Low	Low	Low/Medium
Barakat 2014	Low	Low	Unclear	Unclear	Low	Unclear	Low/Medium
Barakat 2019	Low	Low	High	Unclear	Low	Unclear	Low/Medium
Barquiel 2023	Low	Unclear	Unclear	Unclear	Low	Low	Low/Medium
Brownfoot 2016	Low	Low	High	Unclear	Low	Low	Low/Medium
Buckingham 2019	Unclear	Unclear	High	Unclear	Low	Unclear	High
Cahill 2018	Low	Unclear	Unclear	Low	Low	Unclear	Low/Medium
Chan 2018	Low	Low	High	Low	Low	Unclear	Low/Medium
Da Silva 2017	Low	Low	High	Low	Low	Low	Low/Medium
Deng 2022	Low	Low	High	High	Low	Low	Low/Medium
Ding 2021	Low	Low	High	Low	Unclear	Low	Low/Medium
Eslami 2018	Unclear	Low	High	Low	Low	Low	Low/Medium
Ferrera 2020	Low	Unclear	High	Low	Low	Unclear	Low/Medium
Gonzalez-Plaza 2022	Low	Low	Unclear	Unclear	High	Low	High
Hajian 2020	Low	Low	Unclear	Unclear	Low	Unclear	Low/Medium
Herring 2016	Low	Low	Unclear	Unclear	Low	Low	Low/Medium
Horn 2018	Low	Low	High	Low	Low	Unclear	Low/Medium
Jing 2015	Low	Low	Unclear	Unclear	Low	Low	Low/Medium
Ko 2014	Low	Unclear	Unclear	Low	Low	Low	Low/Medium
Kong 2014	Low	Low	High	Unclear	Low	Low	Low/Medium
Korpi-Hyovalti 2012	Low	Low	High	High	Low	High	High
Liu 2022	Low	Unclear	Unclear	Low	Low	Low	Low/Medium

McDonald 2021	Low	Unclear	Unclear	Unclear	Low	Low	Low/Medium
Michalopoulou 2023	Low	Low	High	Unclear	Low	Low	Low/Medium
Okesene-Gafa 2019	Low	Low	High	Low	Low	Unclear	Low/Medium
Parat 2019	High	Low	High	Unclear	Low	Unclear	High
Perales 2016a	Low	Unclear	High	Low	High	Low	High
Polley 2002	Unclear	Unclear	Unclear	Unclear	Low	Low	High
Price 2012	Low	Low	High	Unclear	High	Unclear	High
Quinlivan 2011	Low	Low	Unclear	Low	Low	Low	Low/Medium
Rakhshani 2012	Low	Low	High	Low	High	Low	High
Roland 2023	Low	Unclear	High	Unclear	Low	Low	Low/Medium
Sadiya 2022	High	Unclear	High	Unclear	Low	Low	High
Seneviratne 2016	Low	Low	Unclear	Unclear	Low	Low	Low/Medium
Simmons 2016	Low	Low	Unclear	Low	Low	Low	Low/Medium
Thornton 2009	Low	Unclear	Unclear	Unclear	Low	Low	Low/Medium
Tomic 2013	High	High	Unclear	Unclear	Low	Low	High
Trak-Fellermeier 2020	Low	Low	High	Unclear	Low	Unclear	Low/Medium
Uria-Minguito 2022	Low	Unclear	Unclear	Unclear	low	Low	Low/Medium
Vesco 2014	Low	Unclear	Unclear	Unclear	Low	Low	Low/Medium
Wang 2016	Unclear	Unclear	High	Unclear	Low	Low	High
Wang 2023	High	Unclear	Unclear	High	Low	Unclear	High
Xu 2021	Low	Low	High	Unclear	High	Unclear	High
Xu 2023	High	Unclear	Unclear	Unclear	Low	Unclear	High

Appendix 9: Definitions for all variables collected in the IPD meta-analysis

Variable label	Variable name	Description
Anthropometric measurements		
Height (cm)	ht	
Pre-pregnancy weight (kg)	pp_wt	
Pre-pregnancy BMI	pp_bmi	
Early pregnancy weight (kg)	ep_wt	
Early pregnancy BMI	ep_bmi	
Gestational age at baseline (weeks)	b_ga_wks	
Gestational age at baseline (days)	b_ga_dys	
Gestational age at follow-up (weeks)	f_ga_wks	
Gestational age at follow-up (days)	f_ga_dys	
Follow-up weight (kg)	f_wt	
Follow-up BMI	f_bmi	
Total weight gain (kg)	totgwg	
Weight post delivery	pn_wt	
Babies birth weight (grams)	baby_wt	
Socioeconomic variables		
Age (years)	age	
Land of birth	ethn_country	
Race/ Ethnicity*	ethn_race	1 = Caucasian, 2 = Asian, 3 = Black, 4 = Central/South American, 5 = Middle East, 6 = Other, 9 = NK
Education Mum (detail)	edu_detail	
Education Mum (categorical)**	edu_cat	1 = Low, 2 = Middle, 3 = High, 9 = NK
Smoking status		
Current smoker	smoker_curr	0 = No, 1 = Yes, 9 = NK
Ex-smoker (pre pregnancy)	smoker_ex	0 = No, 1 = Yes, 9 = NK
Allocation adherence		
Allocation***	trt	0 = Control, 1 = Intervention1, 2 = Intervention2, 9 = NK
Unit of randomisation	unit_rand	*e.g. participantID, centre ID …*
Pregnancy variables		
Number of fetuses	no_fetus	1 = Singleton, 2 = Twin or more, 9 = NK
GA at delivery (weeks)	ga_delivery	
Mode of delivery	mode_delivery	1=nvd, 2=instrumental/vacuum/forceps, 3=cs, 9=nk
Number of times giving birth before this pregnancy	parity	
Previous Miscarriages	prev_miscarr	0 = No, 1 = Yes, 9 = NK

Gravidity (nr of times pregnant)	gravida	
Baseline Risk		
Obesity (>30 BMI)	b_obesity	0 = No, 1 = Yes, 9 = NK
Previous large baby (4.5kg+)	b_macrosom	0 = No, 1 = Yes, 9 = NK
Previous GDM	b_prevgdm	0 = No, 1 = Yes, 9 = NK
Family history of diabetes	b_famhistdm	0 = No, 1 = Yes, 9 = NK
Baseline GDM	b_gdm	0 = No, 1 = Yes, 9 = NK
Baseline DM	b_dm	0 = No, 1 = Yes, 9 = NK
Baseline PIH	b_pih	0 = No, 1 = Yes, 9 = NK
Baseline hypertension	b_hyperten	0 = No, 1 = Yes, 9 = NK
Complication Outcomes for mother		
Type of GDM test	outcm_gdmtesttype	
Gestational diabetes	outcm_gdm	0 = No, 1 = Yes, 9 = NK
Pregnancy induced hypertension	outcm_pih	0 = No, 1 = Yes, 9 = NK
Pre-Eclampsia	outcm_pe	0 = No, 1 = Yes, 9 = NK
Preterm delivery****	outcm_pretermdel	0 = No, 1 = Yes, 9 = NK
Caesarean section	outcm_cs	0 = No, 1 = Unspecified CS, 2 = Elective CS, 3 = Emergency CS, 9 = NK
Complication Outcomes for baby		
Intrauterine death	outcb_death	0 = No, 1 = Yes, 9 = NK
Small for gestational age	outcb_sga	0 = No, 1 = Yes, 9 = NK
Large for gestational age	outcb_lga	0 = No, 1 = Yes, 9 = NK
Admission to NICU	outcb_nicu	0 = No, 1 = Yes, 9 = NK
Shoulder dystocia	outcb_shoulder	0 = No, 1 = Yes, 9 = NK
Birth trauma	outcb_trauma	0 = No, 1 = Yes, 9 = NK
Long term neurological sequelae	outcb_neuro	0 = No, 1 = Yes, 9 = NK
Long term metabolic sequelae	outcb_metab	0 = No, 1 = Yes, 9 = NK
Glucose variables		
Blood glucose unit	glu_unit	
OGTT glucose load	glu_ogtt_load	
Unit of OGTT glucose load	glu_ogtt_load_unit	
Glucose (range of GA)		
Blood glucose at <24 weeks gestation - 0h	gluless24_0h	
Blood glucose at <24 weeks gestation - 1h	gluless24_1h	
Blood glucose at <24 weeks gestation - 2h	gluless24_2h	
Blood glucose at <24 weeks gestation - 3h	gluless24_3h	
Blood glucose at 24-30 weeks gestation - 0h	glu2430_0h	
Blood glucose at 24-30 weeks gestation - 1h	glu2430_1h	
Blood glucose at 24-30 weeks gestation - 2h	glu2430_2h	
Blood glucose at 24-30 weeks gestation - 3h	glu2430_3h	
Blood glucose at >30 weeks gestation - 0h	glumore30_0h	

Blood glucose at >30 weeks gestation - 1h	glumore30_1h	
Blood glucose at >30 weeks gestation - 2h	glumore30_2h	
Blood glucose at >30 weeks gestation - 3h	glumore30_3h	
Glucose GA		
Gestational age	gestational_age	
Blood glucose 0h	gluless_0h	
Blood glucose 1h	gluless_1h	
Blood glucose 2h	gluless_2h	
Blood glucose 3h	gluless_3h	

NK: Not known

*: White Caucasian European also includes Russians and Australians; Asian also includes SE Asians; Black includes both Africans and African Americans; Central/SouthAmerican also includes Antillen and El Salvador; Middle East also includes Iran and Turkey; Other also includes Fiji, New Zealand, Native American, Greenland)

**: for example: 1= <12years, 2 = 12 years / a-level, 3=uni/graduate

***: for multiple interventions, the most complex one is coded as 2

****: preferred definition if available: <37 weeks

Appendix 10: Effect estimates derived from IPD meta-analysis (all interventions combined)-GDM (any definition)

Intervention type and study	Odds ratio	95% CI	% Weight
Diet			
Al Wattar 2019	0.798	0.566, 1.125	5.31
Assaf-Balut 2017	0.751	0.531, 1.062	5.26
Bruno 2016	0.599	0.297, 1.205	2.26
Khoury 2005	1.089	0.187, 6.355	0.45
McCarthy 2016	1.02	0.608, 1.71	3.45
Vitolo 2011	2.127	0.426, 10.623	0.53
Walsh 2012	0.977	0.337, 2.835	1.13
Wolff 2008	0.694	0.091, 5.315	0.34
Subgroup, REML+HKSJ	**0.813**	**0.687, 0.961**	**18.73**
Mixed approach			
Arthur 2020	1.415	0.8, 2.503	3.03
Bogaerts 2012	0.93	0.364, 2.381	1.41
Chao 2017	2.032	0.075, 54.891	0.13
Dodd 2014	1.321	1.01, 1.729	6.36
Dodd 2019	1.057	0.633, 1.764	3.48
El Beltagy 2013	0.117	0.006, 2.207	0.17
Garmendia 2020	1.26	1.028, 1.545	7.34
Guelinckx 2010	2.385	0.357, 15.953	0.39
Harrison 2013	0.809	0.413, 1.586	2.39
Hawkins 2014	0.97	0.217, 4.347	0.61
Hui 2011	0.469	0.096, 2.292	0.55
Hui 2014	0.451	0.061, 3.312	0.35
Jeffries 2009	1.111	0.501, 2.465	1.85
Kennelly 2018	0.948	0.569, 1.578	3.51
Olson 2018	1	0.58, 1.724	3.22
Petrella 2013	0.215	0.071, 0.655	1.05
Phelan 2011	1.129	0.023, 55.749	0.1
Phelan 2018	0.969	0.507, 1.851	2.54
Poston 2013	0.834	0.419, 1.659	2.32
Poston 2015	0.952	0.739, 1.227	6.6

Renault 2013	0.464	0.191, 1.125	1.55
Rono 2018	1.302	0.667, 2.543	2.42
Sagedal 2016	1.331	0.763, 2.323	3.13
Vinter 2011	1.146	0.442, 2.974	1.37
Kunath 2019	0.848	0.435, 1.654	2.42
Rauh 2013	0.474	0.169, 1.329	1.2
Luoto 2011	1.676	0.98, 2.867	3.28
Willcox 2017	0.336	0.1, 1.129	0.9
Subgroup, REML+HKSJ	**1.048**	**0.912, 1.205**	**63.66**
Physical Activity			
Baciuk 2008	0.809	0.018, 35.676	0.1
Barakat 2008	0.616	0.289, 1.315	2
Barakat 2011	0.888	0.296, 2.665	1.07
Barakat 2012a	0.573	0.213, 1.541	1.29
Barakat 2016	0.493	0.222, 1.092	1.85
Barakat 2018	0.061	0.003, 1.076	0.17
Bisson 2015	0.57	0.11, 2.957	0.51
Cordero 2014	0.153	0.027, 0.853	0.47
Dekker 2015	1.053	0.015, 76.177	0.08
Garnaes 2016	0.247	0.049, 1.245	0.53
Khaledan 2010	1.837	0.048, 69.835	0.11
Nascimento 2011	0.589	0.18, 1.935	0.93
Ong 2009	0.469	0.017, 13.287	0.13
Oostdam 2012	0.532	0.187, 1.514	1.17
Peleaz 2019	0.496	0.144, 1.702	0.87
Perales 2014	1.548	0.527, 4.549	1.11
Ruiz 2013	0.536	0.288, 0.996	2.7
Stafne 2012	1.326	0.693, 2.538	2.53
Subgroup, REML+HKSJ	**0.64**	**0.484, 0.845**	**17.61**
Overall, REML+HKSJ	**0.901**	**0.799, 1.016**	**100**

Appendix 11: Effect estimates derived from IPD meta-analysis (all interventions combined)-GDM (NICE)

Intervention Type and Study	Odds ratio	95% CI	% Weight
Diet			
Al Wattar 2019	0.75	(0.53, 1.07)	10.3
Assaf-Balut 2017	0.75	(0.47, 1.18)	7.1
Bruno 2016	0.28	(0.1, 0.79)	1.77
Subgroup, REML+HKSJ	**0.7**	**(0.33, 1.49)**	**19.16**
Mixed approach			
Dodd 2014	1.24	(0.94, 1.63)	13.35
Dodd 2019	1.03	(0.62, 1.71)	6.13
Garmendia 2020	1.21	(0.94, 1.57)	14.11
Harrison 2013	1.04	(0.56, 1.92)	4.48
Kennelly 2018	0.78	(0.38, 1.6)	3.45
Petrella 2013	0.56	(0.19, 1.65)	1.62
Phelan 2018	1.07	(0.44, 2.61)	2.32
Poston 2013	0.7	(0.3, 1.62)	2.59
Poston 2015	1.03	(0.75, 1.43)	11.14
Rono 2018	0.71	(0.37, 1.39)	3.93
Sagedal 2016	1.48	(0.85, 2.56)	5.35
Kunath 2019	1.08	(0.44, 2.63)	2.31
Rauh 2013	0.78	(0.23, 2.58)	1.33
Luoto 2011	1.23	(0.57, 2.66)	2.99
Subgroup, REML+HKSJ	**1.1**	**(0.98, 1.23)**	**75.12**
Physical Activity			
Bisson 2015	0.08	(0, 6.48)	0.1
Dekker 2015	0.95	(0.02, 44.28)	0.14
Garnaes 2016	0.24	(0.05, 1.13)	0.81
Ong 2009	0.77	(0.02, 25.97)	0.16
Stafne 2012	1.36	(0.74, 2.5)	4.51
Subgroup, REML+HKSJ	**0.65**	**(0.18, 2.31)**	**5.72**
Overall, REML+HKSJ	**0.98**	**(0.84, 1.13)**	**100**

Appendix 12: Effect estimates derived from IPD meta-analysis (all interventions combined)-GDM (IADPSG)

Intervention Type and Study	Odds ratio	95% CI	% Weight
Diet			
Assaf-Balut 2017	0.78	(0.51, 1.18)	12.92
Bruno 2016	0.48	(0.2, 1.14)	2.92
Subgroup, REML+HKSJ	**0.71**	**(0.06, 7.88)**	**15.84**
Mixed approach			
Dodd 2019	0.82	(0.37, 1.8)	3.63
Harrison 2013	0.67	(0.37, 1.24)	6.01
Kennelly 2018	0.93	(0.56, 1.54)	8.68
Petrella 2013	0.27	(0.09, 0.84)	1.71
Phelan 2018	1.38	(0.57, 3.31)	2.9
Poston 2013	0.82	(0.4, 1.68)	4.41
Poston 2015	0.93	(0.72, 1.21)	33.17
Rono 2018	0.93	(0.46, 1.9)	4.42
Kunath 2019	0.91	(0.43, 1.92)	4.03
Rauh 2013	0.6	(0.19, 1.91)	1.66
Luoto 2011	0.98	(0.64, 1.49)	12.63
Subgroup, REML+HKSJ	**0.89**	**(0.76, 1.03)**	**83.25**
Physical Activity			
Bisson 2015	1.56	(0.1, 24.34)	0.3
Dekker 2015	0.64	(0.07, 6.15)	0.43
Ong 2009	0.95	(0.03, 31.8)	0.18
Subgroup, REML+HKSJ	**0.92**	**(0.28, 3.08)**	**0.91**
Overall, REML+HKSJ	**0.86**	**(0.75, 0.97)**	**100**

Appendix 13: Effect estimates derived from IPD meta-analysis (all interventions combined)-GDM (modified IADPSG)

Intervention Type and Study	Odds ratio	95% CI	% Weight
Diet			
Al Wattar 2019	0.64	(0.46, 0.87)	7.86
Assaf-Balut 2017	0.75	(0.52, 1.07)	7.26
Bruno 2016	0.29	(0.12, 0.69)	2.82
Subgroup, REML+HKSJ	**0.64**	**(0.32, 1.3)**	**17.94**
Mixed approach			
Dodd 2014	1.34	(1.01, 1.76)	8.38
Dodd 2019	1.04	(0.57, 1.89)	4.61
Garmendia 2020	1.39	(1.12, 1.74)	9.1
Harrison 2013	0.72	(0.38, 1.34)	4.36
Kennelly 2018	1.1	(0.6, 2.02)	4.53
Petrella 2013	0.41	(0.13, 1.29)	1.86
Phelan 2018	1.78	(0.7, 4.57)	2.51
Poston 2013	0.72	(0.34, 1.56)	3.38
Poston 2015	0.99	(0.75, 1.3)	8.4
Rono 2018	0.96	(0.48, 1.92)	3.89
Sagedal 2016	2.04	(1.15, 3.64)	4.81
Kunath 2019	0.83	(0.41, 1.66)	3.85
Rauh 2013	0.59	(0.09, 3.8)	0.78
Luoto 2011	0.78	(0.51, 1.21)	6.33
Subgroup, REML+HKSJ	**1.08**	**(0.89, 1.31)**	**66.77**
Physical Activity			
Bisson 2015	3.91	(0.22, 69.54)	0.34
Dekker 2015	0.39	(0.01, 25.21)	0.16
Garnaes 2016	0.56	(0.19, 1.64)	2.03
Ong 2009	0.95	(0.03, 31.8)	0.23
Perales 2014	0.71	(0.11, 4.78)	0.74
Ruiz 2013	0.94	(0.64, 1.37)	6.98
Stafne 2012	0.83	(0.47, 1.48)	4.81
Subgroup, REML+HKSJ	**0.88**	**(0.7, 1.09)**	**15.29**
Overall, REML+HKSJ	**0.92**	**(0.78, 1.1)**	**100**

Appendix 14: All software libraries and packages used in the IPD meta-analysis

R v4.0.2 (2020-06-22)

R Studio v2023.03.1 Build 446

R Packages: lme4 v1.1-26, data.table v1.13.0, logistf v1.24.1, tidyr v1.2.0, sjlabelled v1.2.0, table1 v1.4.2, readxl v1.4.0, dplyr v1.0.8

Stata/SE 17.0 for Windows (64-bit x86-64)

Stata Packages: ipdmetan, metan, moremata, tab3way, firthlogit, confunnel, postrcspline, mvmeta

Appendix 15: Forest plot for IPD meta-analysis with IPD and non IPD trials

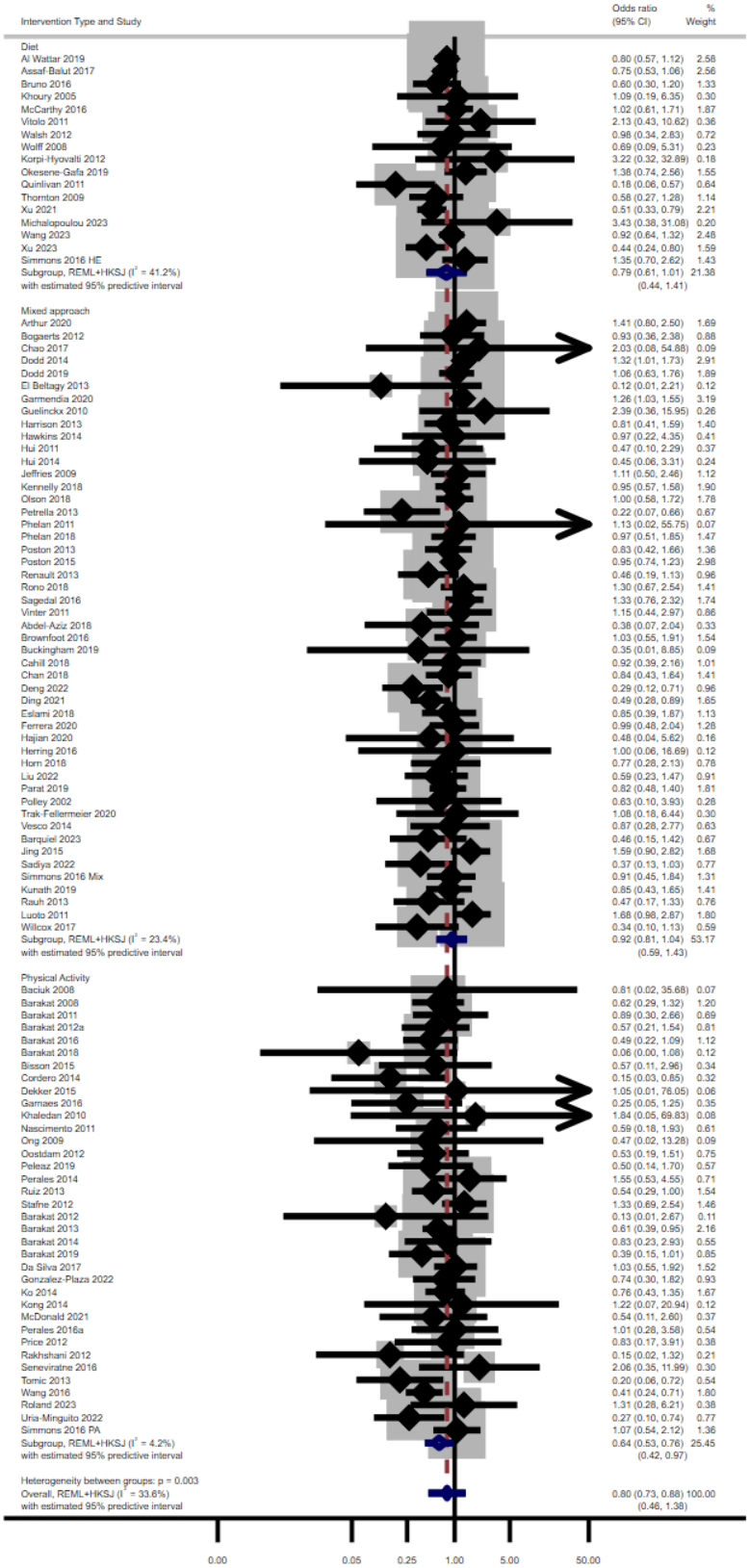


Figure 9.1: Forest plot showing the effect of lifestyle interventions on GDM (trial authors' definition) from IPD and aggregate data

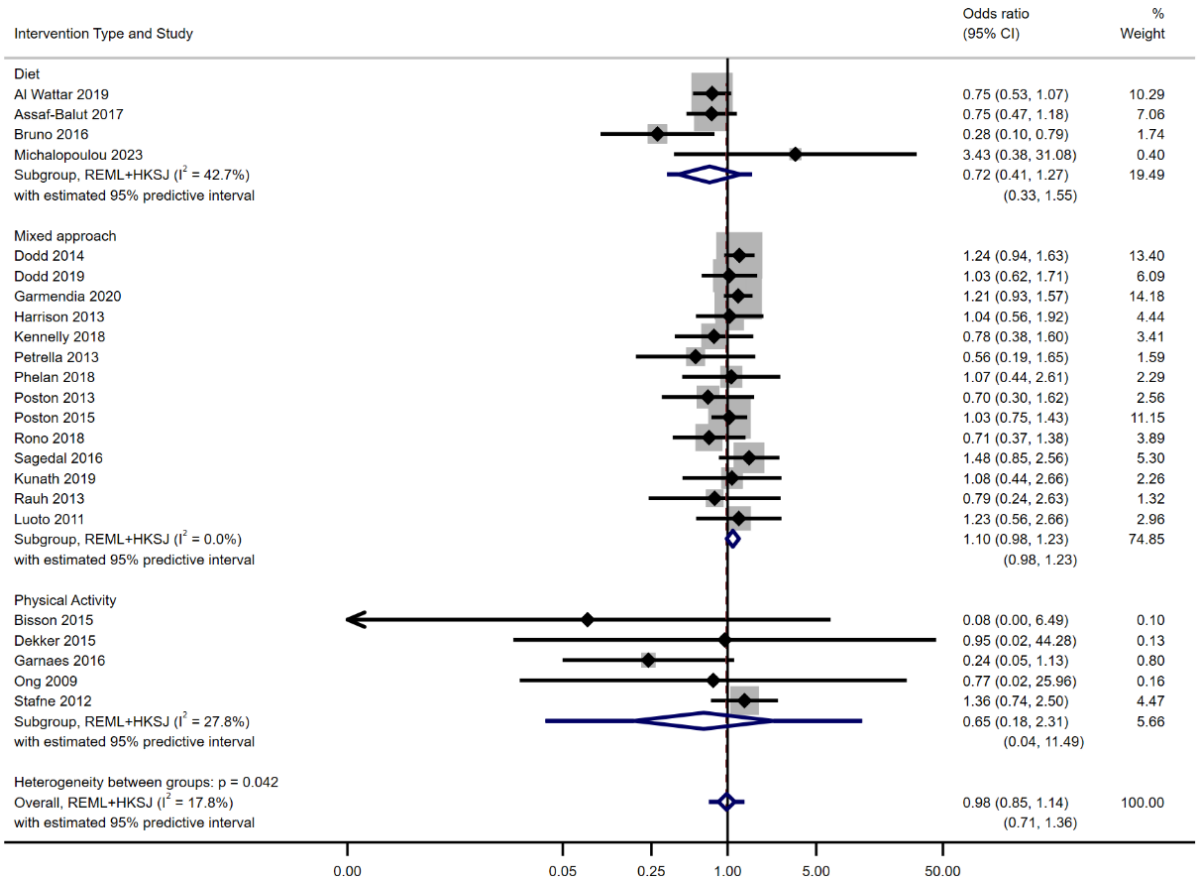


Figure 9.2: Forest plot showing the effect of lifestyle interventions on GDM (NICE) from IPD and aggregate data

Appendix 16: Forest plot for IPD meta-analysis with only low risk of bias trials

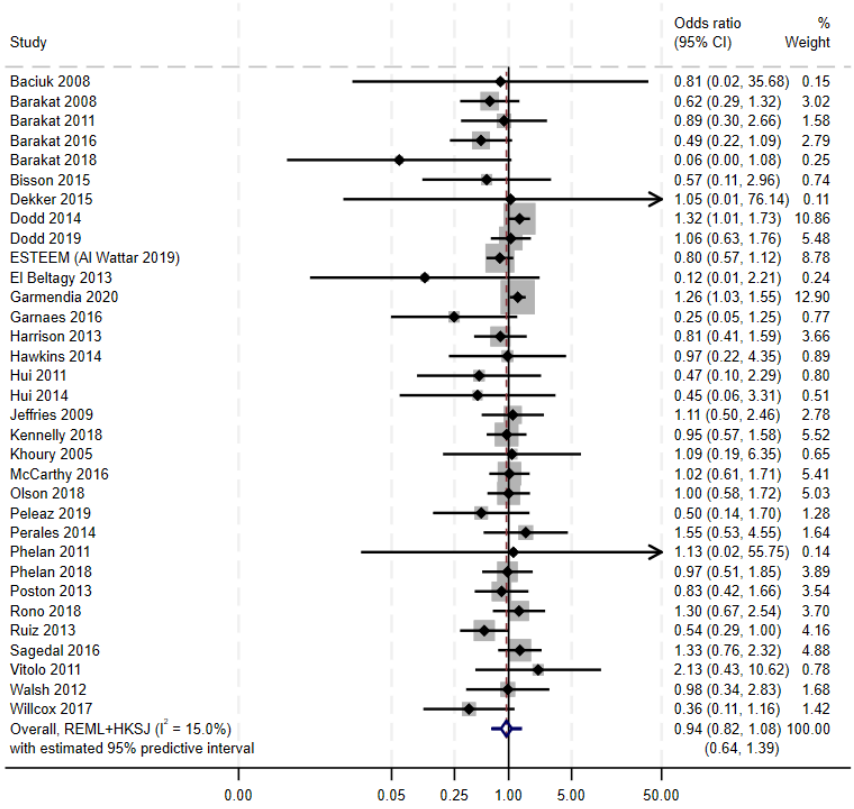


Figure 9.3: Forest plot showing the effect of lifestyle interventions on GDM (trial authors' definition) including only IPD trials rated low/medium risk of bias

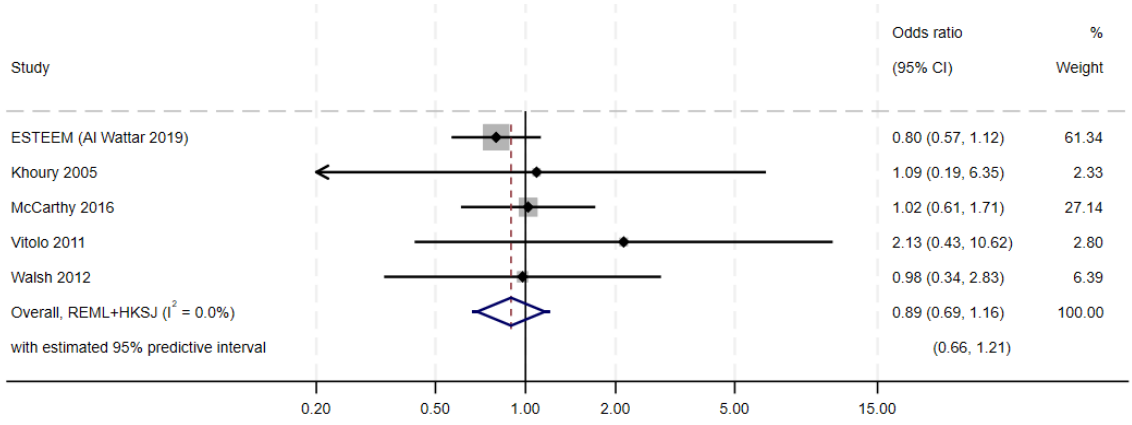


Figure 9.4: Forest plot showing the effect of diet interventions on GDM (trial authors' definition) including only IPD trials rated low/medium risk of bias

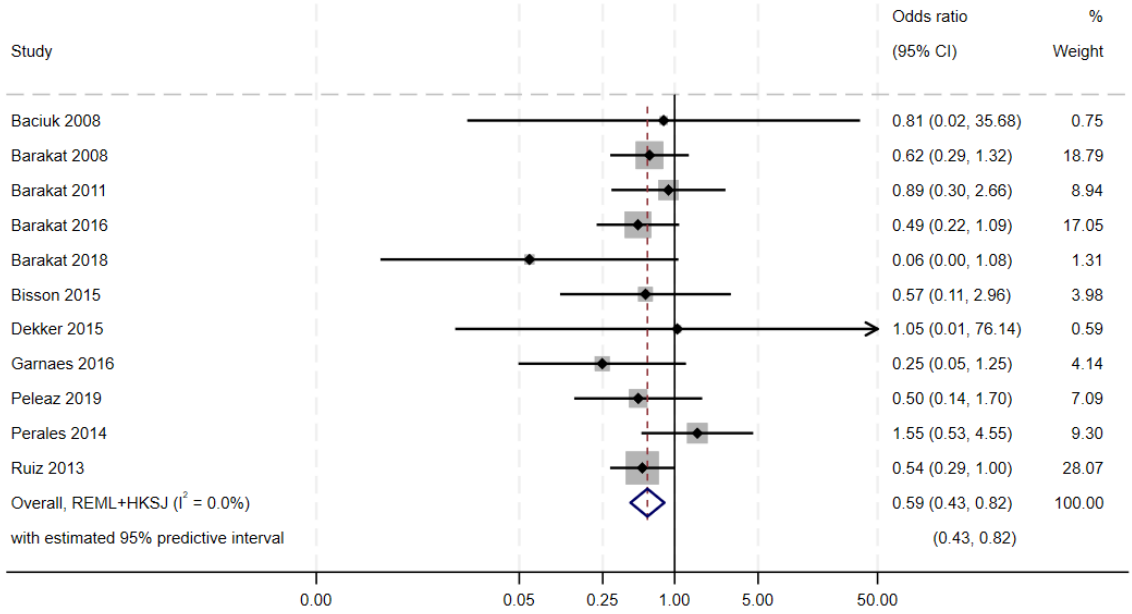


Figure 9.5: Forest plot showing the effect of physical activity interventions on GDM (trial authors' definition) including only IPD trials rated low/medium risk of bias

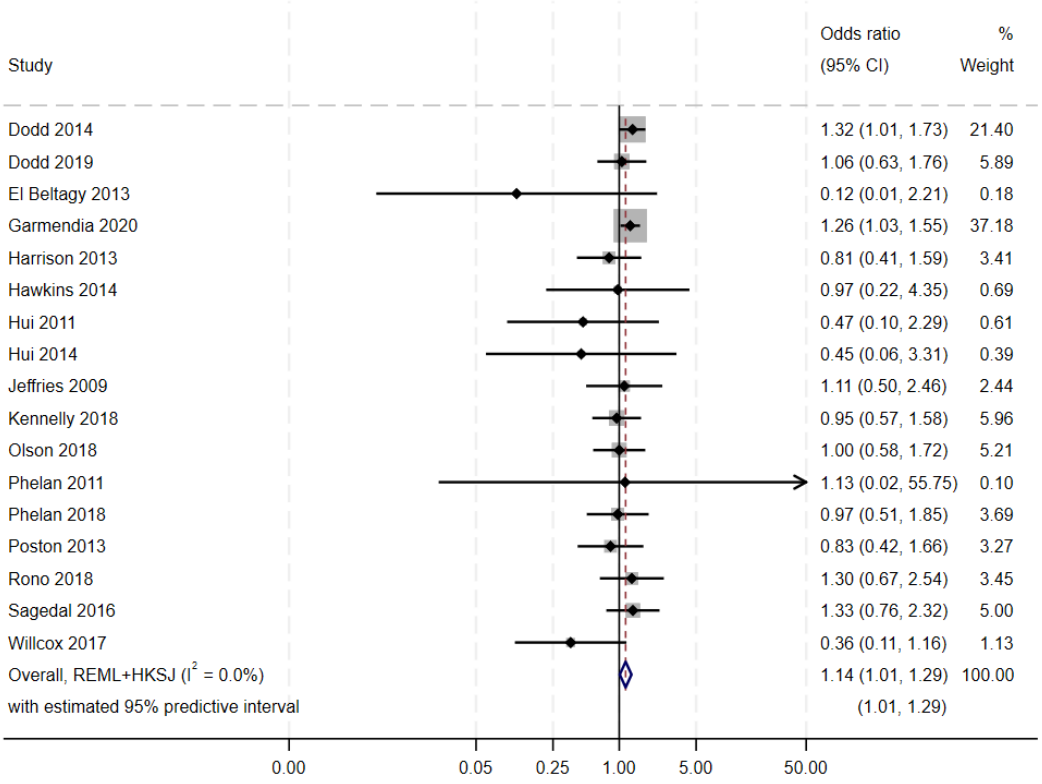


Figure 9.6: Forest plot showing the effect of mixed interventions on GDM (trial authors' definition) including only IPD trials rated low/medium risk of bias

Appendix 17: Funnel plots for trials with NICE, IADPSG and modified IADPSG definitions and continuous glucose measurements

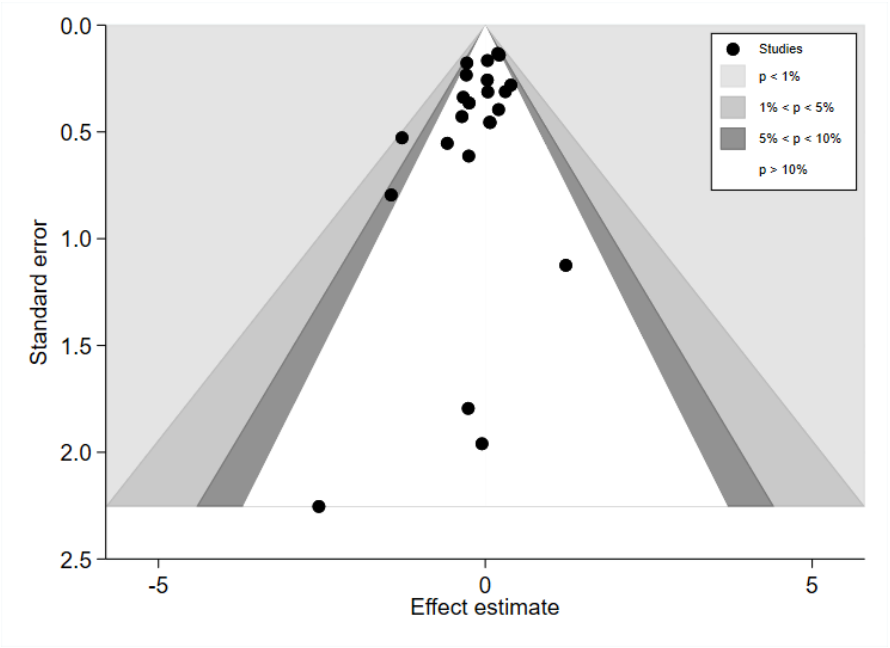


Figure 9.7: Contour-enhanced funnel plot for overall intervention effects on GDM (NICE) (IPD & aggregate data)

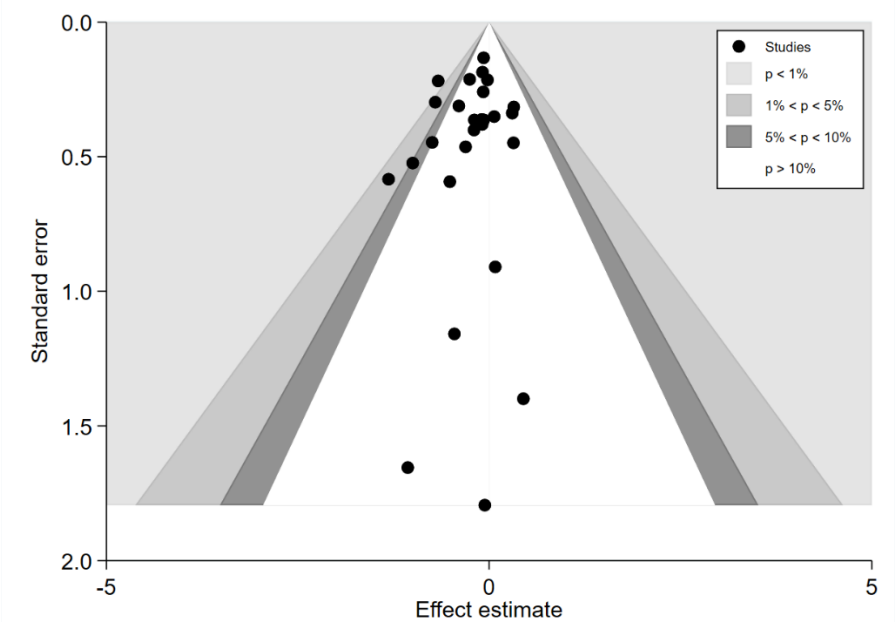


Figure 9.8: Contour-enhanced funnel plot for overall intervention effects on GDM (IADPSG) (IPD & aggregate data)

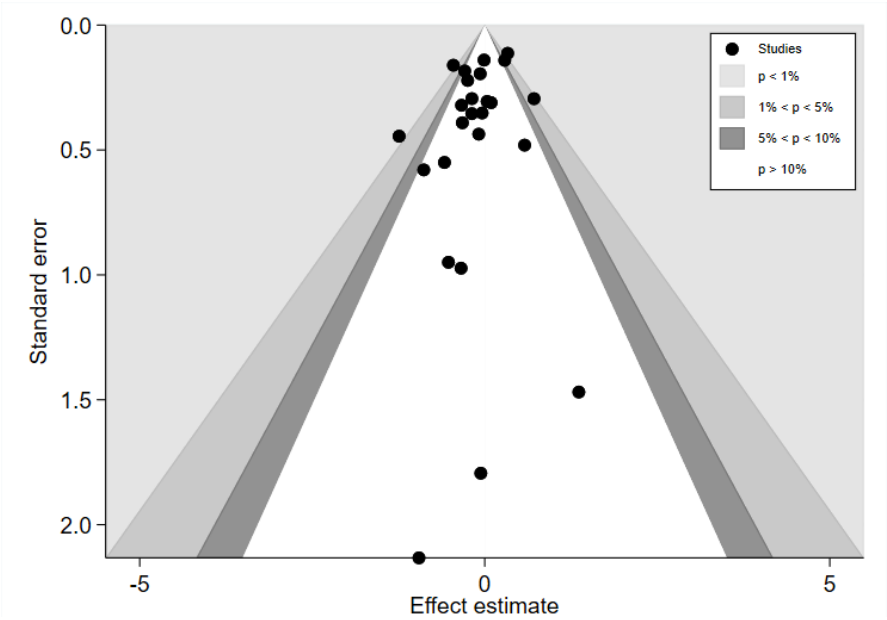


Figure 9.9: Contour-enhanced funnel plot for overall intervention effects on GDM (mod IADPSG) (IPD & aggregate data)

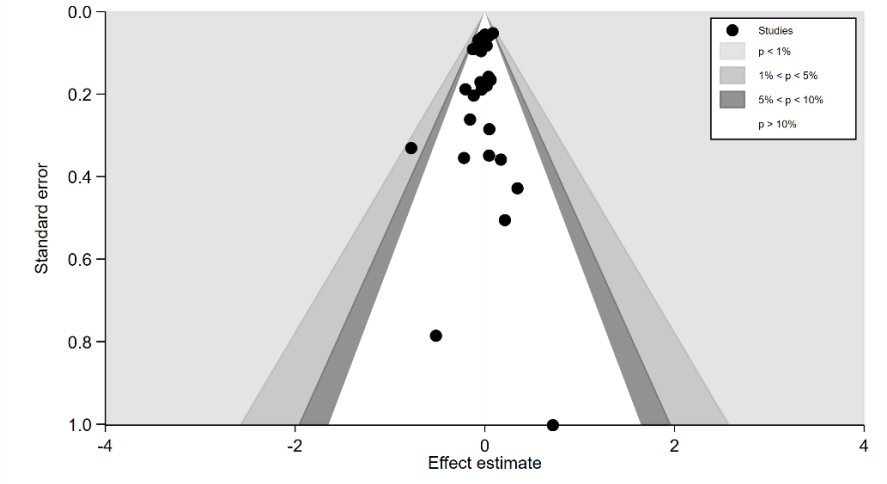


Figure 9.10: Contour-enhanced funnel plot for intervention effects on GDM (continuous 0-hour glucose measurement) taken at less than 24 weeks (IPD only)

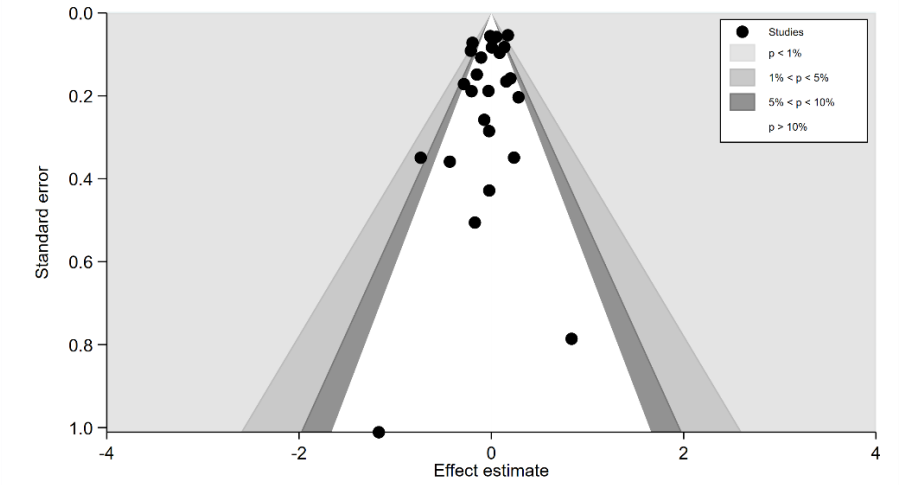


Figure 9.11: Contour-enhanced funnel plot for intervention effects on GDM (continuous 2-hours glucose measurement) taken at less than 24 weeks (IPD only)

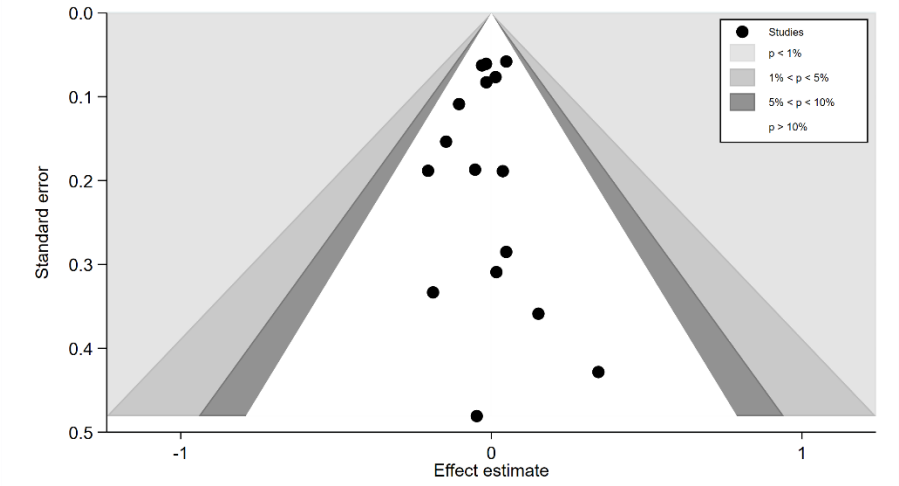


Figure 9.12: Contour-enhanced funnel plot for intervention effects on GDM (continuous 0-hour glucose measurement) taken between 24-30 weeks (IPD only)

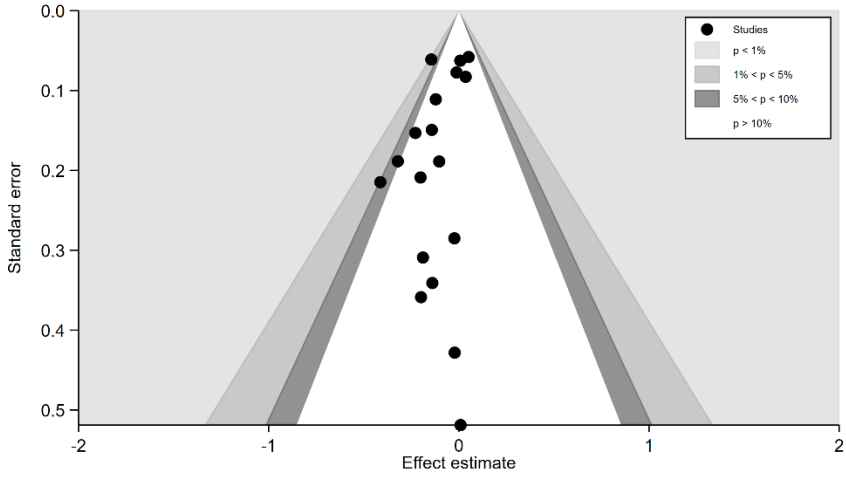


Figure 9.13: Contour-enhanced funnel plot for intervention effects on GDM (continuous 2-hours glucose measurement) taken between 24-30 weeks (IPD only)

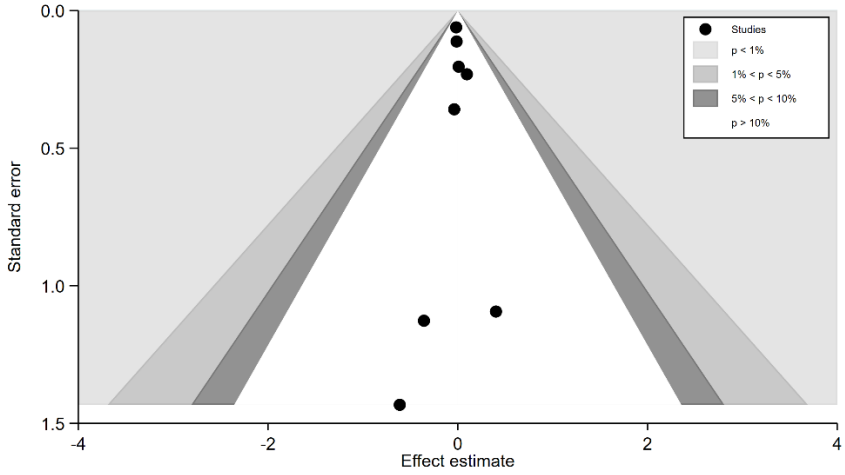


Figure 9.14: Contour-enhanced funnel plot for intervention effects on GDM (continuous 0-hour glucose measurement) taken after 30 weeks (IPD only)

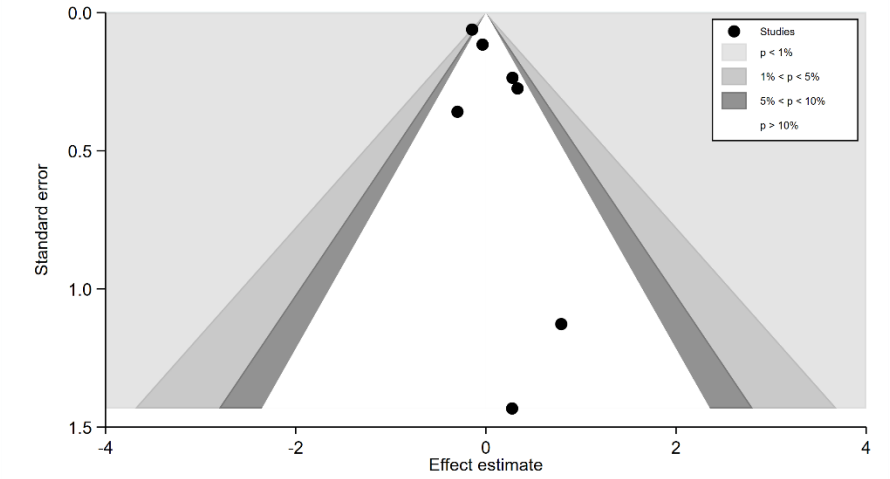


Figure 9.15: Contour-enhanced funnel plot for intervention effects on GDM (continuous 2-hours glucose measurement) taken after 30 weeks (IPD only)

Appendix 18: TiDIER intervention core components of IPD studies

Study name	Intervention type	Theory (Yes/No)	Resources	Structure	Method	Facilitators	Prior training	Location	Duration	Number of sessions	Ongoing support	Gestation week
Arthur 2020	Mixed	No	Self-monitoring tool	Individual	Face-to-face	NA	No/NR	Other	Moderate	Low	No	≥20
Assaf-Balut 2017	Diet	No	None	Group	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	Low	Low	No	<20
Baciuk 2008	Exercise	No	Other resource	Group	Face-to-face	Allied health staff	No/NR	Exercise Centre	High	High	No	<20
Barakat 2008	Exercise	No	Other resource	Group	Face-to-face	Allied health staff	Yes	Hospital/ Antenatal clinic	Moderate	High	Yes	≥20
Barakat 2011	Exercise	No	None	Group	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	High	High	No	<20
Barakat 2012a	Exercise	No	None	Group	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	High	High	No	<20
Barakat 2016	Exercise	No	None	Group	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	High	High	No	<20

Barakat 2018	Exercise	No	None	Group	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	High	High	No	<20
Bisson 2015	Exercise	No	None	Individual	Face-to-face	Allied health staff	No/NR	Exercise Centre	Low	High	No	<20
Bogaerts 2012	Mixed	Yes	Other resource	Group	Face-to-face	Medical staff	Yes	Hospital/ Antenatal clinic	Moderate	Low	No	<20
Bruno 2016	Mixed	No	Self-monitoring tool	Individual	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	High	Low	No	<20
Chao 2017	Mixed	Yes	Self-monitoring tool	Individual	Face-to-face + Remote	Allied health staff	Yes	Hospital/ Antenatal clinic	Moderate	High	Yes	<20
Cordero 2014	Exercise	No	None	Group	Face-to-face	Allied health staff	No/NR	Exercise Centre	High	High	No	<20
Dekker 2015	Exercise	No	Other resource	Individual	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	High	Low	Yes	<20
Dodd 2014	Mixed	Yes	Combination	Individual	Face-to-face	Allied health staff	Yes	Hospital/ Antenatal clinic	Moderate	Low	Yes	<20
Dodd 2019	Mixed	Yes	Combination	Individual	Face-to-face	Allied health staff	Yes	Hospital/ Antenatal clinic	Moderate	Low	Yes	<20

ESTEEM (Al Wattar 2019)	Diet	Yes	None	Individual	Face-to-face	Allied health staff	Yes	Hospital/ Antenatal clinic	Moderate	Low	Yes	<20
El Beltagy 2013	Mixed	No	Combination						Low			<20
Garmendia 2020	Mixed	No	None	Individual	Face-to-face	Allied health staff	Yes	Hospital/ Antenatal clinic	High	High	No	<20
Garnaes 2016	Exercise	Yes	Self-monitoring tool	Group	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	Moderate	High	No	<20
Guelinckx 2010	Mixed	Yes	Other resource	Group	Face-to-face	Allied health staff	Yes	Hospital/ Antenatal clinic	Moderate	Low	No	<20
Harrison 2013	Mixed	Yes	Combination	Individual	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	Low	Low	No	<20
Hawkins 2014	Mixed	Yes	Combination	Individual	Face-to-face + Remote	Other	Yes	Hospital/ Antenatal clinic	High	Moderate	Yes	<20
Hui 2011	Mixed	No	Combination	Group	Face-to-face	Allied health staff	No/NR	Exercise Centre	Low	Moderate	No	≥20
Hui 2014	Mixed	No	Combination	Group	Face-to-face + Remote	Allied health staff	No/NR	Exercise Centre	Low	High	No	≥20
Jeffries 2009	Mixed	No	Self-monitoring tool	Individual	Face-to-face	Medical staff	No/NR	Hospital/ Antenatal clinic	High	Low	No	<20

Kennelly 2018	Mixed	Yes	Other resource	Group	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	High	Low	Yes	<20
Khaledan 2010	Exercise	No	None	Group	Face-to-face	Other	No/NR	Hospital/ Antenatal clinic	Low	High	No	≥20
Khoury 2005	Diet	No	Other resource	Individual	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	Moderate	Low	No	<20
Kunath 2019	Mixed	No	Combination	Individual	Face-to-face	Medical staff	Yes	Hospital/ Antenatal clinic	Moderate	Low	No	<20
Luoto 2011	Mixed	Yes	Other resource	Individual	Face-to-face	Medical staff	Yes	Hospital/ Antenatal clinic	High	Moderate	Yes	<20
McCarthy 2016	Diet	No	Combination	Individual	Face-to-face	Medical staff	No/NR	Hospital/ Antenatal clinic	Moderate	Low	Yes	≥20
Nascimento 2011	Exercise	No	Self-monitoring tool	Group	Face-to-face	Allied health staff	Yes	Hospital/ Antenatal clinic	Low	Moderate	No	≥20
Olson 2018	Mixed	Yes	Combination	Individual	Remote	NA	NA	Other	Moderate	NA	Yes	≥20
Ong 2009	Exercise	No	Other resource	Individual	Face-to-face	Other	No/NR	Other	Low	High	No	<20
Oostdam 2012	Exercise	No	None	Group	Face-to-face	Allied health staff	Yes	Hospital/ Antenatal clinic	Low	High	No	≥20

Peleaz 2019	Exercise	No	None	Group	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	High	High	No	<20
Perales 2014	Exercise	No	None	Group	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	High	High	No	<20
Petrella 2013	Mixed	No	Self-monitoring tool	Individual	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	High	Low	No	<20
Phelan 2011	Mixed	Yes	Combination	Individual	Face-to-face	Allied health staff	No/NR	Other	Moderate	Low	Yes	<20
Phelan 2018	Mixed	Yes	Combination	Individual	Face-to-face	Allied health staff	No/NR	Other	Moderate	Moderate	No	<20
Poston 2013	Mixed	Yes	Combination	Individual	Face-to-face + Remote	Allied health staff	Yes	Hospital/ Antenatal clinic	High	Moderate	Yes	≥20
Poston 2015	Mixed	Yes	Combination	Group	Face-to-face + Remote	Other	Yes	Hospital/ Antenatal clinic	Low	Moderate	Yes	<20
Rauh 2013	Mixed	Yes	Self-monitoring tool	Individual	Face-to-face	Other	Yes	Hospital/ Antenatal clinic	Low	Low	No	≥20
Renault 2013	Diet	No	Self-monitoring tool	Individual	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	High	Moderate	Yes	<20

Rono 2018	Mixed	No	None	Individual	Face-to-face	Medical staff	No/NR	Hospital/ Antenatal clinic	High	Low	No	<20
Ruiz 2013	Exercise	No	None	Group	Face-to-face	Allied health staff	No/NR	Exercise Centre	High	High	No	<20
Sagedal 2017	Mixed	No	Other resource	Group	Face-to-face + Remote	Allied health staff	Yes	Exercise Centre	Moderate	High	Yes	≥20
Stafne 2012	Exercise	No	None	Group	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	Low	Moderate	No	≥20
Vinter 2011	Mixed	Yes	Self-monitoring tool	Group	Face-to-face	Allied health staff	No/NR	Exercise Centre	Moderate	High	No	<20
Vitolo 2011	Diet	No	Other resource	Individual	Face-to-face	Other	No/NR	Hospital/ Antenatal clinic	Low	Low	No	≥20
Walsh 2012	Diet	No	Other resource	Group	Face-to-face	Allied health staff	No/NR	Hospital/ Antenatal clinic	Moderate	Low	No	<20
Willcox 2017	Mixed	Yes	Combination	Individual	Face-to-face + Remote	Allied health staff	No/NR	Hospital/ Antenatal clinic	Low	Moderate	Yes	≥20
Wolff 2008	Diet	No	None	Individual	Face-to-face	Allied health staff	Yes	Hospital/ Antenatal clinic	NA	Moderate	No	<20

Appendix 19: Forest plots for treatment covariate interaction effects for GDM (trial authors' definition)

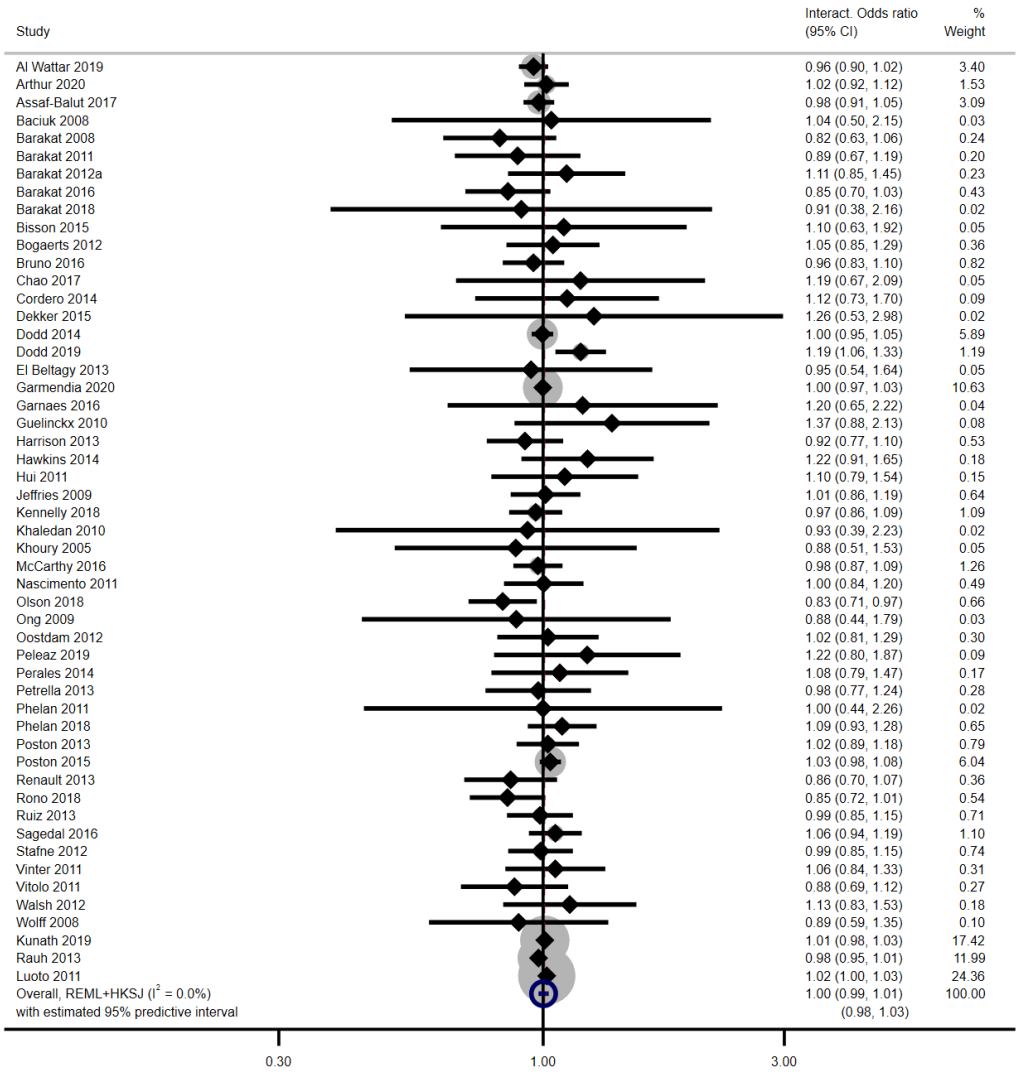


Figure 9.16: Forest plot showing the effect of the interaction between lifestyle interventions and age (continuous) on GDM (trial authors' definition) using IPD meta-analysis

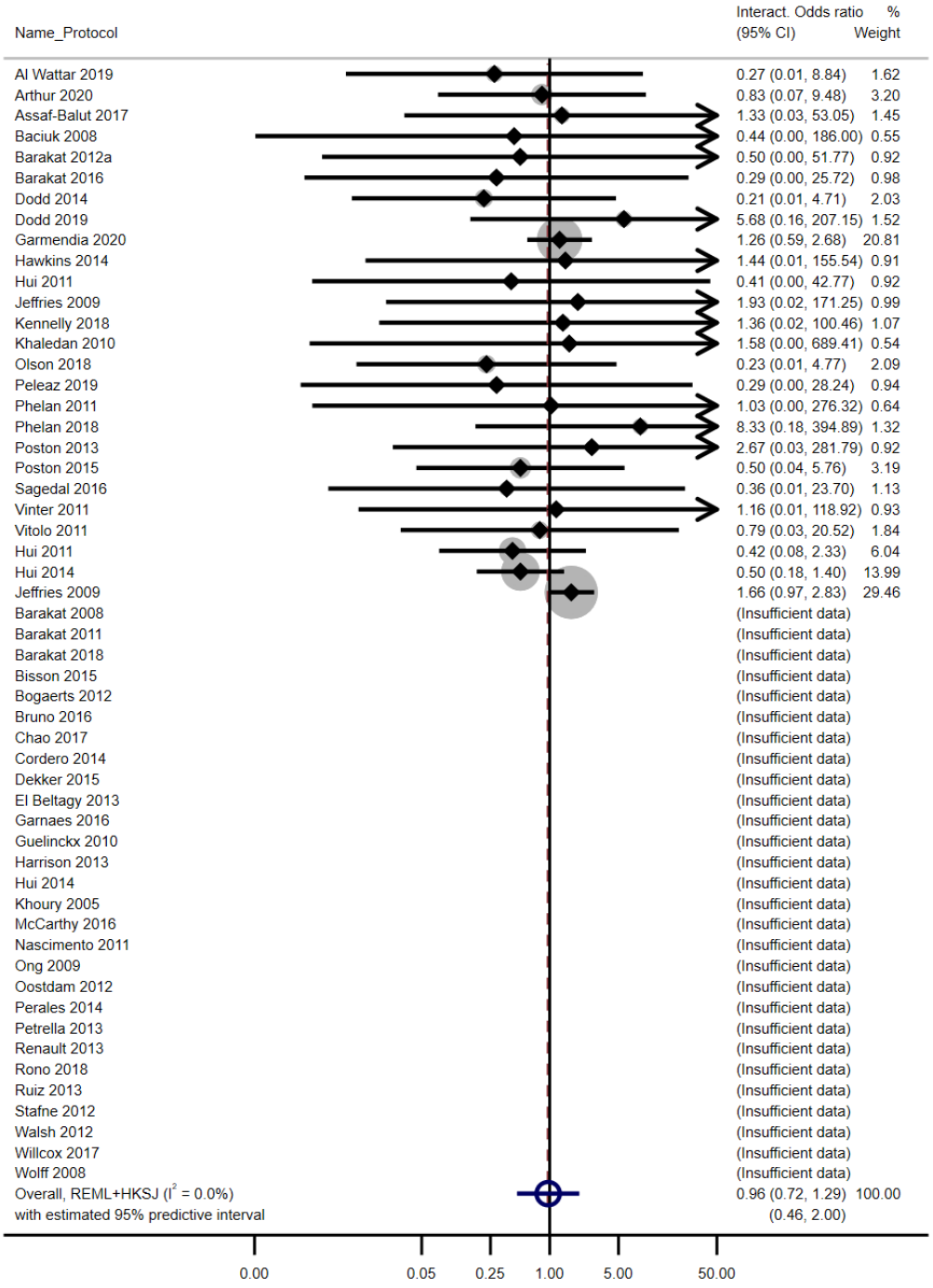


Figure 9.17: Forest plot showing the effect of the interaction between lifestyle interventions and age (categorical) on GDM (trial authors' definition) using IPD meta-analysis

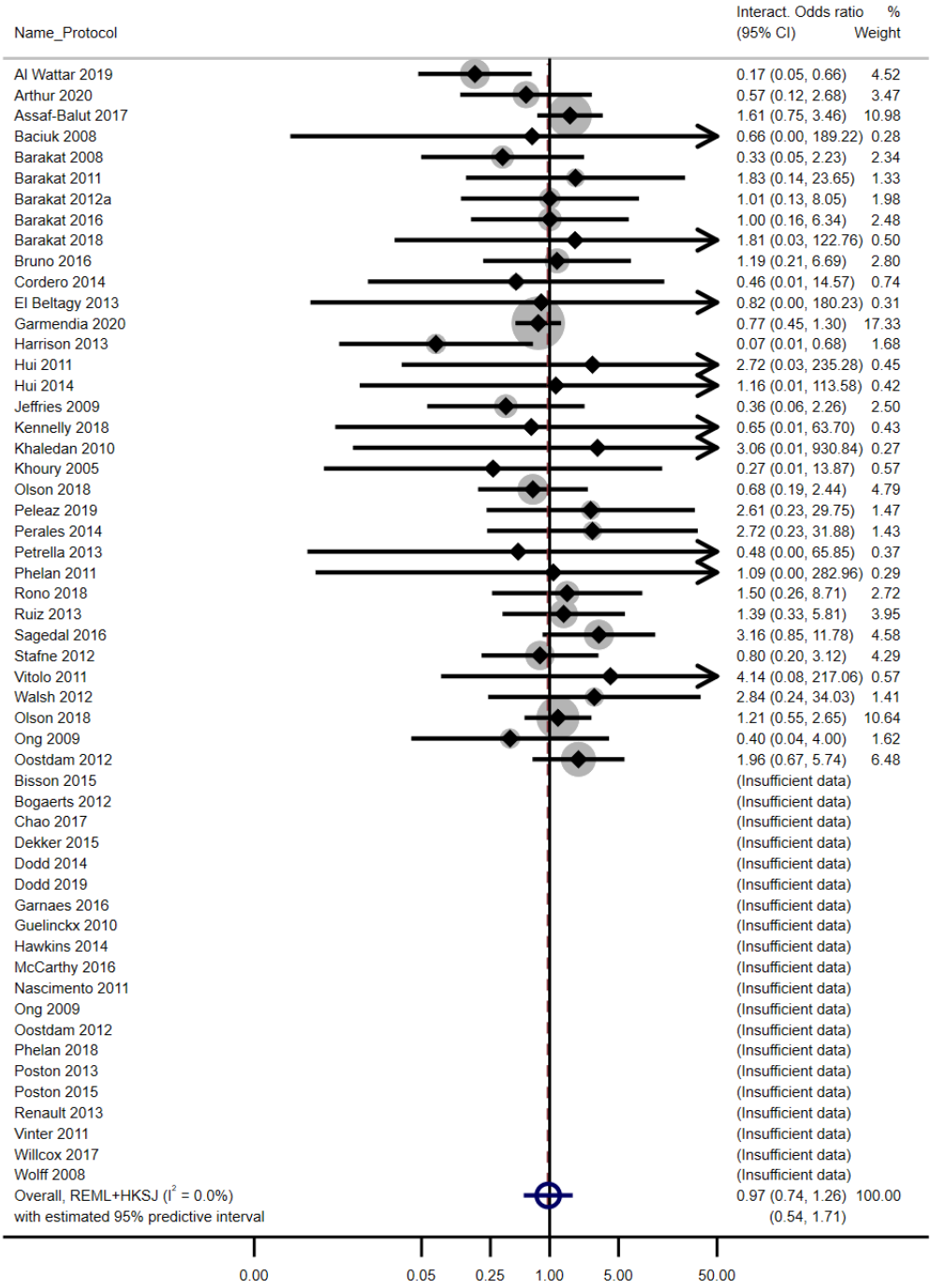


Figure 9.18: Forest plot showing the effect of the interaction between lifestyle interventions and BMI (overweight) on GDM (trial authors' definition) using IPD meta-analysis

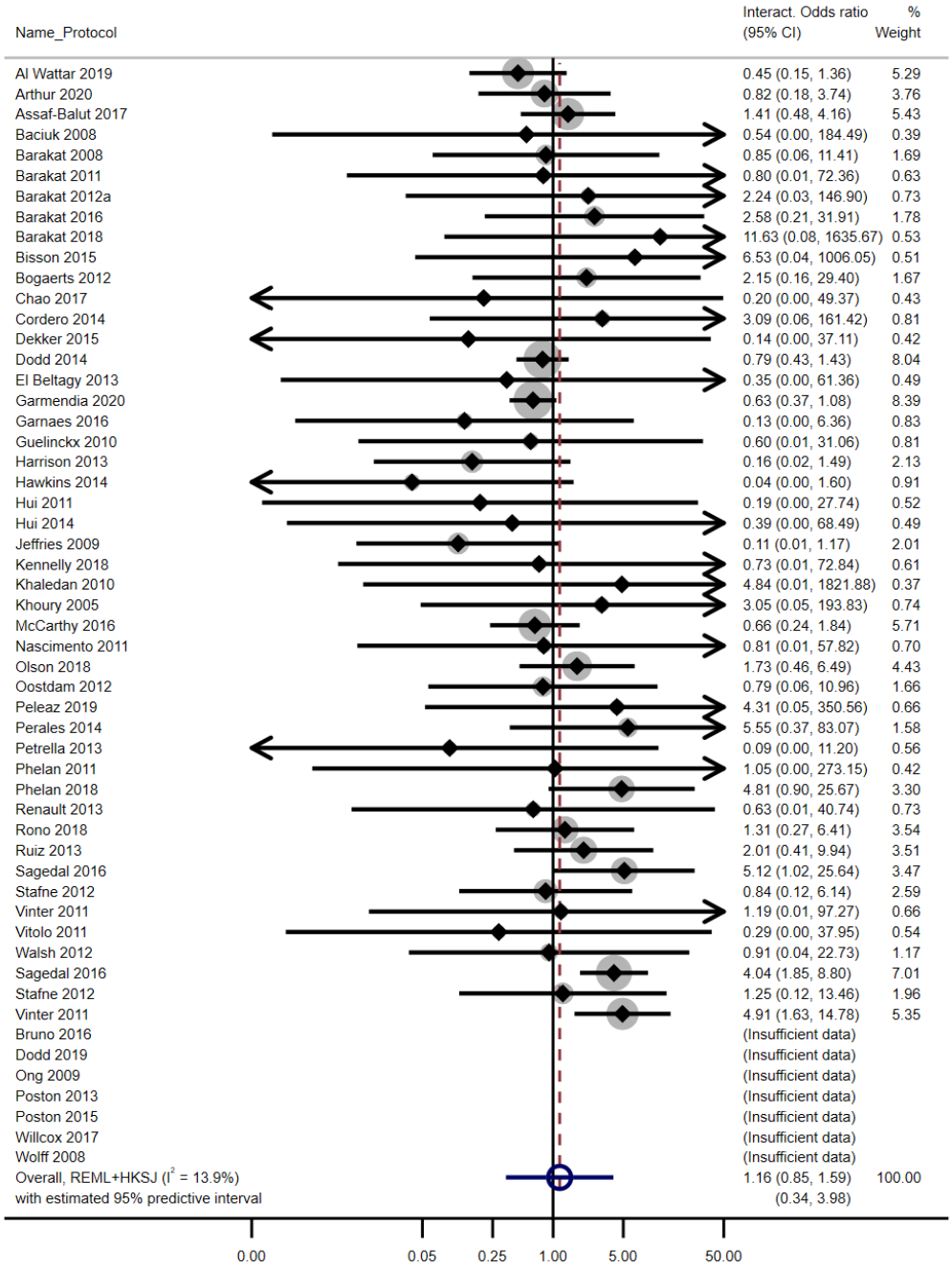


Figure 9.19: Forest plot showing the effect of the interaction between lifestyle interventions and BMI (obese) on GDM (trial authors' definition) using IPD meta-analysis

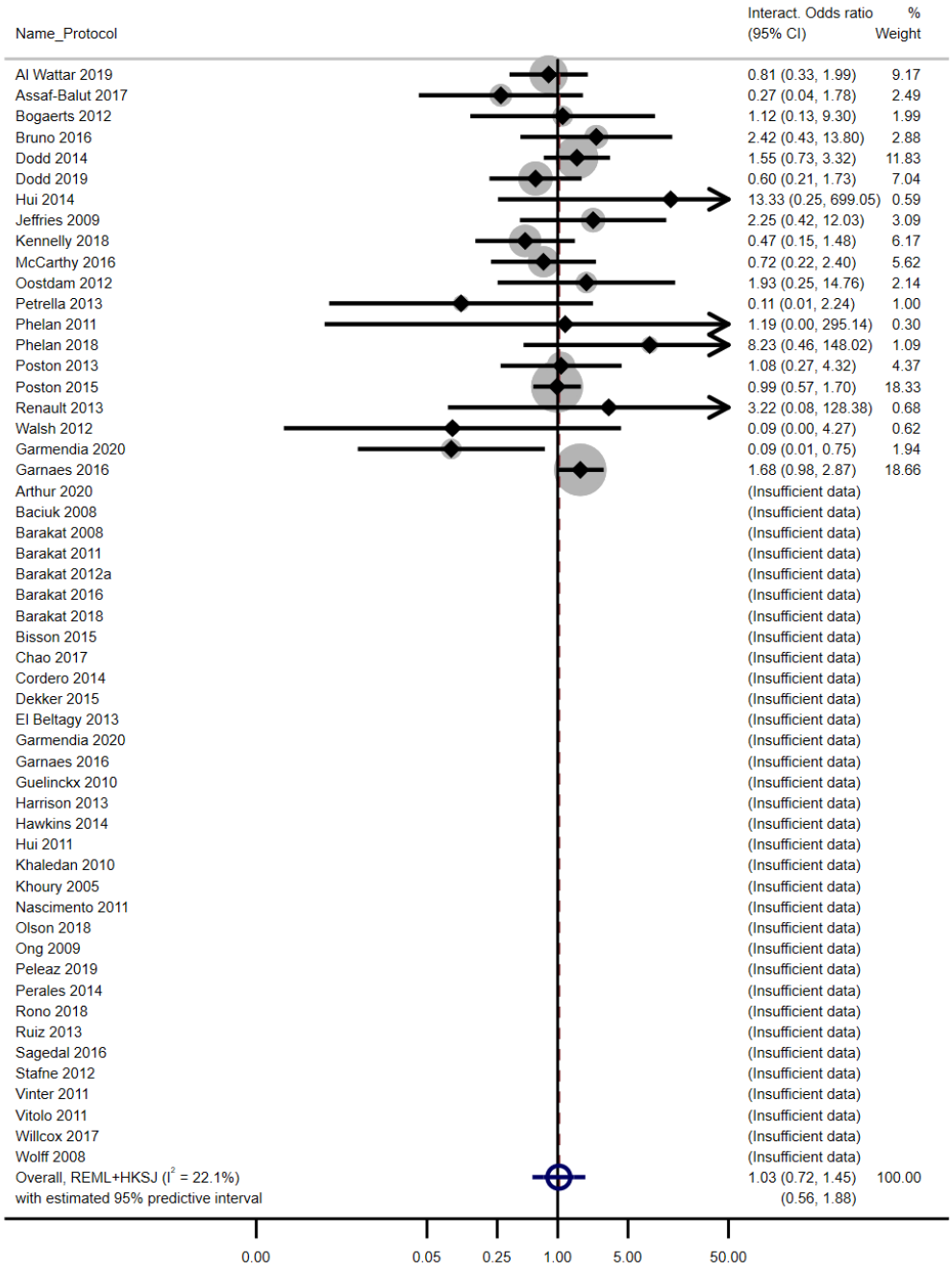


Figure 9.20: Forest plot showing the effect of the interaction between lifestyle interventions and ethnicity on GDM (trial authors' definition) using IPD meta-analysis

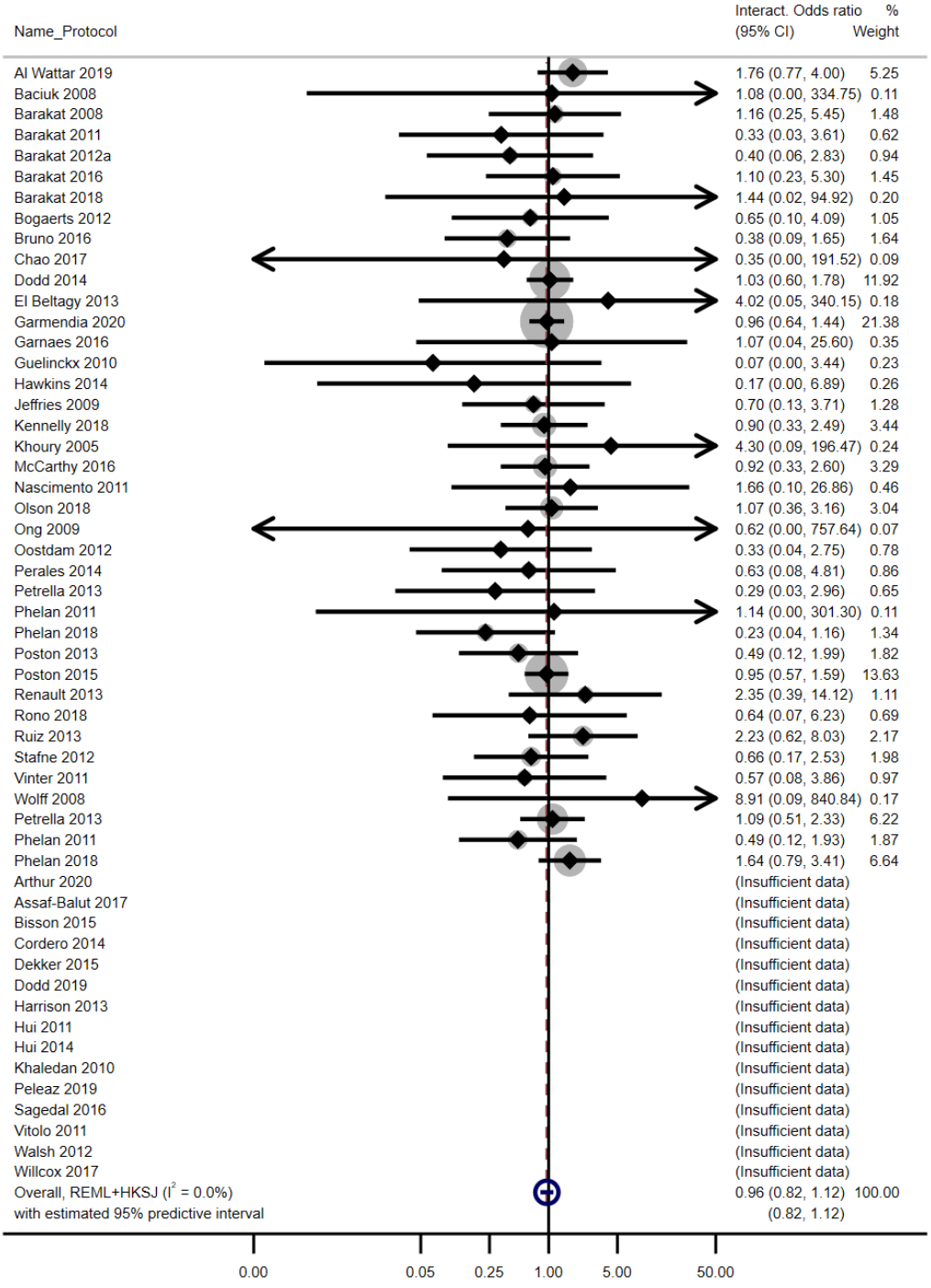


Figure 9.21: Forest plot showing the effect of the interaction between lifestyle interventions and parity on GDM (trial authors' definition) using IPD meta-analysis

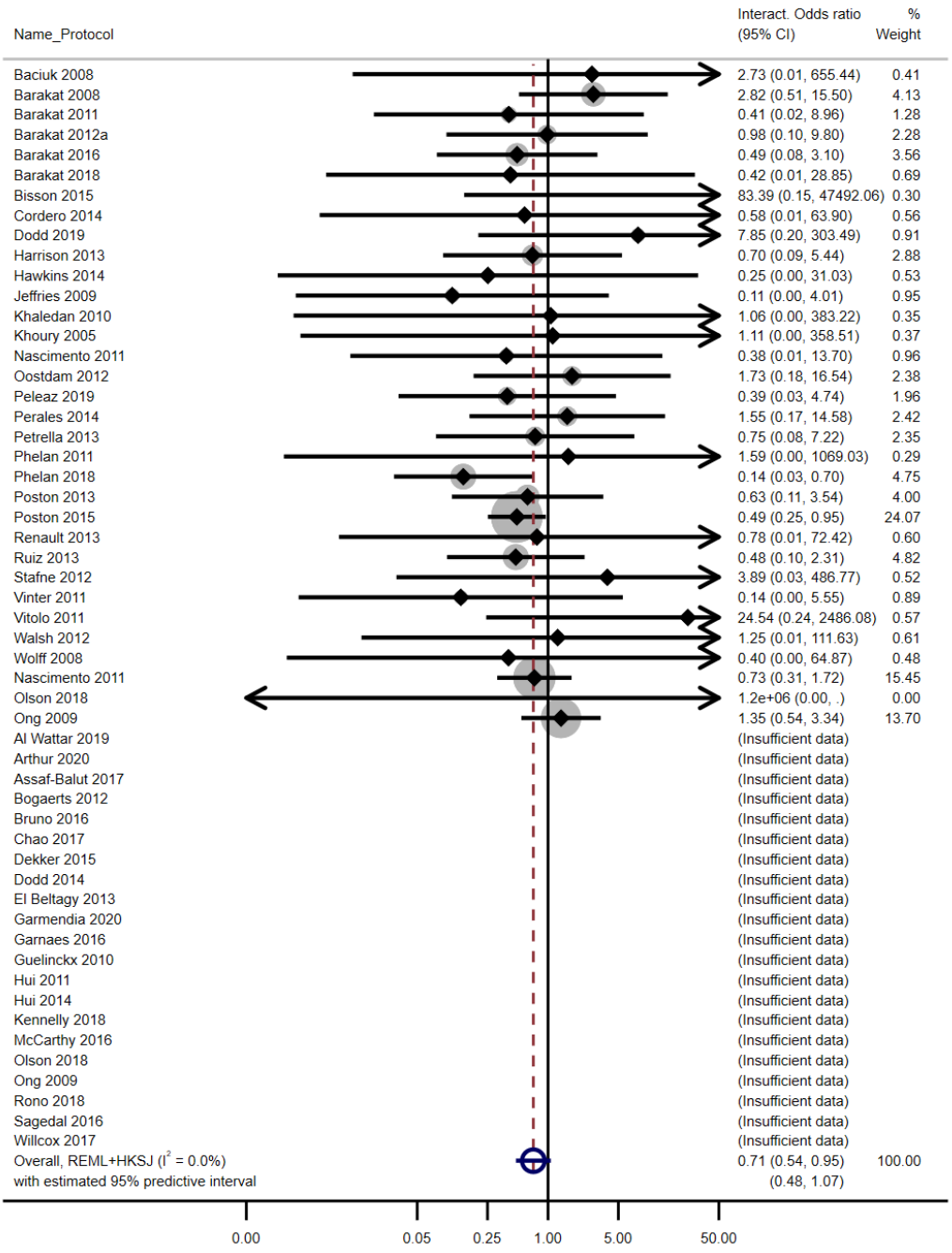


Figure 9.22: Forest plot showing the effect of the interaction between lifestyle and education (mid) on GDM (trial authors' definition) using IPD meta-analysis

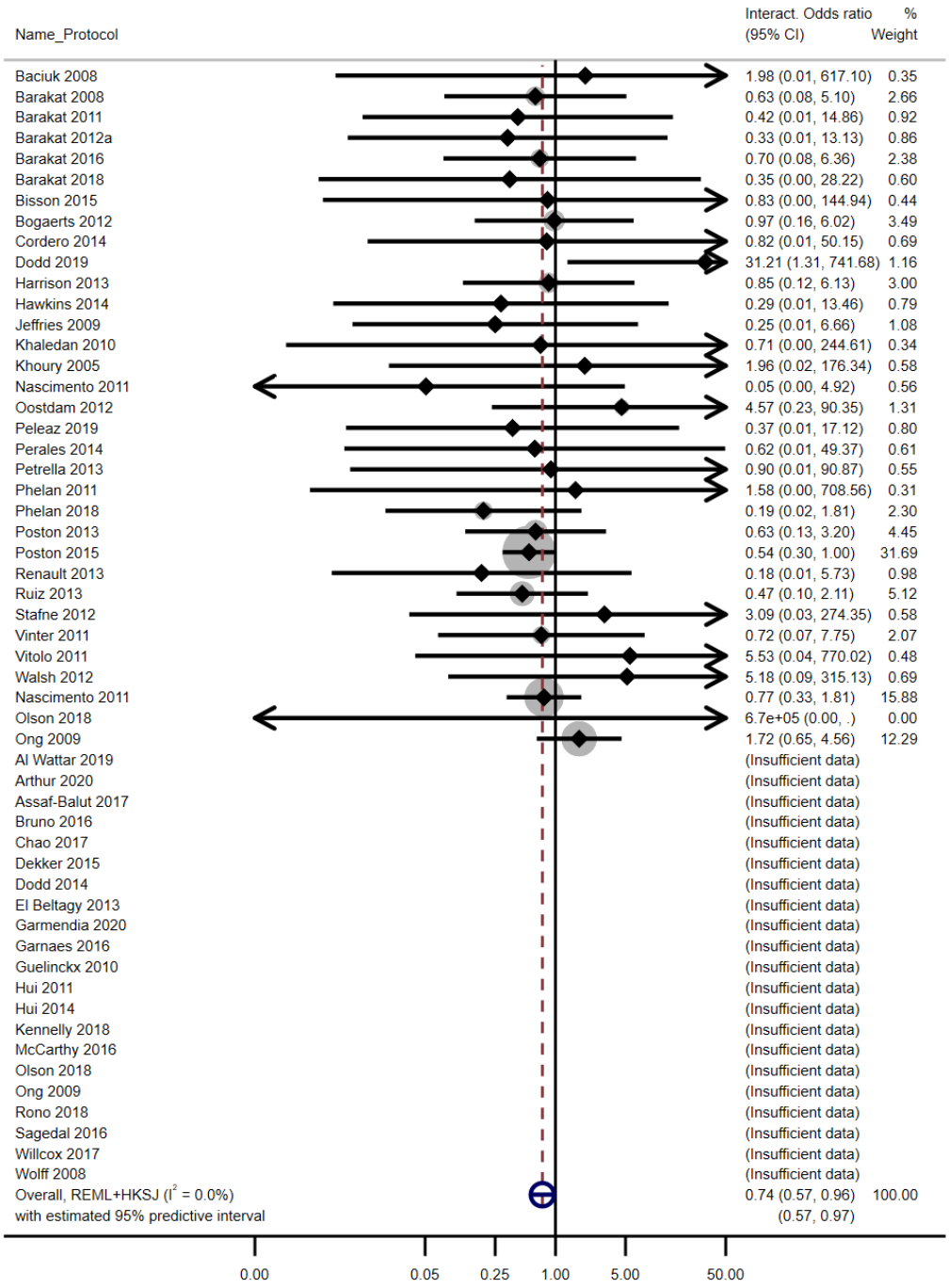


Figure 9.23: Forest plot showing the effect of the interaction between lifestyle and education (high) on GDM (trial authors' definition) using IPD meta-analysis

Appendix 20: Forest plots for treatment covariate interaction effects for GDM (NICE definition)

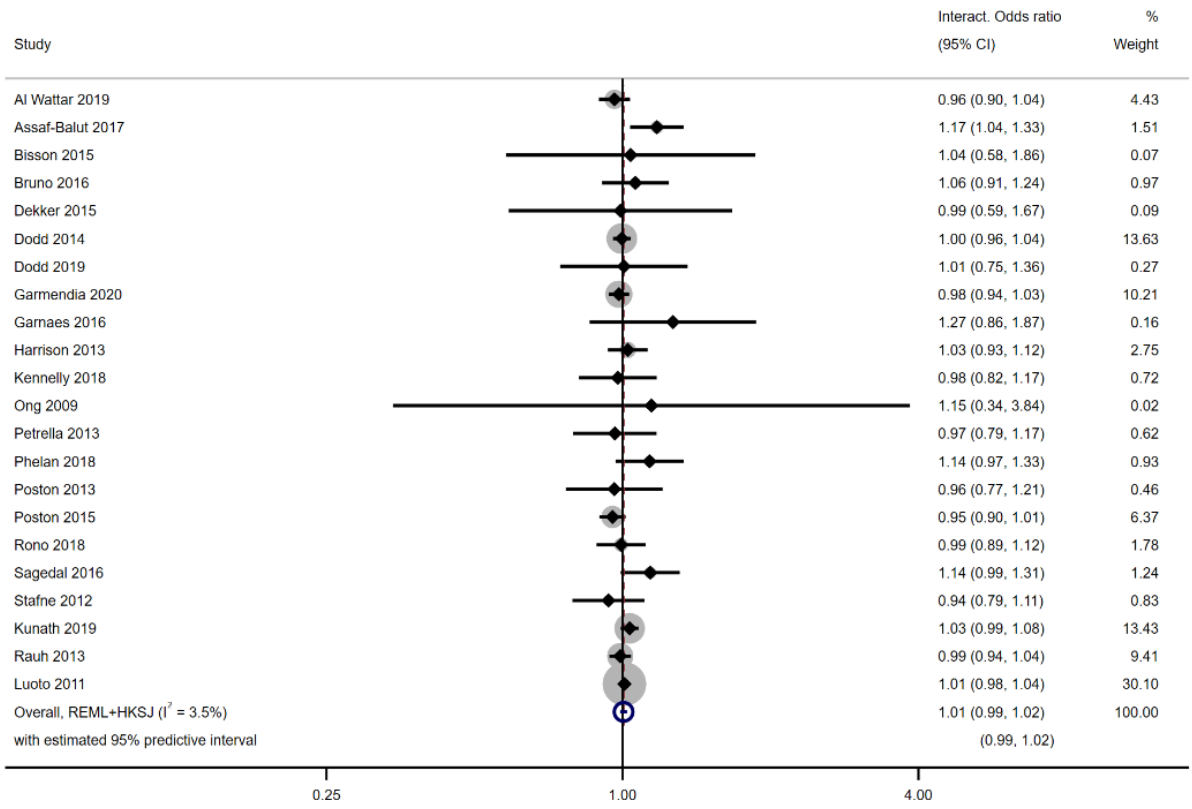


Figure 9.24 : Forest plot showing the effect of the interaction between lifestyle interventions and age (continuous) on GDM (NICE definition) using IPD meta-analysis

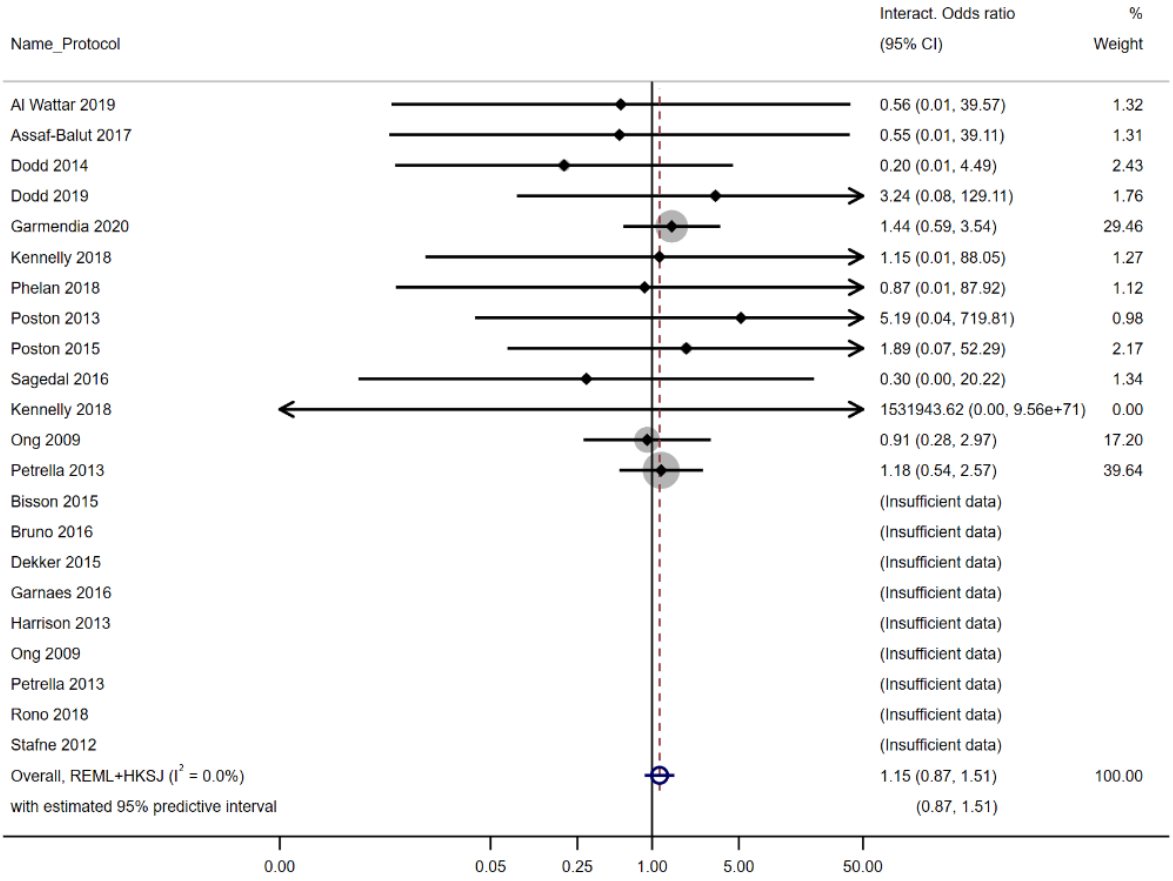


Figure 9.25: Forest plot showing the effect of the interaction between lifestyle interventions and age (categorical) on GDM (NICE definition) using IPD meta-analysis

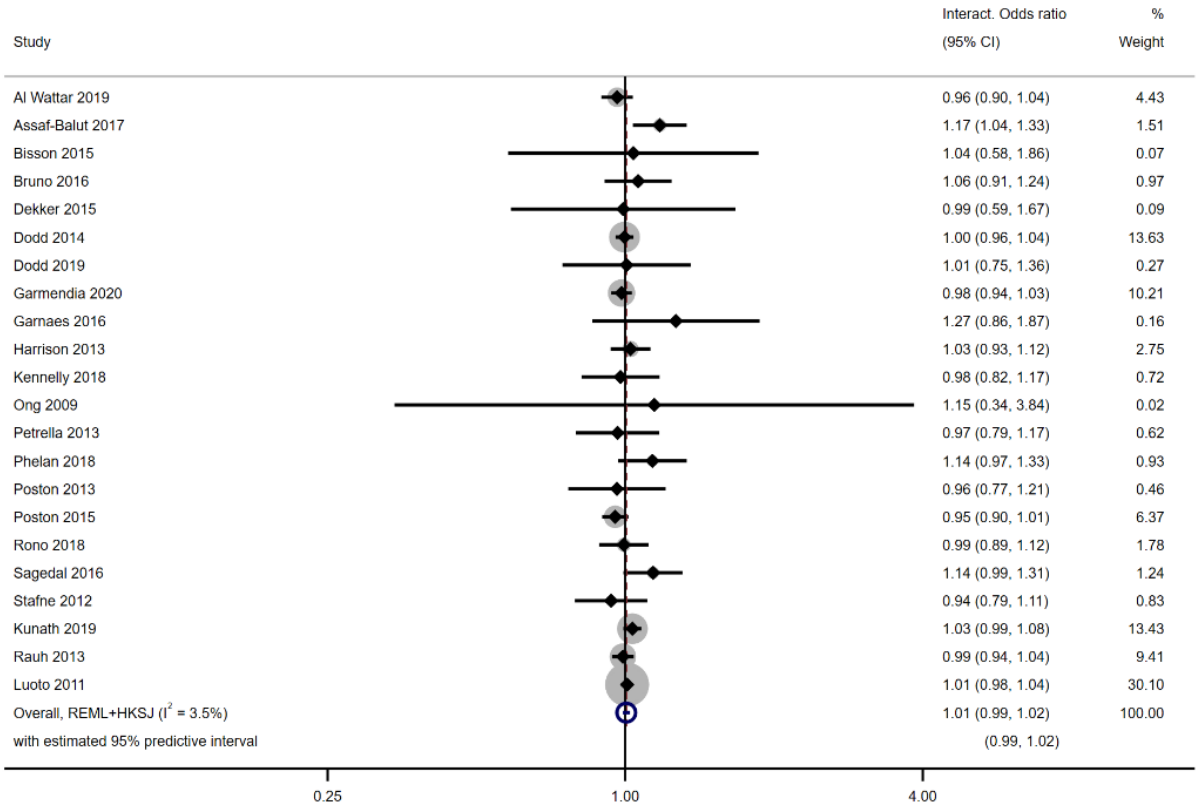


Figure 9.26: Forest plot showing the effect of the interaction between lifestyle interventions and BMI (continuous) on GDM (NICE definition) using IPD meta-analysis

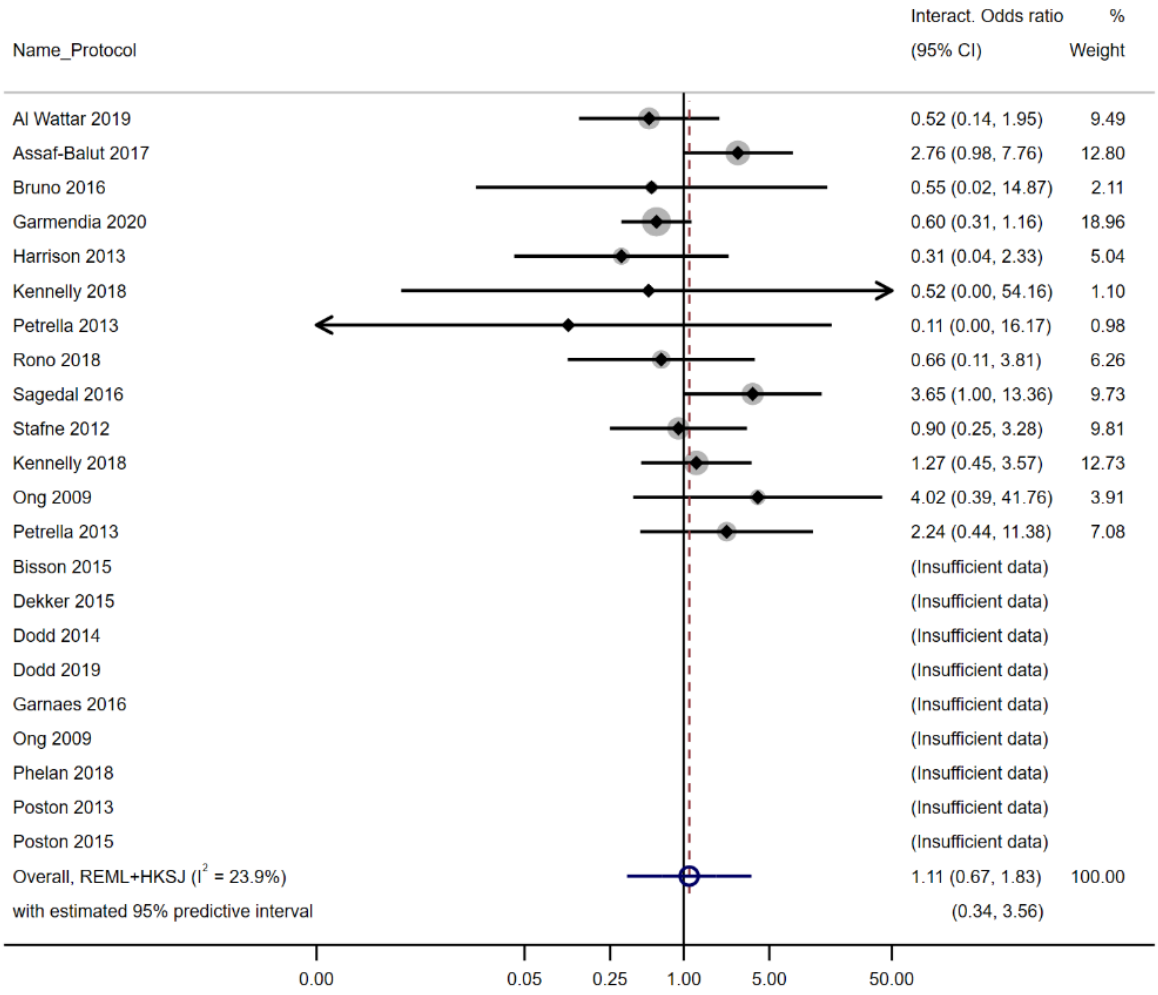


Figure 9.27: Forest plot showing the effect of the interaction between lifestyle interventions and BMI (overweight) on GDM (NICE definition) using IPD meta-analysis

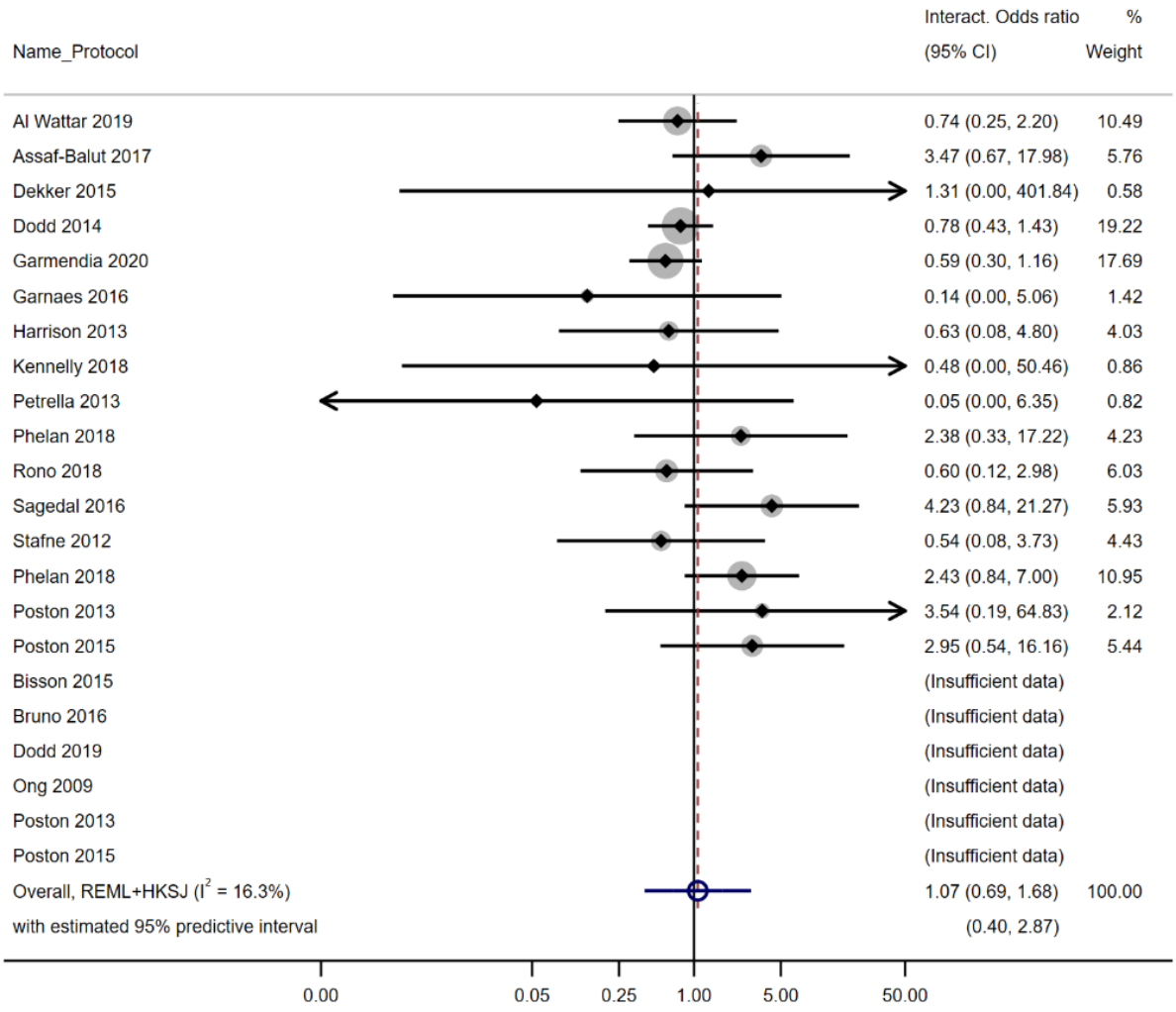


Figure 9.28: Forest plot showing the effect of the interaction between lifestyle interventions and BMI (obese) on GDM (NICE definition) using IPD meta-analysis

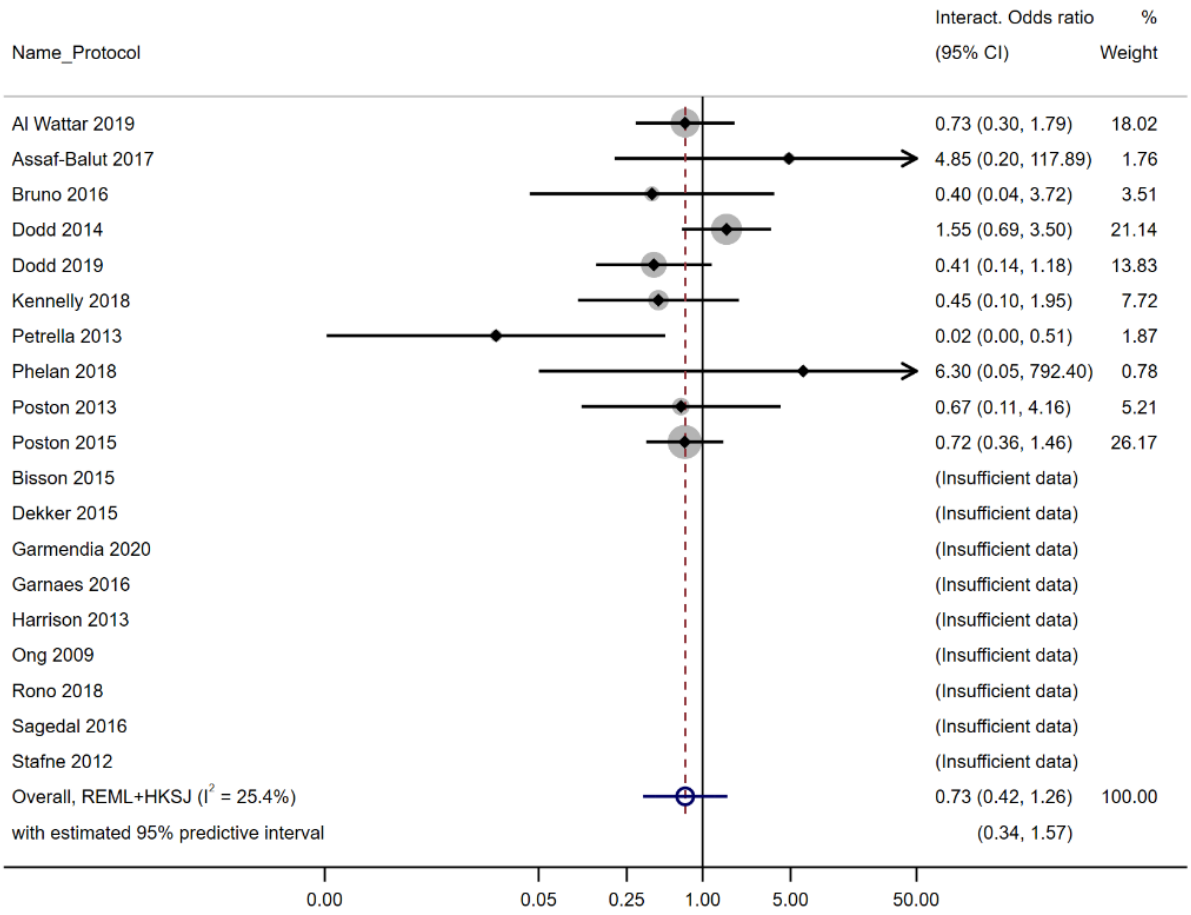


Figure 9.29: Forest plot showing the effect of the interaction between lifestyle interventions and ethnicity on GDM (NICE definition) using IPD meta-analysis

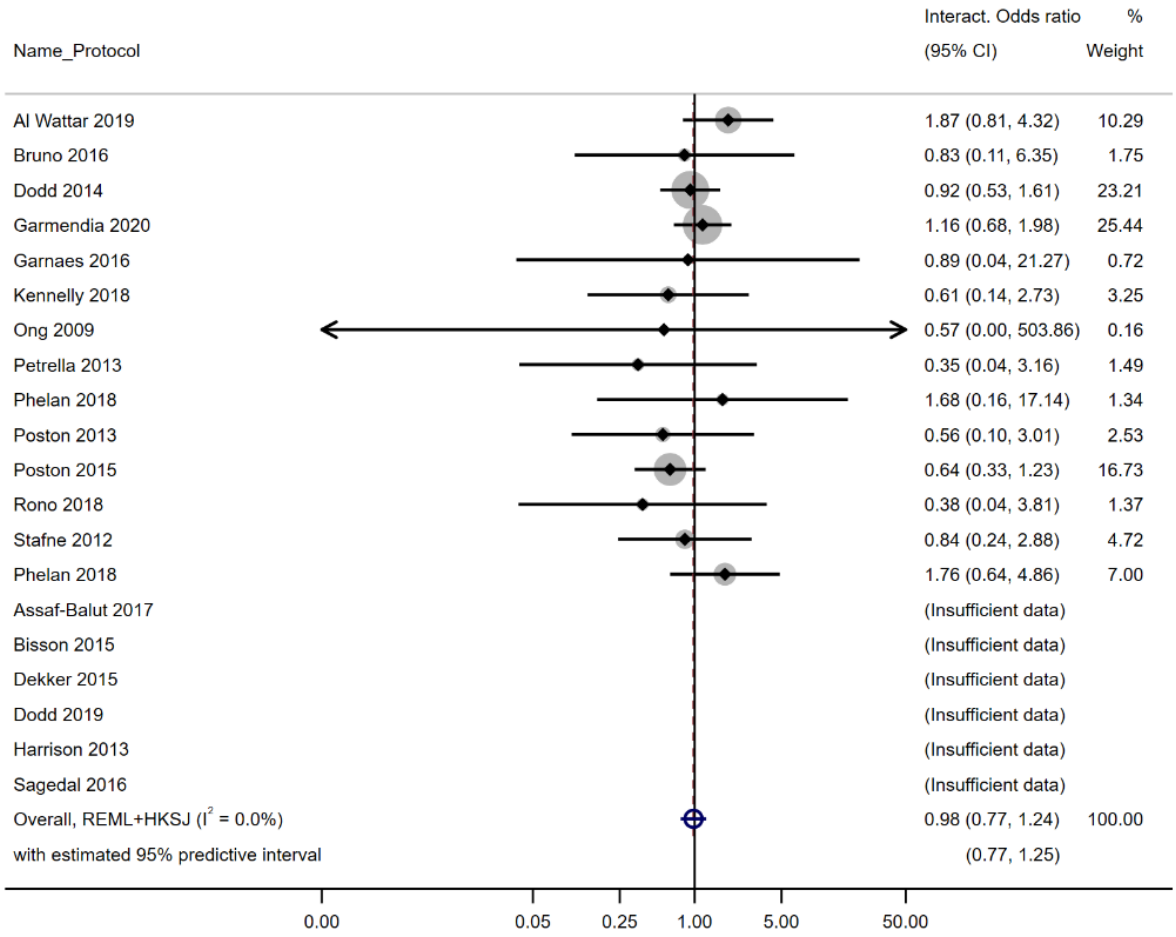


Figure 9.30: Forest plot showing the effect of the interaction between lifestyle interventions and parity on GDM (NICE definition) using IPD meta-analysis

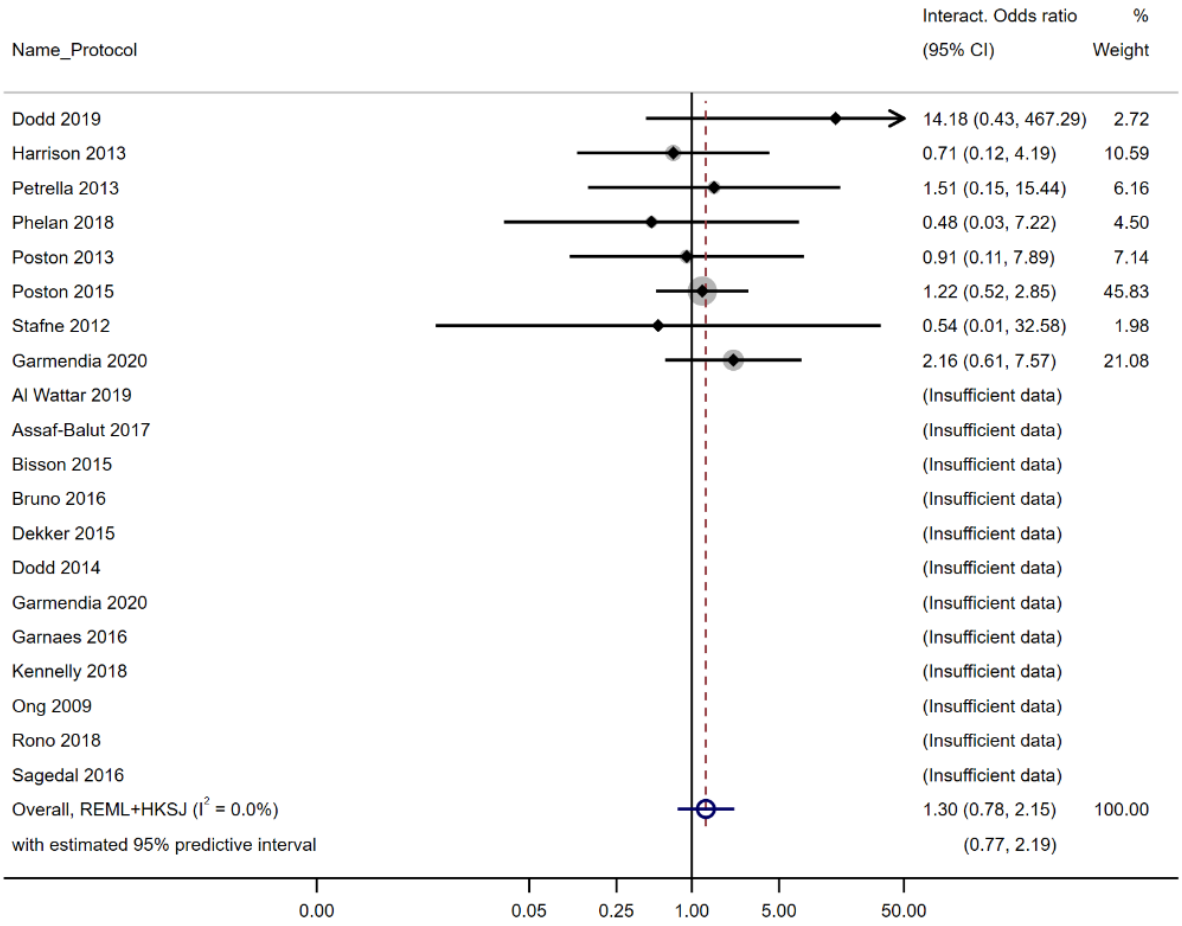


Figure 9.31: Forest plot showing the effect of the interaction between lifestyle interventions and mother's education (mid) on GDM (NICE definition) using IPD meta-analysis

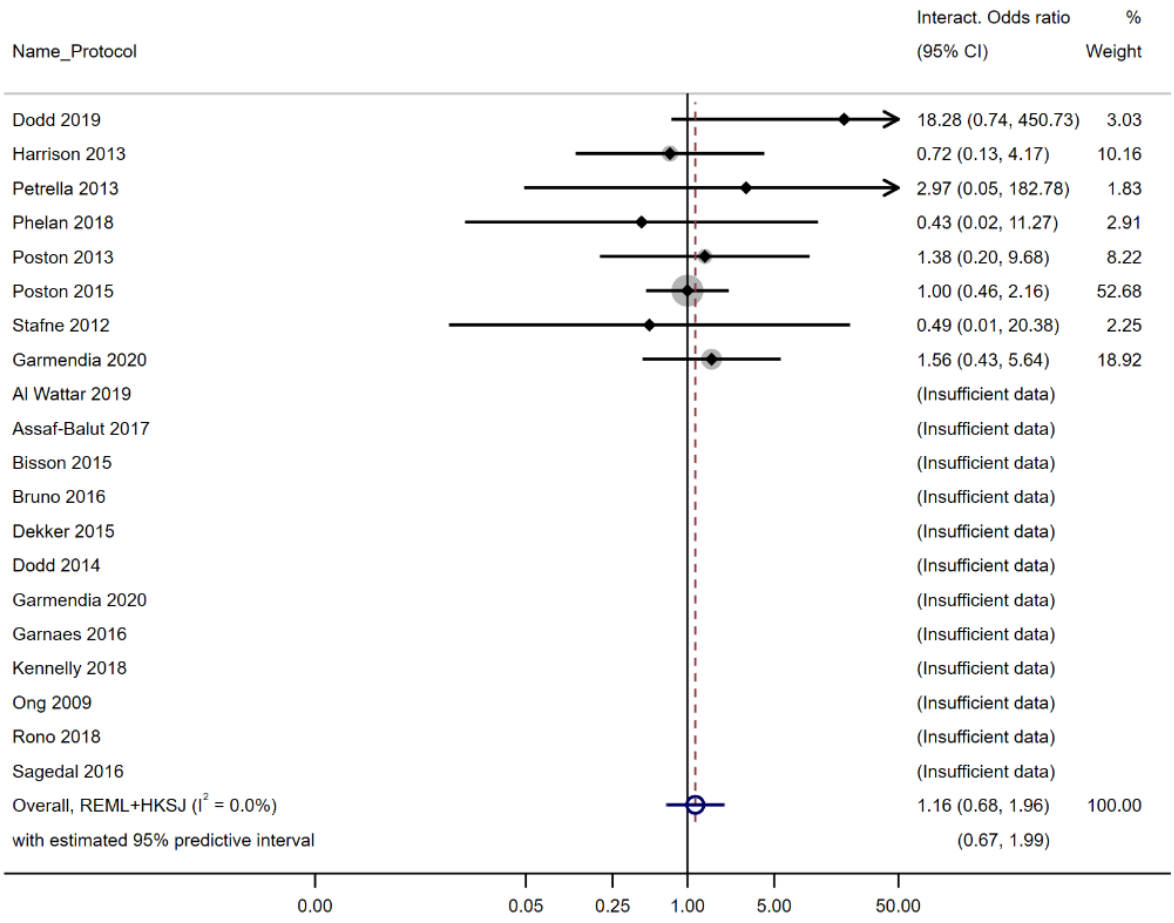


Figure 9.32: Forest plot showing the effect of the interaction between lifestyle interventions and mother's education (high) on GDM (NICE definition) using IPD meta-analysis

Appendix 21: Forest plots of maternal & offspring complications in women with GDM (trial authors' definition)

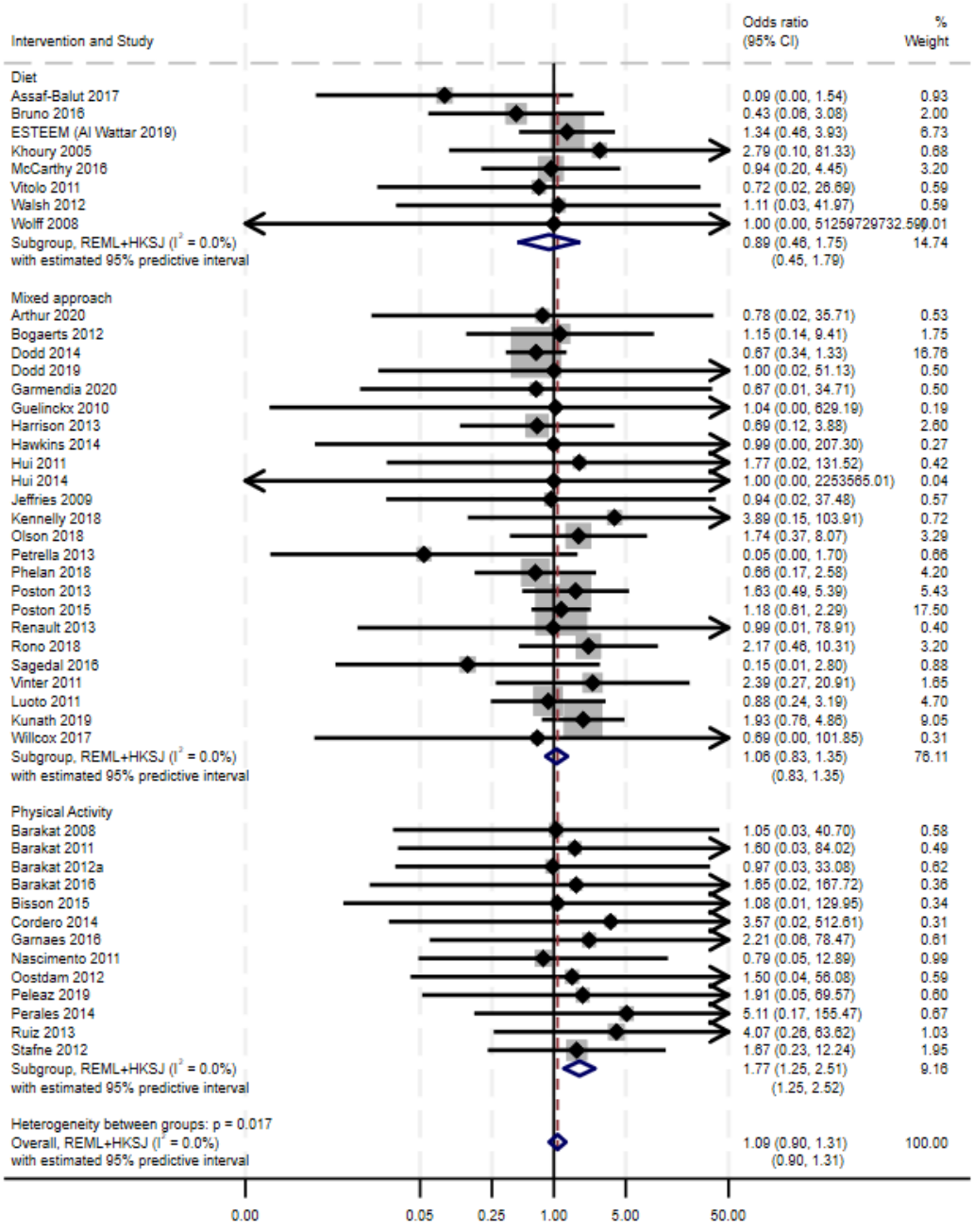


Figure 9.33: Forest plot showing the effect of lifestyle interventions on hypertensive diseases among women with GDM (trial authors' definition) from IPD meta-analysis

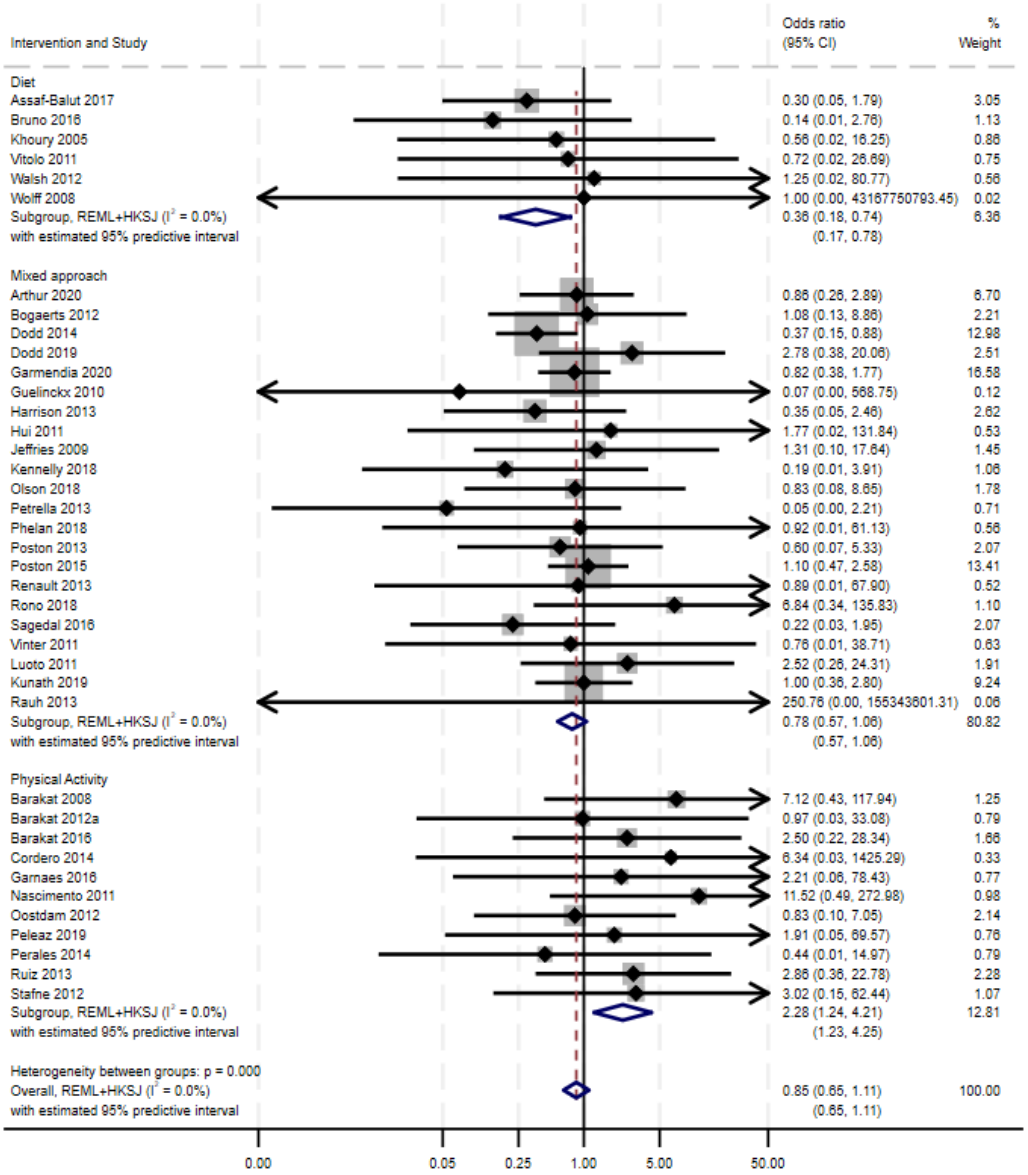


Figure 9.34: Forest plot showing the effect of lifestyle interventions on preterm delivery among women with GDM (trial authors' definition) from IPD meta-analysis

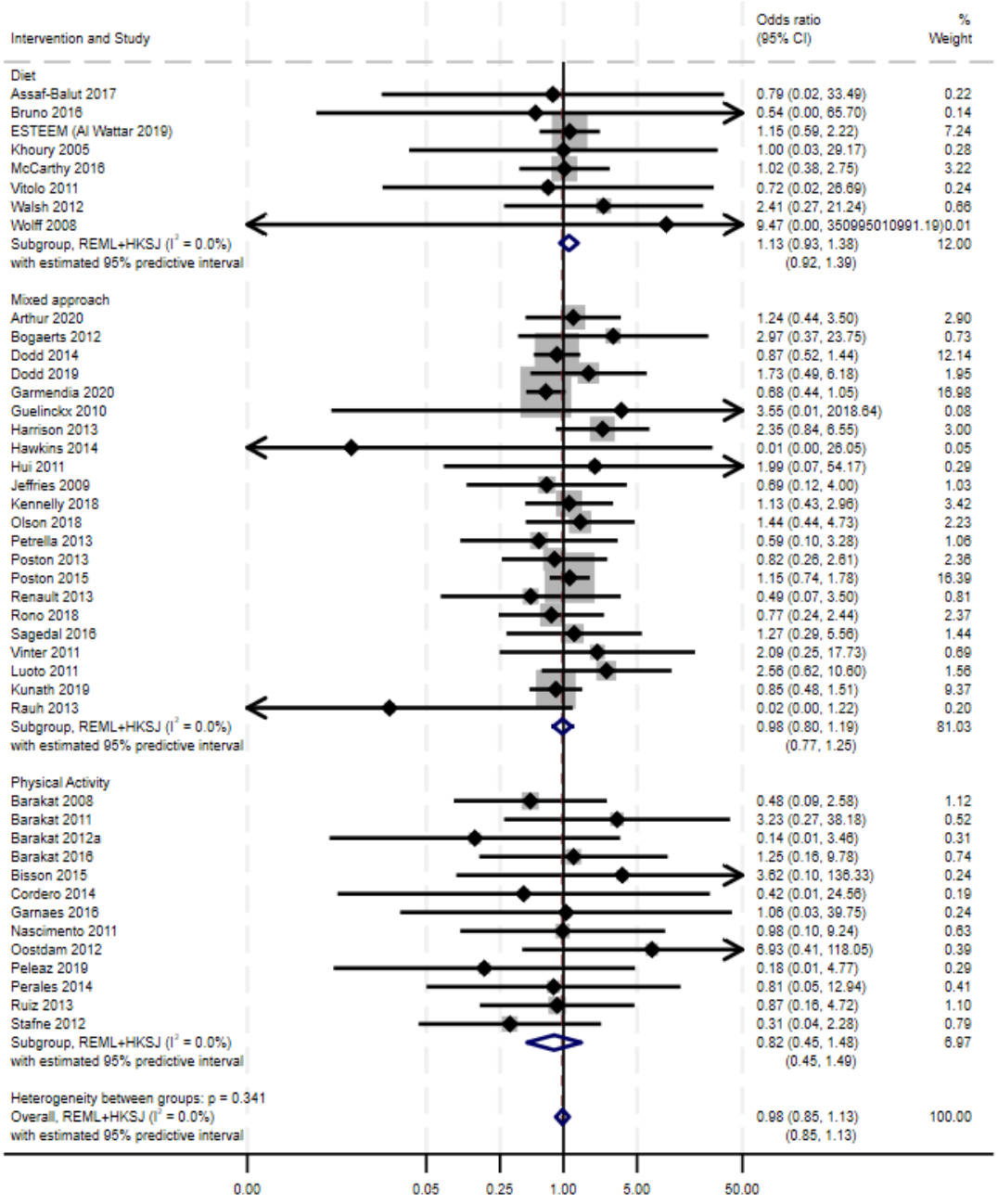


Figure 9.35: Forest plot showing the effect of lifestyle interventions on caesarean section among women with GDM (trial authors' definition) from IPD meta-analysis

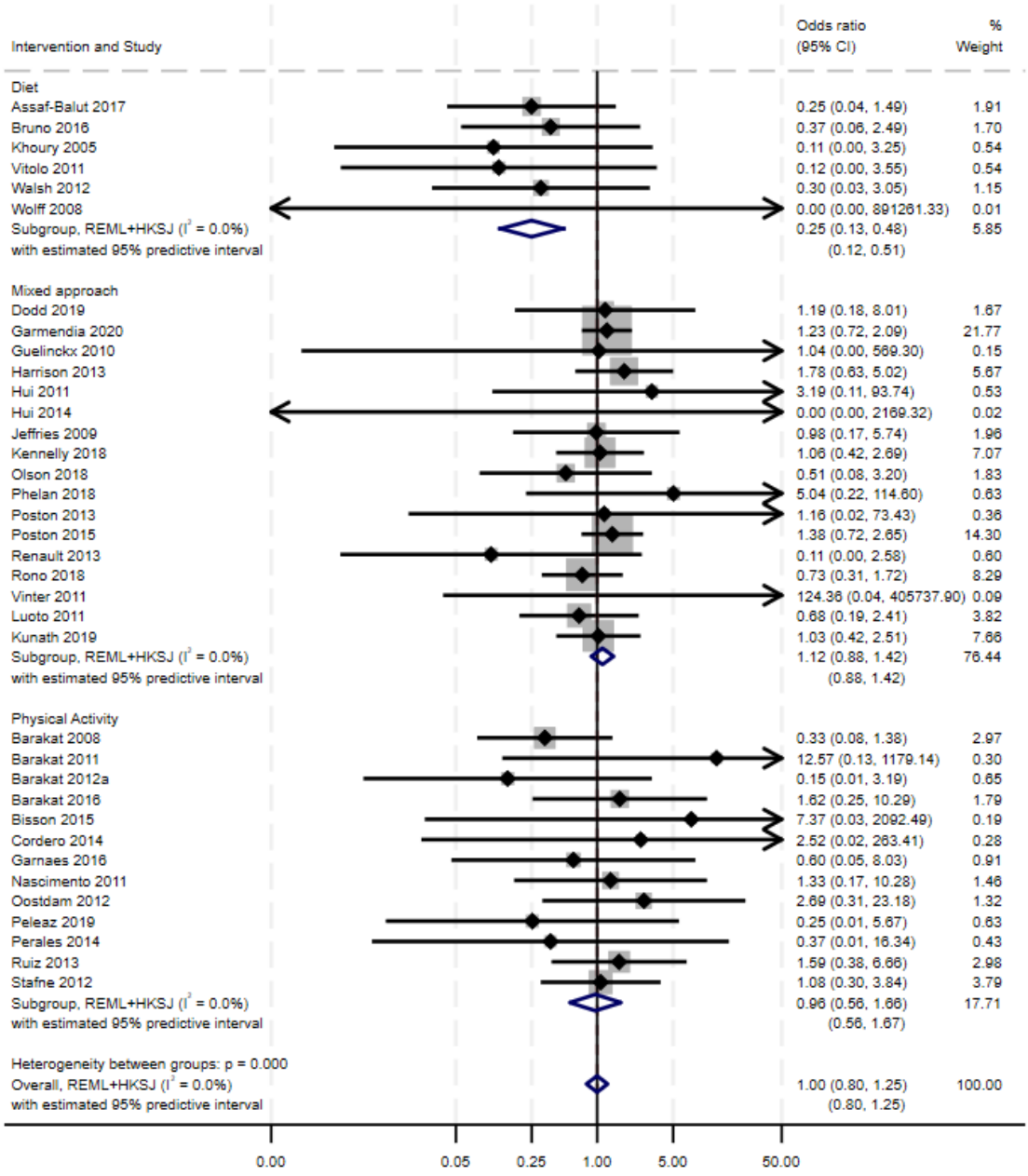


Figure 9.36: Forest plot showing the effect of lifestyle interventions on LGA among women with GDM (trial authors' definition) from IPD meta-analysis

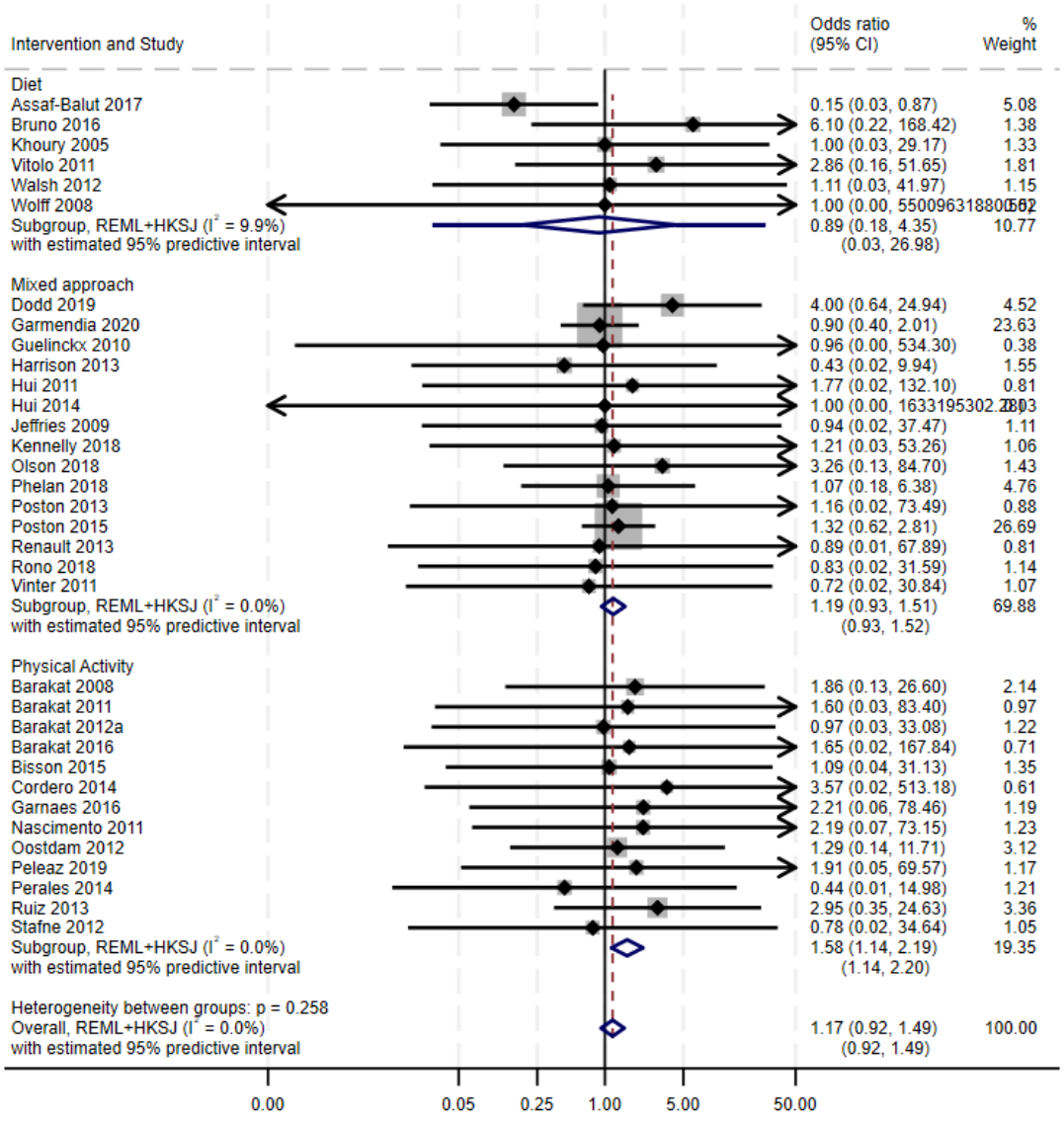


Figure 9.37: Forest plot showing the effect of lifestyle interventions on SGA among women with GDM (trial authors' definition) from IPD meta-analysis

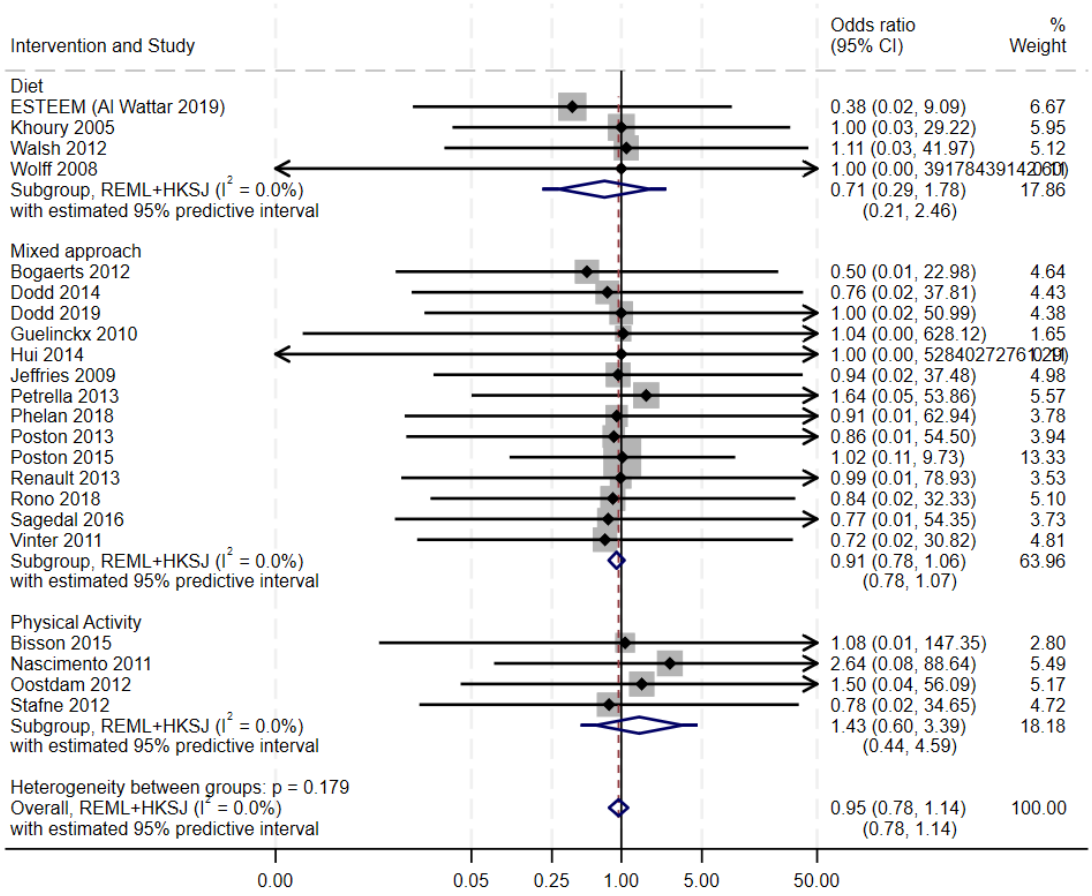


Figure 9.38: Forest plot showing the effect of lifestyle interventions on stillbirths among women with GDM (trial authors' definition) from IPD meta-analysis

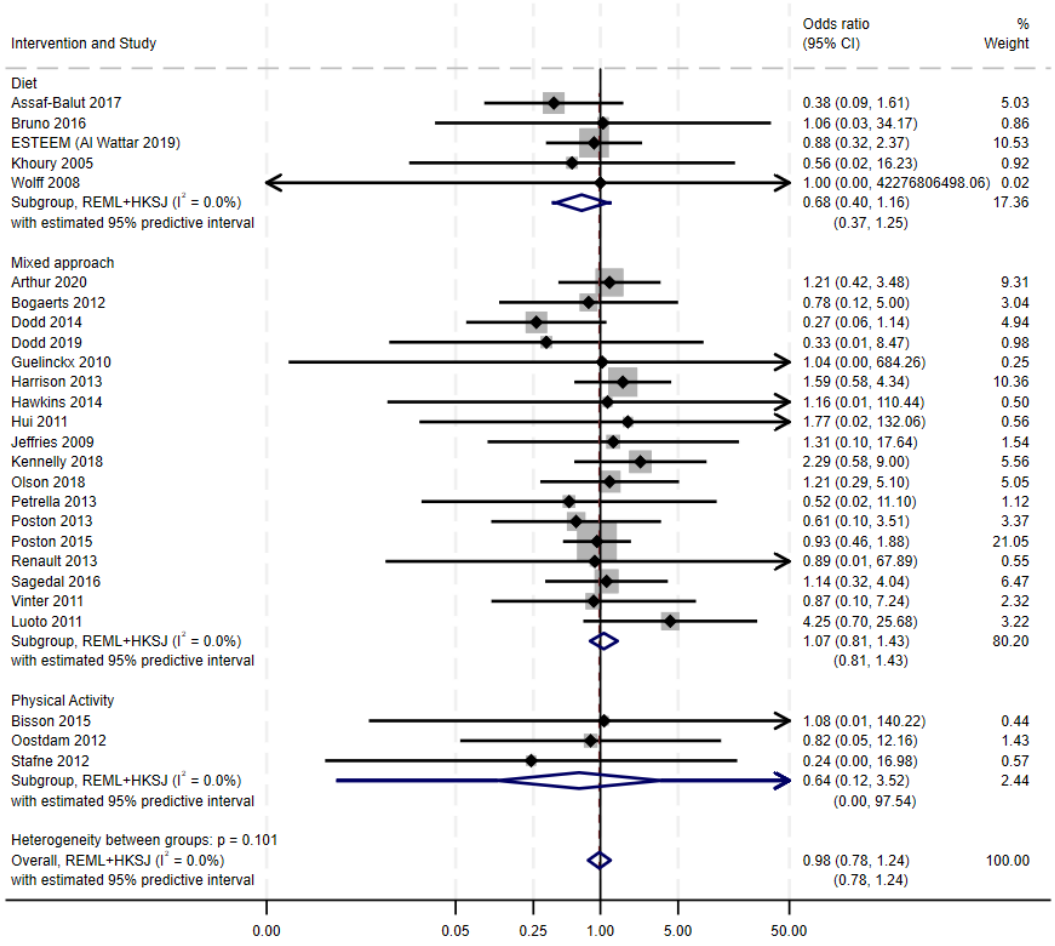


Figure 9.39: Forest plot showing the effect of lifestyle interventions on NICU admission among women with GDM (trial authors' definition) from IPD meta-analysis

Appendix 22: Calculation of probabilities for cost-effectiveness analysis

Parameter	Source	Description
CS	Hospital Episode Statistics 2018-2019, Method of Delivery, Table 3a	Divided #CS by #births excluding unknowns
Non-CS	Hospital Episode Statistics 2018-2019, Method of Delivery, Table 3a	1-P(CS)
CS (FGR)	Assumption	
FGR	Vieira 2019[353], NICE guidelines	10% of all babies are SGA, and 1/3 of them are FGR
Sensitivity of ultrasound scan	Haragan, 2015[354]	USAC <5th percentile to predict BW <10 percentile
Sensitivity of SFH measurement	Pay, 2015[355]	Accuracy of SF height for the prediction of SGA defined as BW ≥ 2 SDs below the mean
Specificity of ultrasound scan	Haragan 2015[354]	USAC <5th percentile to predict BW <10 percentile
Specificity of SFH measurement	Pay 2015[355]	Accuracy of SF height for the prediction of SGA defined as BW ≥ 2 SDs below the mean
Sensitivity of prediction model	Prediction model, IPPIC HTA Report	Probability threshold 0.08
Specificity of prediction model	Prediction model, IPPIC HTA Report	Probability threshold 0.08
Parameter	Source	Description
CS	Hospital Episode Statistics 2018-2019, Method of Delivery, Table 3a	Divided #CS by #births excluding unknowns
Non-CS	Hospital Episode Statistics 2018-2019, Method of Delivery, Table 3a	1-P(CS)
CS (FGR)	Assumption	
FGR	Vieira 2019[353], NICE guidelines	10% of all babies are SGA, and 1/3 of them are FGR
Sensitivity of ultrasound scan	Haragan, 2015[354]	USAC <5th percentile to predict BW <10 percentile
Sensitivity of SFH measurement	Pay, 2015[355]	Accuracy of SF height for the prediction of SGA defined as BW ≥ 2 SDs below the mean
Specificity of ultrasound scan	Haragan 2015[354]	USAC <5th percentile to predict BW <10 percentile

Specificity of SFH measurement	Pay 2015[355]	Accuracy of SF height for the prediction of SGA defined as BW ≥ 2 SDs below the mean
Sensitivity of prediction model	Prediction model, IPPIC HTA Report	Probability threshold 0.08
Specificity of prediction model	Prediction model, IPPIC HTA Report	Probability threshold 0.08

Appendix 23: Calculation of costs for cost-effectiveness analysis

Parameter	Source	Description
CS	NHS reference cost: National schedule of reference costs: the main schedule, Total HRG's	Weighted average of planned (NZ50C) and emergency section (NZ51C)
Non-CS	NHS reference cost: National schedule of reference costs: the main schedule, Total HRG's	Weighted average of NZ30C, NZ31C, NZ40C, NZ41C
SFH measurement	PSSRU (2006)[356]	
Ultrasound fetal growth scan	NHS reference cost: National schedule of reference costs: the main schedule, DADS	NZ73Z

Appendix 24: Expected Net Benefit (NB) and number of True Positives (TP), False Positives (FP), True Negatives (TN) and False Negatives (FN) per 1000 women using the model at different predicted probability thresholds, based on FGR model's apparent performance in full development data

Threshold probability	**TP per 1000**	**FP per 1000**	**TN per 1000**	**FN per 1000**	**Sensitivity**	**Specificity**	**NB per 1000**
0	7	993	0	0	100%	0%	7
0.01	6	47	946	1	88.3%	95.3%	6
0.02	6	30	963	1	85.7%	97%	6
0.03	6	23	969	1	81.9%	97.7%	5
0.04	6	20	973	2	78.6%	98%	5
0.05	5	17	975	2	75%	98.3%	5
0.06	5	16	977	2	72.7%	98.4%	4
0.07	5	14	978	2	70.1%	98.5%	4
0.08	5	13	979	2	67.8%	98.7%	4
0.09	5	12	980	2	66.5%	98.8%	4
0.10	5	12	981	3	65.2%	98.8%	3
0.11	5	11	982	3	63.9%	98.9%	3
0.12	5	10	982	3	62.6%	99%	3
0.13	4	10	983	3	61.6%	99%	3
0.14	4	9	983	3	60.6%	99.1%	3
0.15	4	9	984	3	59.5%	99.1%	3
0.16	4	9	984	3	58.7%	99.1%	3
0.17	4	8	985	3	58%	99.2%	3
0.18	4	8	985	3	57.1%	99.2%	2
0.19	4	7	985	3	56.4%	99.2%	2
0.20	4	7	986	3	55.4%	99.3%	2
0.30	3	4	988	4	46.4%	99.6%	2
0.40	3	2	991	5	34.8%	99.8%	1
0.50	1	1	992	6	19.1%	99.9%	1
0.60	1	0	992	7	9.5%	100%	0
0.70	0	0	993	7	5.8%	100%	0
0.80	0	0	993	7	3.2%	100%	0
0.90	0	0	993	7	0.8%	100%	0

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