

Effectiveness of Smartphone-Based Lifestyle Interventions on Women with Gestational Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Background: Gestational diabetes mellitus (GDM) is a condition that causes poor glucose tolerance during pregnancy and usually resolves after birth. Having GDM impacts the mother and baby. Smartphone-based lifestyle interventions may offer innovative solutions.

Aim: To examine the effects of smartphone-based lifestyle interventions on compliance, Hemoglobin A1c (HbA1c), maternal outcomes, infant outcomes, psychological status, satisfaction, and cost effectiveness among women with GDM.

Methods: Randomized controlled trials (RCTs) of smartphone-based lifestyle interventions for women with GDM aged over 18 years were included. A systematic search of PubMed, Embase, Web of Science, CINAHL, and Cochrane Library for articles published from January 2007 to March 2022 and updated on 12 October 2022. Data were extracted independently by two researchers, and the risk of bias in individual trials was rated using the Cochrane risk-of-bias tool (RoB 2). Meta-analysis was conducted by using RevMan 5.3.

Results: Ten studies were included involving 1626 participants. The mean ages of the women were 32.42 ± 4.68 years. Eight out of 10 studies were conducted in developed countries. Meta-analysis found that smartphone-based lifestyle interventions statistically improved compliance [SMD = 7.36, 95% CI = (4.05 to 10.68), $P < 0.0001$] and decreased the incidences of neonatal intensive care unit (NICU) admission [RR = 0.64, 95% CI = (0.47, 0.86), $P = 0.003$], compared with controls. However, intervention effects on HbA1c, maternal outcomes, neonatal hypoglycemia, and infant birth weight were non significant. Moreover, the satisfaction of intervention is high in this review. Contrastingly, no significant effects were observed for psychological status and cost-effectiveness.

Conclusion: Smartphone-based lifestyle interventions may improve patient compliance and reduce NICU admissions. These findings may aid in developing future intervention strategies, help elucidate future research directions, and guide clinical practice for women with GDM. Future high-quality RCTs must be further studied at larger scales to examine smartphone-based lifestyle interventions' long-term effects and cost-effectiveness.

Keywords: smartphone, women, gestational diabetes mellitus, lifestyle interventions, systematic review, meta-analysis

Introductions

GDM refers to any degree of glucose intolerance that occurs or is first detected during pregnancy.¹ GDM is one of the most common pregnancy complications, with a global prevalence of 10.6%.² Women with GDM are seven times more likely to develop Type 2 diabetes mellitus (T2DM) later in life than women with normal glycemia during pregnancy.³ Women with GDM are more likely to have adverse maternal and infant outcomes, including caesarean section, higher need for induced labor and pre-eclampsia, and congenital disabilities in infants.^{4,5} In addition, children exposed to

chronic high blood sugar in utero have a higher risk of obesity, insulin resistance, metabolic syndrome, T2DM, or cardiovascular disease.⁶ Thus, GDM must be managed effectively.

The current management model for GDM focuses on lifestyle interventions that aim to provide patients with the skills and strategies required to promote and change their behavior. Due to their low cost and potential for scalability with no side effects,⁷ lifestyle interventions are recommended as a first-line approach to improve physical activity and dietary modification in women with GDM.⁸ Lifestyle interventions for women with GDM during pregnancy and postpartum can normalize glycemic levels, reducing the incidence of adverse maternal and infant outcomes^{5,8–10} and improving diabetes-related risk factors (eg, insulin resistance and weight reduction).¹¹ Meanwhile, a meta-analysis of eight studies from seven countries unveiled that lifestyle interventions reduced T2DM incidence by 25% in women with GDM.¹¹ However, traditional lifestyle interventions often require intensive provider support, ongoing follow-ups, and frequent counselling for young mothers.¹² As a result, previous studies have reported implementation with a 54.1% recruitment response rate and 65.0% attendance rate,¹³ well below the benchmark rate of over 80%.¹⁴ Researchers reported challenges for women with GDM participating in lifestyle interventions in clinical practice, including guilt about leaving their children, work-life imbalance, time constraints, and the need for more flexible schedules.¹² These findings are consistent with reports that the main barriers to attending in-person health promotion programs are family/childcare responsibility and transportation.¹⁵ These problems may be alleviated by using technology. As the COVID-19 pandemic spreads, the development of mobile health interventions as alternatives to traditional face-to-face approaches to providing real-time healthcare to patients is becoming increasingly popular.¹⁶

Lifestyle interventions delivered through smartphones can be cost effective, innovative, secure, and user friendly.¹⁷ The unique features of smartphone app or text message can be used to track and modify the patient's diet, exercise or health behavior diet, weight, and physical activity.¹⁸ The data collection function of smartphones can also be used to develop a tailored intervention.¹⁹ Furthermore, smartphones can provide real-time feedback through a graphical display and encourage self-monitoring.²⁰ Smartphone-based interventions can be embedded with behavior change technologies, such as feedback, reminders, information delivery, self-monitoring, and tailoring to adjust an individual's diet and physical activity.²¹ A systematic review including 29 studies suggests that smartphone-based lifestyle interventions are feasible and acceptable for health care during pregnancy.²² Many smartphone-based health lifestyle interventions have been applied in chronic disease management and have shown great potential in providing personalized guidance.^{23,24} Smartphone-based lifestyle interventions are promising in improving the management of maternal obesity and excessive gestational weight gain.^{17,22,25} Women with GDM are interested in receiving health information on their smartphones and are willing to use them.^{20,26} These data suggest that smartphones are a promising medium for women with GDM to use in the behavior change.

Recently published systematic review has highlighted lifestyle-based interventions as practical strategies that delay the onset of T2DM among at-risk populations.²⁷ However, due to the scarcity of available studies, knowledge gaps were observed regarding the effect of lifestyle-based interventions on the health-related outcomes for GDM.²⁷ Meanwhile, several previous systematic reviews and meta-analyses have evaluated the effects of technology-based lifestyle interventions in managing diabetes (T1DM, T2DM, and GDM), most of which involve heterogeneous technologies. They examined the effectiveness of smartphone-based interventions combining other types of technology (eg, wearable devices and primarily web-based programs).^{28–32} Moreover, a systematic review, which included six studies (n = 408), suggested that mHealth-apps may improve health-related outcomes among pregnant women with GDM.³³ However, this paper was a narrative synthesis and failed to draw solid conclusions for health-related outcomes due to heterogeneity, a small number of trials, the research design was not limited to RCT. Drawing reliable conclusions about the effectiveness of smartphone-based lifestyle interventions for patients with GDM is difficult. To a large extent, evidence is sparse on the impacts of smartphone-based lifestyle interventions on GDM. Thus, we performed a systematic review and meta-analysis of available evidence from RCT studies to quantify the evidence on smartphone-based lifestyle interventions for health-related outcomes and satisfaction and cost effectiveness for GDM. Therefore, this study aimed to assess the efficacy of smartphone-based lifestyle interventions in improving compliance, HbA1c, maternal outcomes, infant outcomes, and psychological status, as well as investigate the satisfaction and cost effectiveness in women with GDM compared to control groups.

Methods

Eligibility Criteria

Studies that were RCTs published in the English language and met the following criteria were included: 1) Study participants were adults who had GDM history or a confirmed diagnosis of GDM. 2) Smartphone-based lifestyle interventions were defined as interventions achieved through smartphones, for example real-time doctor-patient communication, activity/diet tracking, coaching, goal setting. Telemedicine portals or portals based on electronic medical records used for mobile phones are not eligible (eg, website). 3) Studies that examined at least one of the following outcomes: compliance, HbA1C, maternal outcomes (gestational weight gain, gestational age at delivery, normal vaginal delivery, and cesarean delivery), infant outcomes (infant birth weight (grams), neonatal hypoglycemia, NICU admission), and psychological status (depression and anxiety).

The exclusion criteria are as follows: 1) used qualitative data as an outcome measure, 2) were not written in English, and 3) did not use smartphone-based technology for GDM. A PRISMA checklist is outlined in Figure 1.

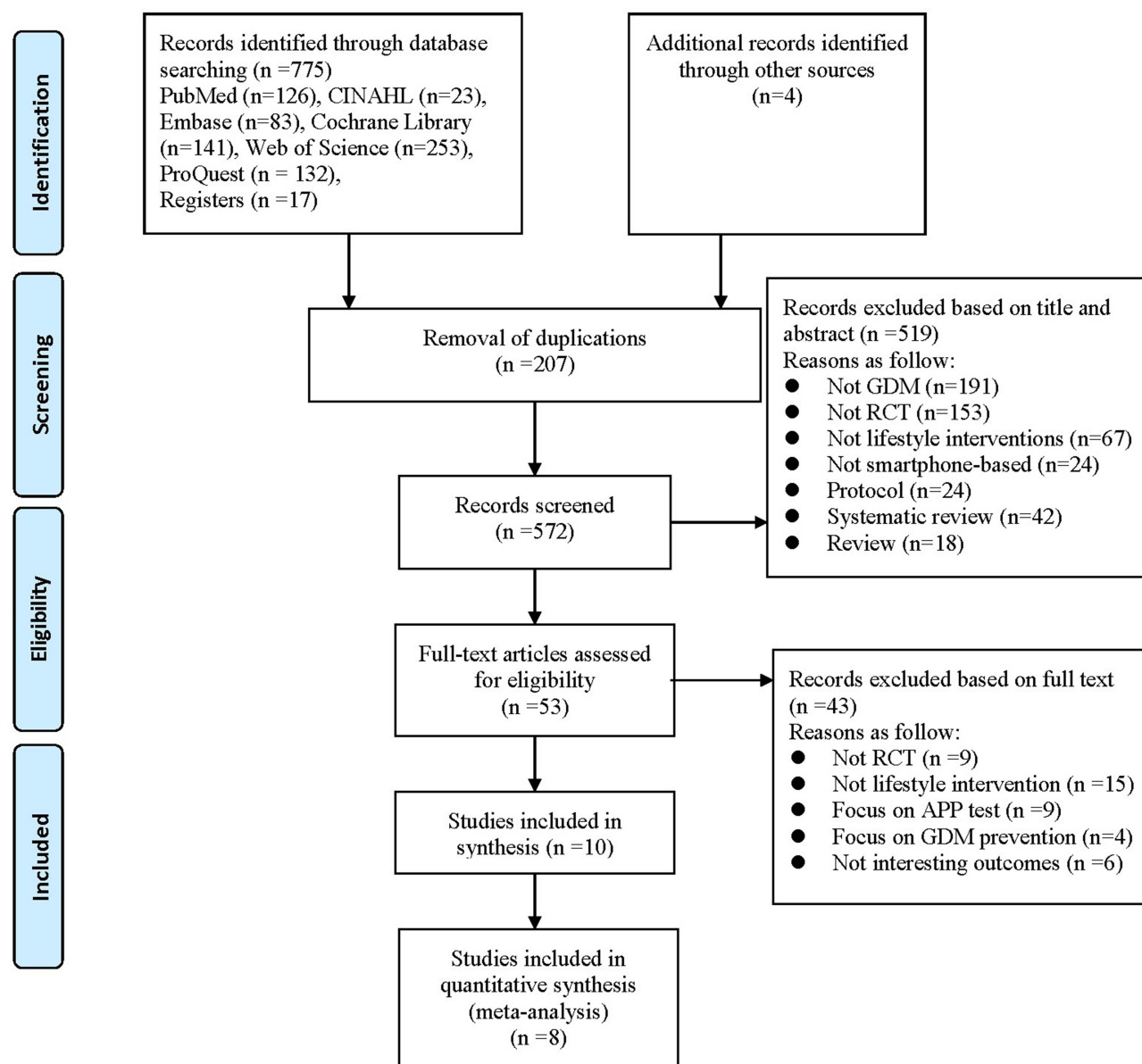


Figure 1 PRISMA flow diagram.

Notes: PRISMA figure adapted from Liberati A, Altman D, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Journal of clinical epidemiology*. 2009;62(10). Creative Commons.³⁴

Data Source and Search Strategy

A systematic search of PubMed, Web of Science, Embase, CINAHL and Cochrane Library was carried out. These five databases were chosen because they contain a wealth of valuable biomedical literature that maximizes journal coverage and ensures the inclusion of all relevant research.^{35,36} ClinicalTrials.gov, Grey Literature (<http://www.opengrey.eu>), ProQuest Dissertations, and ongoing trials were also searched to find unpublished and ongoing trials. Smartphones with touch screens were popular among the population and rapidly developed from 2007.³⁷ Therefore, only studies published from January 2007 to March 2022 were included. The search was updated on 12 October 2022. Comprehensive search strategies were developed under the supervision of a medical librarian. [Appendix 1](#) shows the detailed search strategies. Additional studies were identified for screening by manually retrieving the list of references and systematic reviews cited in eligible studies. Eligible studies' citations were searched on the Web of Science to find potential studies and avoid missing eligible studies.

Study Selection and Data Extraction

Searched records were imported into Endnote X9.1 reference manager (Clarivate Analytics, PA, USA), and duplicated references were removed using the software and by hand. Two reviewers (HJW and YYJ) worked independently to screen titles, abstracts, and full texts to decide the eligibility of the studies. Any discrepancies were resolved by a third reviewer (LG). The consensus was achieved in all studies included.

Data were extracted by two reviewers (HJW, YYJ) independently from the 10 trials using a standardized data collection sheet. Any disagreements between two reviewers during the data collection were resolved through further discussion. If necessary, a third reviewer (LG) was invited to arbitrate until an agreement was reached.

Characteristics of each study included general information (authors, year, and country), methods (study design), participants' characteristics (sample size, mean age, mean BMI, HbA1c at diagnosis, gestation week at recruitment, OGTT-2h, history of previous GDM, attrition rate) (see [Table 1](#)), detailed descriptions of interventions (content of intervention, venue, provider, dosage and framework) (see [Table 2](#)), outcome measures (compliance, HbA1c, gestational weight gain, gestational age at delivery, normal vaginal delivery, cesarean delivery, infant birth weight, neonatal hypoglycemia, NICU admission, depression, anxiety) (see [Table 3](#)).

Risk of Bias Assessment

The Cochrane risk-of-bias tool (RoB 2) was utilized to evaluate the quality of the included

studies by two independent investigators.³⁸ This tool assessed the methodological quality of studies in five domains: (1) random allocation, (2) deviation from intended interventions, (3) management of missing data, (4) outcome measurement, and (5) data analysis. The risk of bias for each domain was categorized into three levels: low, some concerns, high. Any disagreements between the investigators were resolved through discussion or consultation with a senior reviewer (LG). The critical appraisal results are reported in narrative form and a table ([Table 4](#)).

Data Analysis

The RevMan Version 5.3.5 was used to conduct the data analysis (available from the website for free: <http://tech.cochrane.org/revman/download>). Mean difference (MD)/standardized mean difference (SMD) was calculated for continuous outcomes, and dichotomous variables were presented as risk ratio (RR) with forest plots. I^2 test was carried out to assess the heterogeneity, and a value of $I^2 > 50\%$ means high heterogeneity.³⁹ A fixed-effects model was considered to calculate the pooled effect size if the data were not significantly heterogeneous; otherwise, a random-effects model was used. A narrative synthesis was used for quantitative studies that do not extract data to be included in the meta-analysis. A sensitivity analysis was performed by excluding one study at a time to confirm the consistency of the findings. Given that number of reviewed studies is small, subgroup analysis was not conducted. The funnel plot was visually inspected to assess any publication bias.

Table 1 Characteristics of Included Studies

Study, Year (Reference); Location, Design	Sample Characteristic (P)								Intervention Characteristic (I)						Framework	Drop Out (%)
	Group	N	Age (Years) Mean \pm SD	Mean BMI (kg/m ²) Mean \pm SD	HbA1c at Diagnosis (%) Mean \pm SD	Gestation at Recruitment (Weeks) Mean \pm SD	Plasma Glucose on OGTT (mmol/L) 2h	History of Previous GDM n (%)	Content	Intervention Period	Technical Support	Frequency	Venue	Interventionist		
Sophie E. Poulter, 2022, ⁴³ Australia. A single-center, two-arm pilot RCT.	I	98	31.9 \pm 5.4	NR	NR	28.2 \pm 2.1	NR	15 (15)	NET-Health smartphone application intervention and routine care. NET-Health allowed automatic upload of BGL values and generate alert if it was not an eligible target.	24–30 weeks of gestation to delivery	NET-Health App	Everyday	Home	A dietitian or a licensed diabetes educator	NR	0
	C	94	32.4 \pm 5.7	NR	NR	28.6 \pm 1.7	NR	11 (12)	Routine care, including dietary and lifestyle modifications, self-blood glucose monitoring, and record blood glucose level in a paper diary		Paper diary	Reviewed every 2–4 weeks	Hospital	By phone, email, or clinic review	NR	0
Tong Wei Yew, 2021, ⁴¹ Singapore. A single-center, two-arm RCT	I	170	31.7 \pm 4.0	25.5 \pm 5.5	5.3 \pm 0.4	27.0 \pm 3.2	8.6 \pm 1.4	19 (11.3)	12 interactive lessons including diet, SMBG, physical activity, and weight tracking tools; and a messaging platform with health care professionals.	12–30 weeks of gestation to delivery	Habits-GDM App	12 interactive lessons feedback every day.	Home	Health care teams	Health Belief Model	1.76%
	C	170	32.2 \pm 4.4	25.6 \pm 5.7	5.3 \pm 0.4	26.7 \pm 3.7	8.6 \pm 1.3	21 (12.7)	Education session: the sessions covered pathophysiology and complications of GDM, healthy eating, carbohydrate exchange, SMBG, and future risk of diabetes. Advice on diet and lifestyle modification and initiation of insulin and/or metformin was individualized on the basis of SMBG results.		NR	2–3 days a week	Hospital	A diabetes nurse educator and dietitian	NR	3.5%
Karen Lim, 2021, ⁴² Singapore. A single-center, two-arm RCT	I	96	32.6 \pm 4.5	X	5.4 \pm 0.3	27.1 \pm 2.0	8.4 \pm 1.4	13 (13.5)	Interactive Smartphone App: Goal Setting, Food choices and recommendations. Activity and steps tracker, Interactive video lessons, Healthcare Professionals Support	Between six weeks and four months after postpartum	Nutritionist Buddy (nBuddy)	A total of 16 video clips (3 minutes per video). Feedback every day.	Home	Dieticians, a physiotherapist, and an occupational therapist.	Obesity-Related Behavioral Intervention Trials model	5.9%
	C	93	32.4 \pm 4.2	X	5.2 \pm 0.4	27.0 \pm 1.7	8.7 \pm 1.2	13 (14.0)	A follow-up appointment at 6 weeks postpartum include providing dietary advice and performing an OGTT.		NR	NR	Hospital	Clinician		12.1%
Iren Borgen, 2019, ⁴⁰ Norway. A multi-center, two-arm RCT	I	112	NR	NR	NR	NR	NR	23 (33.8)	Pregnant+ app and usual care: diet, being physically active, management of GDM and receiving feedback on their blood glucose levels. It contains four main icons: "Blood glucose", "Physical activity", "Food and beverages", and "Diabetes information".	\leq 33 weeks of gestation to delivery	Pregnant+ app	Every day	Home	NR	NR	2.6%
	C	121	NR	NR	NR	NR	NR	19 (31.7)	Usual care consists of information about a healthy diet, regular physical activity, measure / record blood glucose levels.		Paper diary	Every second week	Hospital	Midwives and/or diabetes nurses	NR	1.6%

(Continued)

Table I (Continued).

Study, Year (Reference); Location, Design	Sample Characteristic (P)								Intervention Characteristic (I)						Framework	Drop Out (%)
	Group	N	Age (Years) Mean \pm SD	Mean BMI (kg/m ²) Mean \pm SD	HbA1c at Diagnosis (%) Mean \pm SD	Gestation at Recruitment (Weeks) Mean \pm SD	Plasma Glucose on OGTT (mmol/L) 2h	History of Previous GDM n (%)	Content	Intervention Period	Technical Support	Frequency	Venue	Interventionist		
H. Guo, 2019 ⁴⁸ China. A single-center, two-arm RCT	I	64	31.2 \pm 4.1	25.7 \pm 3.3	6.0 \pm 0.4	24.7 \pm 5.1	9.7 \pm 1.3	10 (15.6)	Standard care and mobile health. Additional mobile medical management refers to nurse providing personalized online instruction which include diet, exercise, blood glucose monitoring, insulin injection.	24–28 weeks of gestation to delivery	Dnurse App	Every day	Home	Outpatient service doctor and education nurse.	NR	0
	C	60	30.6 \pm 3.1	25.6 \pm 2.9	5.9 \pm 0.3	25.1 \pm 3.5	9.9 \pm 1.5	9 (15.0)	Standard care: diet, exercise, monitoring blood glucose and performing OGTT after delivery 3 months.		Paper diary	One visit a week for 3 consecutive weeks. at least 3 days per week until delivery.	Hospital	Educational nurse	NR	0
Ji-Hee Sung, 2019, ⁴⁵ Korea. A single-center, two-arm pilot RCT	I	11	35.0 \pm 2.76	24.69 \pm 4.45	NR	27.29 \pm 1.92	NR	NR	Standard antenatal care and tailored mobile health care services. The application comprised 4 sections: clinical data, nutrition and diet, medication, and messaging system and information.	24–28 weeks of gestation to delivery	Mobile phone application	Twice a week	Home	Health care providers	NR	0
	C	10	31.7 \pm 4.92	26.28 \pm 3.51	NR	27.39 \pm 1.61	NR	NR	Standard antenatal care including record their blood glucose, blood pressure, and intake meal.		NR	Biweekly visits up to 36 weeks of gestation, followed by weekly visits until delivery	Hospital	Obstetricians and endocrinologists	NR	0
Hadas Miremborg, 2018, ⁴⁷ Israel. A single-center, two-arm RCT	I	60	31.7 \pm 4.2	27.1 \pm 5.1	5.2 \pm 0.33	NR	NR	12 (20)	Stand care and smartphone-based intervention. Patients received individualized feedback from clinic team regarding her daily glycemic control, eg, dietary tips, insulin treatment.	< 34 weeks of gestation to delivery	Mobile application	Every day (including weekends)	Home	Maternal-fetal medicine specialist and endocrinologist)	NR	7.7%
	C	60	32 \pm 6.3	27.1 \pm 5.2	5.2 \pm 0.4	NR	NR	18 (30)	Standard care: routine prenatal care, physical activity, blood pressure monitoring, urine dipstick for proteinuria, and blood glucose measurements.		Paper diary	Bi-weekly visits up to visits from 35 weeks of gestation, weekly visits from 35 weeks of gestation until delivery	Hospital	Medicine specialist, nurse, dietician	NR	1.6%
Lucy Mackillop, 2018, ⁴⁴ UK. A single-center, two-arm RCT	I	101	33.9 \pm 5.5	31.1 \pm 6.7	5.42 \pm 0.34	30.9 \pm 3.6	7.4 \pm 2.2	10 (13.8)	Additional daily detailed feedback from the clinic team via mobile app containing advice about diet, dose adjustments of hypoglycemic medications, and messages of encouragement.	< 34 weeks of gestation to delivery	GDm-health app	Once a week	Home	Diabetes midwife	NR	1.9%
	C	102	33 \pm 5.6	31.6 \pm 7.3	5.39 \pm 0.35	31 \pm 3.4	7.0 \pm 1.9	7 (11.7)	Standard Care: routine biweekly prenatal clinic care		Paper diary	Every 2 to 4 weeks, until delivery.	Hospital	Diabetes midwife	NR	1%

Ping Yang, 2018, ⁴⁹ China, A single-center, three-arm RCT	I	57	31.61 ± 4.16	NR	NR	NR	8.90 ± 1.82	NR	Individualized dietary advice, self-monitor glucose levels	24–28 weeks of gestation to delivery	WeChat platform system	Every day.	Home	Obstetrician and qualified dietitian	NR	0
	C	50	32.22 ± 4.69	NR	NR	NR	9.84 ± 1.77	NR	Usual care: routine outpatient clinic treatment and health education guidance.		NR	NR	Hospital	NR	NR	0
Natalia Pérez-Ferre, 2010, ⁴⁶ Spain, A single-center, two-arm RCT	I	49	33.33 ± 5.58	NR	5.03 ± 0.38	NR	NR	4 (8.2)	Short messaging Service (SMS): patients send their blood glucose values via SMS and the professional makes recommendations.	24–28 weeks of gestation to delivery	Short messaging Service	Every day	Home	An endocrinologist and a diabetes nurse educator	NR	2%
	C	48	34.19 ± 5.18	NR	5.10 ± 0.41	NR	NR	9 (18.8)	Usual care: face-to-face outpatient clinic visits		Paper diary	Any time	Hospital	NR	NR	4%

Note: X refers to data not available.

Abbreviations: RCT, Randomized Controlled Trials; NR, Not Report; I, Intervention; C, Control; OGTT, Oral Glucose Tolerance Test; SMBG, Self-Monitoring of Blood Glucose; HbA1c, Hemoglobin A1c.

Table 2 Content of Lifestyle Interventions of Included Studies

Study, Year, (Reference);	Lifestyle Interventions							
	Diet	Physical Activity	SMBG	Weight Tracking	A Messaging Feedback/ Interaction	Health Education	Blood Glucose	Insulin Treatment
Sophie E. Poulter, 2022 ⁴³	X	X			X		X	
Tong Wei Yew, 2021 ⁴¹	X	X	X	X	X			
Karen Lim, 2021 ⁴²	X	X			X	X		
Iren Borgen, 2019 ⁴⁰	X	X			X	X	X	
H. Guo, 2019 ⁴⁸	X	X	X		X	X	X	X
Ji-Hee Sung, 2019 ⁴⁵	X	X			X	X	X	
Hadas Miremborg, 2018 ⁴⁷	X				X	X	X	X
Lucy Mackillop, 2018 ⁴⁴	X				X	X	X	
Ping Yang, 2018 ⁴⁹	X			X	X	X	X	
NataliaPérez-Ferre, 2010 ⁴⁶	X				X		X	X

Note: X refers to the content of lifestyle interventions available.

Abbreviation: SMBG, Self-Monitoring of Blood Glucose.

Results

Search Results

A total of 779 articles were retrieved in the initial search of databases, of which 207 were duplicates. A total of 519 studies were excluded on the basis of the title and abstract. There were no eligible studies in the grey literature databases. A total of 53 studies were included in the full-text screening. Ultimately, 10 studies that met the inclusion criteria were included in this systematic review after the screening process. Eight studies were incorporated in the meta-analysis, whereas two studies that did not extract the required outcome data were not incorporated in the meta-analysis. The selection process is shown in [Figure 1](#). Two authors were contacted for more precise data points, but no additional information was received.

Risk of Bias

[Table 4](#) provides the risk of bias summary. Regarding the overall quality of the included studies, six studies had a high risk of bias, and four studies had some concerns about the risk of bias. For the randomization process, four studies reported a low risk of bias for allocation sequence random and allocation sequence concealed; four studies had some concerns, whereas two studies had a high risk of bias. Regarding deviations from intended interventions, most studies ($n = 8$) reported some concerns. The remaining studies had a high risk of bias for the blind participants and interventionists. In terms of missing outcome data, all studies had a low risk of bias. As for the measurement of the outcome, seven out of 10 studies reported a low-risk bias, whereas three studies had a high risk of bias. Concerning the selection of the reported result, four studies reported a low risk of bias; five studies had some concerns, and one study reported a high risk of bias. [Appendix 2](#) presents the details on the risk of bias (graph).

Studies Characteristics

The included studies involved 1626 women with GDM, and sample sizes in each study ranged from 21 to 340 women. One study ($n = 10\%$) was multi-center design. The mean age of the women was 32.42 ± 4.68 years, excluding one study that reported age in a categorical variable.⁴⁰ Regarding research's country, most were performed in developed countries: two in Singapore,^{41,42} one in Australia,⁴³ the UK,⁴⁴ Norway,⁴⁰ Korea,⁴⁵ Spain,⁴⁶ and Israel.⁴⁷ The remaining were conducted in developing countries: China ($n = 2$).^{48,49} Ten studies were conducted during gestation. With respect to GDM diagnosis criteria, three studies reported that GDM diagnosis was used on the basis of the World Health Organization 2013 criteria,^{41,42,49} two studies were based on International Association of Diabetes and Pregnancy

Table 3 Outcome Measures Available for Meta-Analysis

Glycemic Control Outcomes			Maternal and Neonatal Outcomes							Psychology Outcomes	
Study, Year, (Reference);	Compliance	HbA1C (%)	Infant Birth Weight (Grams)	Gestational Age at Delivery (Week)	Neonatal Hypoglycemia, n (%)	NICU Admission, n (%)	Gestational Weight Gain (Kg)	Normal Vaginal Delivery, n (%)	Cesarean Delivery, n (%)	Depression	Anxiety
Sophie E. Poulter, 2022 ⁴³			I:3362 ±445; C:3310± 456	I:38.9 ±1.3; C:38.4 ±1.1	I:19 (19); C:24 (25)	I:22 (22); C:31 (33)		I:11 (11); C:10 (11)	I:37 (37); C:59 (35.8)		
Tong Wei Yew, 2021 ⁴¹	I:12 ±5; C:12 ±6		I:3055.5± 414.9; C: 3064.8± 489.0	I:38.5 ±1.9; C:38.7 ±1.1	I:24 (14.3); C:37 (22.4)	I:12 (7.1); C:21 (12.7)	I:9.03 ±4.99; C:8.44 ±3.88	I:104 (61.9); C:97 (58.8)	I:57 (33.9); C:37 (39)	I:5.1 ±4.1; C:5.3 ±4.3	X
Karen Lim, 2021 ⁴⁶							I:8.84 ±4.2; C:9.19 ±4.7				
Iren Borgen, 2019 ⁴⁰			X			I:14 (12.5); C:20 (16.5)		I:90 (80); C:86 (71)	I:22 (112); C:35 (121)		
H. Guo, 2019 ⁴⁸	I:83.3±12.5; C:70.4 ±10.1	I:4.7 ±0.2; C:5.3 ±0.3		I:38.1±1.6; C:37.8 ±2.5	I:1 (1.6); C:2 (3.3)		I:3.2 ±0.8; C:4.8 ±0.7	I:48 (75); C:40 (66.7)	I:16 (25.0); C:20 (33.3)		
Ji-Hee Sung, 2019 ⁴⁵			I:3280± 530; C: 3210± 370	I:38.74±1.03; C:39.44±0.70			I:1.98 ±2.05; C:3.658 ±1.71				
Hadas Miremberg, 2018 ⁴⁷	I:84±0.16; C:66 ±0.28		I:3097.8± 548.2; C: 3203.3± 414.6	I:38.2±1.7; C:38.5±1.4	I:2 (3.3); C:1 (1.7)	I:6 (10); C:7 (11.6)		I:48 (80); C:40 (67.7)	I:12 (20); C:20 (33.3)		
Lucy Mackillop, 2018 ⁴⁴		X	I:3440± 516 C: 3338±559		I:31 (32.3); C:25 (26.9)	I:5 (5.0); C:12 (12.1)	I:1.23 ±0.96; C:1.19 ±1.20	I:52 (51.4); C:42 (41.2)	I:49(48.5); C:60 (58.8)		
Ping Yang, 2018 ⁴⁹			I:3199.47±389.53; C: 3169.60± 524.03		I:0 (0%); C: 2 (4%)	I: 2 (57); C: 4 (50)		I: 37(57); C:40(50)	I: 18(57); C: 7(50)		
NataliaPérez-Ferre, 2010 ⁴⁶		I:5.3 ±0.4; C:5.4 ±0.4	I:3308.2± 488.8; C: 3370.6± 479.1	I:39.12±1.66; C:39.42±1.42	I: 1 (2%); C: 0 (0%)		I:5.82 ±3.95; C:6.45 ±4.99	I: 20 (40.8); C: 26 (54.2)	I: 17 (34.7); C: 12 (25)		

Note: X refers to data not available.

Abbreviations: I, Intervention; C, Control; HbA1c, Hemoglobin A1c; NICU, Neonatal Intensive Care Unit.

Table 4 Summary of Quality Assessment of Studies by the Cochrane Risk-of-Bias Tool (RoB 2)

Studies	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Overall Bias
Sophie E. Poulter, 2022 ⁴³	Some concerns	Some concerns	Low	High	Some concerns	High
Tong Wei Yew, 2021 ⁴¹	Low	Some concerns	Low	Low	Low	Some concerns
Karen Lim, 2021 ⁴⁶	Low	Some concerns	Low	Low	Some concerns	Some concerns
Iren Borgen, 2019 ⁴⁰	Low	Some concerns	Low	Low	Some concerns	Some concerns
H. Guo, 2019 ⁴⁸	Some concerns	Some concerns	Low	High	Some concerns	High
Ji-Hee Sung, 2019 ⁴⁵	Some concerns	Some concerns	Low	High	Some concerns	High
Hadas Miremberg, 2018 ⁴⁷	Low	High	Low	Low	Low	High
Lucy Mackillop, 2018 ⁴⁴	High	High	Low	Low	High	High
Ping Yang, 2018 ⁴⁹	High	Some concerns	Low	Low	Low	High
Natalia Pérez-Ferre, 2010 ⁴⁶	Some concerns	Some concerns	Low	Low	Low	Some concerns

Study Group criteria,^{43,44} two studies were based on the American Diabetes Society criteria.^{47,48} However, the remaining three studies did not report the GDM diagnosis.^{40,45,46} All of studies were conducted between 2018 and 2022.

Five studies reported a mean BMI of 27.08 ± 4.97 kg/m² at initial study enrollment,^{41,44,45,47,48} whereas other studies did not extract data or did not report it.^{40,42,43,46,49} Six studies reported a mean HbA1C of $5.43 \pm 0.36\%$.^{41,42,44,46–48} Six out of 10 studies said the mean gestational week of 27.58 ± 2.79 weeks.^{41–45,48} Five studies reported a mean OGTT-2h of 8.7 ± 1.48 mmol/L.^{41,42,44,48,49} The majority of the included studies (n = 6) reported women we had with a GDM history.^{40–44,47,48}

Characteristics of Interventions

Intervention Group

Women with GDM in the intervention group received smartphone-based lifestyle interventions using a smartphone app (n = 8),^{40–45,47,48} smart phone social media platform (WeChat) (n = 1),⁴⁹ or short message service (SMS) (N = 1).⁴⁶ Three studies reported research teams, including endocrinologists, diabetes nurse educators, and dietitians,^{42–44} whereas another three studies included obstetricians and endocrinologists,^{46,47,49} one including outpatient service doctors,⁴⁸ the remaining studies did not report the details of the research team.^{40,41,45} The frequency of intervention was every day in eight studies.^{40–43,46–49} Two studies reported a frequency of twice a week⁴⁵ and once a week,⁴⁴ respectively. Only two studies used intervention components that were based on a theoretical framework.^{41,42}

The contents of interventions in our review can be categorized into four primary types: “health education” (provision of diabetes-related behavior education), “self-management behavior reminders” (reminders to conduct specified behavior activities), “data management” (monitoring and recording self-monitoring of blood glucose (SMBG), weight data obtained, data upload, visualization, trend report, and alerts), and “feedback” (system-generated automated messages, system-generated personalized feedback on the basis of pre-designed algorithms, and personalized feedback sent by health-care professionals on the basis of patient data and performance). All the studies incorporated individualized guidance, supervision, and feedback. Ten studies involved diet, eight involved blood glucose; seven performed health education, six included physical activity, and three monitored insulin treatment.^{46–48} Only two studies tracked weight^{41,49} and SMBG.^{41,48}

The attrition of the intervention group ranged from 0% to 7.7%, and the control groups were 0% to 12.7%. The attrition of lifestyle interventions that used a smartphone-based APP in the intervention group ranged from 0% to 7.7%, the control group varied from 0% to 12.1%,^{40–45,47,48} and the WeChat platform was 0% in intervention and control group,⁴⁹ whereas SMS was 2% to 4%.⁴⁶ The reasons for dropout ranged from being too busy, time conflicts, work-related reasons, and spontaneous abortion.

Control Group

Women with GDM in the control group received “usual care”, which generally involved standard outpatient care and/or conventional clinic-based education classes. Six studies reported intervention recorded by paper diary, whereas the other four studies did not report.^{41,42,45,49}

Effects on Compliance and HbA1C

Compliance

Compliance was evaluated in three RCTs^{41,47,48} with two methods. A statistically significant difference in compliance existed between the two groups [$n = 584$, $SMD = 7.36$ 95% CI = (4.05 to 10.68), $z = 4.35$, $P < 0.0001$, $I^2 = 99\%$, random-effects model] (see Figure 2). In two studies,^{47,48} compliance was calculated as the actual blood glucose measurements/instructed measurements $\times 100$, and one study⁴¹ was calculated by frequency of SMBG per week. Heterogeneity did not disappear when we removed study one by one. A high heterogeneity was observed, maybe due to the different measurement criteria of compliance.

HbA1C

HbA1C was assessed in three studies,^{44,46,48} data available were indicated in two studies.^{46,48} As one study did not report the means and standard deviations of the HbA1C values.⁴⁴ Compared to the control group, a non significant difference was observed in two studies after the intervention [$n = 221$, $SMD = -1.30$, 95% CI = (-3.36, 0.77), $z = 1.23$, $P = 0.22$, $I^2 = 98\%$, random-effects model] (see Figure 3).

Effects on Maternal Outcomes

Gestational Weight Gain

Six studies^{41,42,44–46,48} reported the effectiveness of intervention on gestational weight gain. Meta-analysis results revealed non significant improvement in gestational weight gain [$n = 905$, $SMD = -0.47$, 95% CI = (-1.05, 0.11), $z = 1.59$, $P = 0.11$, $I^2 = 94\%$; random-effects model], compared to the control group (see Figure 4). Heterogeneity was reduced from 94% to 30% when Guo's study was excluded [$SMD = -0.02$, 95% CI = (-0.19, 0.16), $z = 0.18$, $P = 0.86$] (figure not shown).

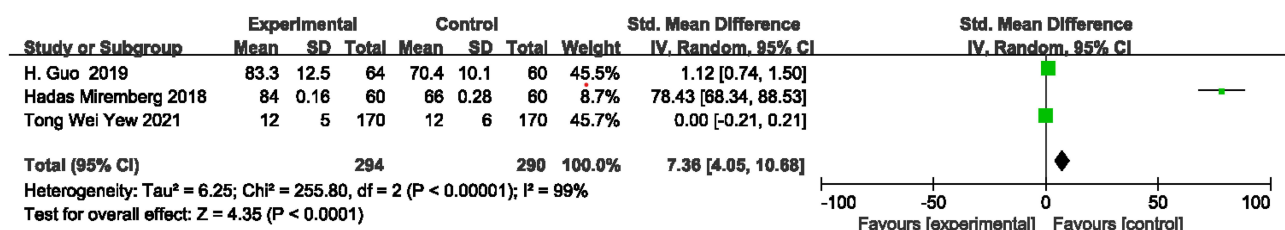


Figure 2 Forest plot of compliance.

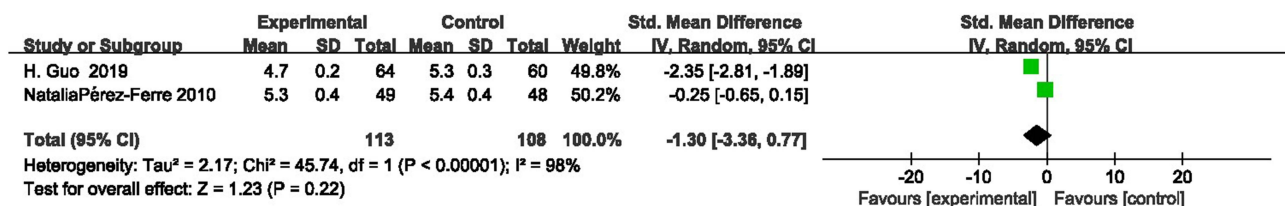


Figure 3 Forest plot of HbA1C.

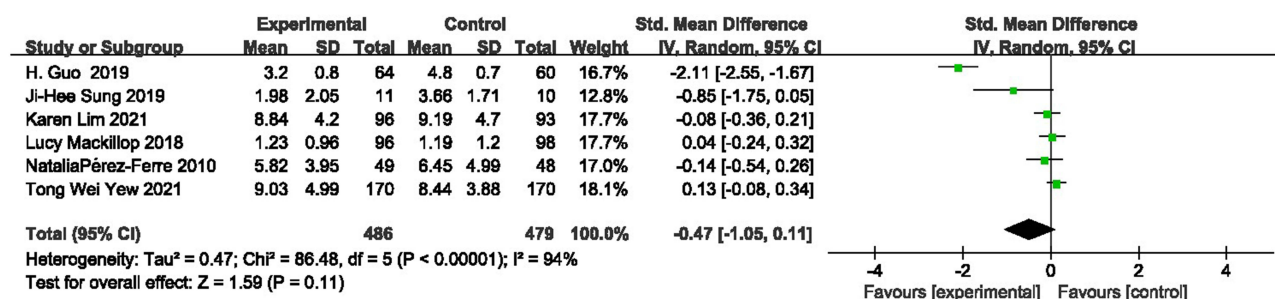


Figure 4 Forest plot of gestational weight gain.

Gestation Age at Delivery

Week of gestation age at delivery was measured in seven RCTs.^{41,43,45–49} Meta-analysis results indicated no beneficial effect on week of gestation age at delivery [$n = 1001$, $SMD = 0.02$, 95% $CI = (-0.21, 0.24)$, $z = 0.15$, $P = 0.88$, $I^2 = 65\%$, random-effects model] (see Figure 5). When the Poulter's study was removed for the analysis, no statistically significant difference was found between two groups with an acceptable heterogeneity ($I^2 = 40\%$, $P = 0.14$) [$SMD = -0.06$, 95% $CI = (-0.25, 0.14)$, $z = 0.59$, $P = 0.56$] (figure not shown).

Normal Vaginal Delivery and Cesarean Birth

Eight studies reported normal vaginal delivery,^{40,41,43,44,46–49} when pooling eight studies, no significant difference was revealed in the groups [$n = 1409$, $RR = 1.19$, 95% $CI = [0.95, 1.51]$, $z = 1.51$, $P = 0.13$, $I^2 = 35\%$, fixed-effects model] (see Figure 6). Similarly, regarding cesarean birth, insignificant differences between two groups were found in risks of cesarean birth as reported in eight studies^{40,41,43,44,46–49} [$n = 1409$, $RR = 0.89$, 95% $CI = [0.77, 1.03]$, $z = 1.58$, $P = 0.11$, $I^2 = 43\%$, fixed-effects model] (see Figure 7).

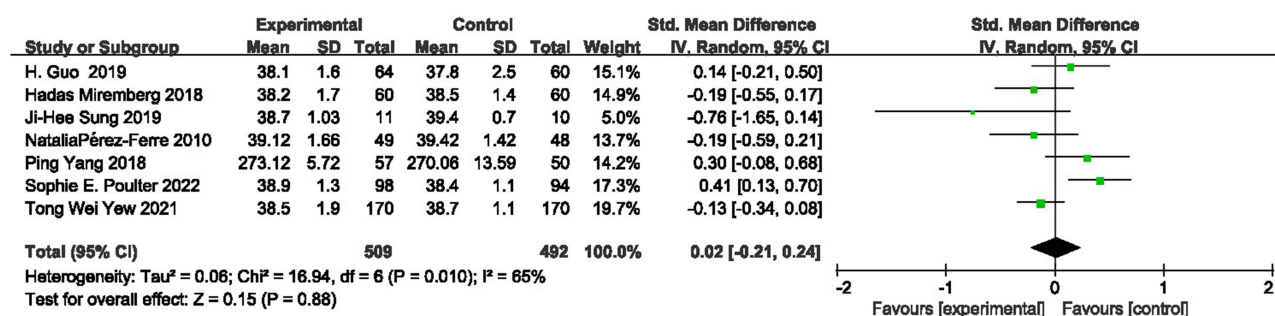


Figure 5 Forest plot of gestational age at delivery.

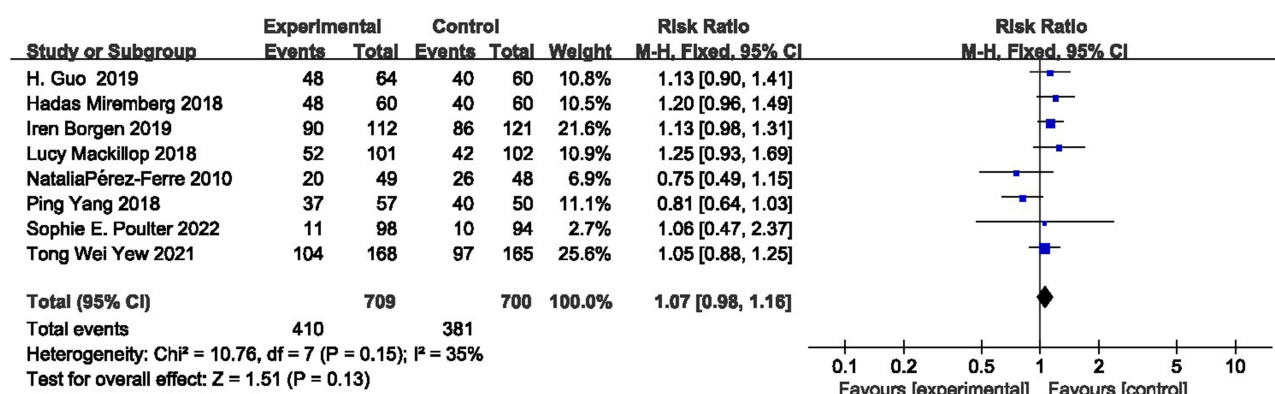


Figure 6 Forest plot of normal vaginal delivery.

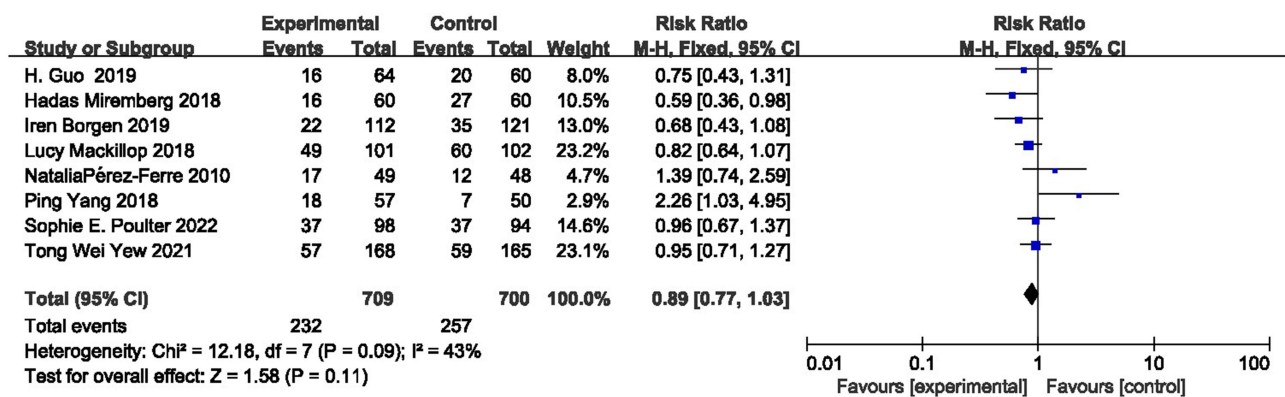


Figure 7 Forest plot of cesarean delivery.

Effects on Infant Outcomes

Infant Birth Weight

Infant birth weight was assessed in eight RCTs. Among which one study was excluded from the meta-analysis due to insufficient data.⁴⁰ Seven studies were performed a meta-analysis,^{41,43–47,49} no statistically significant difference existed in infant birth weight between the intervention group and control group [n = 1072, MD = 9.98, 95% CI = (–46.75 to 66.71), z = 0.34, P = 0.73, I² = 0%, fixed-effects model] (see Figure 8).

Neonatal Hypoglycemia

The overall prevalence of neonatal hypoglycemia was evaluated in eight studies. One out of eight studies could not be pooled for meta-analysis as they did not extract neonatal hypoglycemia values.⁴⁴ Thus, a meta-analysis including seven studies was conducted.^{41,43,44,46–49} The pooled results did not identify a statistically significant amelioration of neonatal hypoglycemia compared with controls [n = 1162, RR = 0.83, 95% CI = (0.64,1.09), z = 1.35, P = 0.18, I² = 6%, fixed-effects model] (see Figure 9).

NICU Admission

Six studies^{40,41,43,44,47,49} reported NICU admission. The results showed that the participants in the intervention group had a significantly reduced risk for NICU admission compared with the control group [n = 1185, RR = 0.64, 95% CI = (0.47,0.86), z = 3.00, P = 0.003, I² = 0%, fixed-effects model] (see Figure 10).^{40,41,43,44,47,49} Table 5 summarizes the effect sizes for primary and secondary outcomes from RCTs.

Psychological Status

Regarding psychology outcomes, one out of 10 studies reported psychological determinants of behavior change (depression and anxiety).⁴¹ Findings revealed no significant difference between the two groups on depression and anxiety after intervention (P > 0.05).

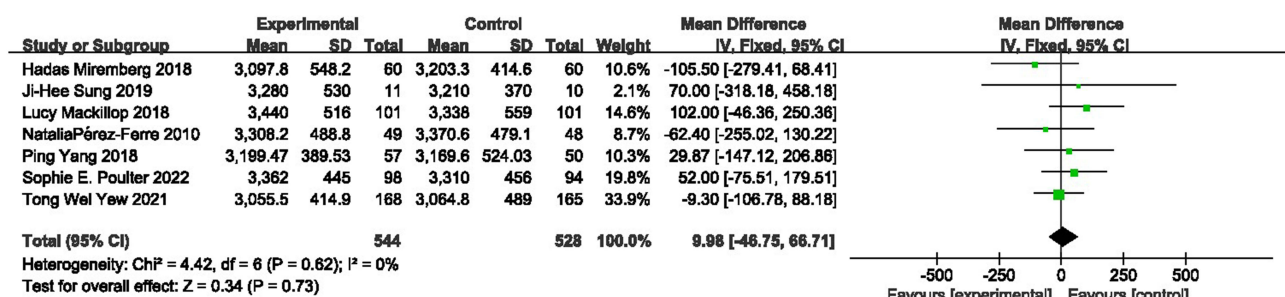


Figure 8 Forest plot of Infant birth weight.

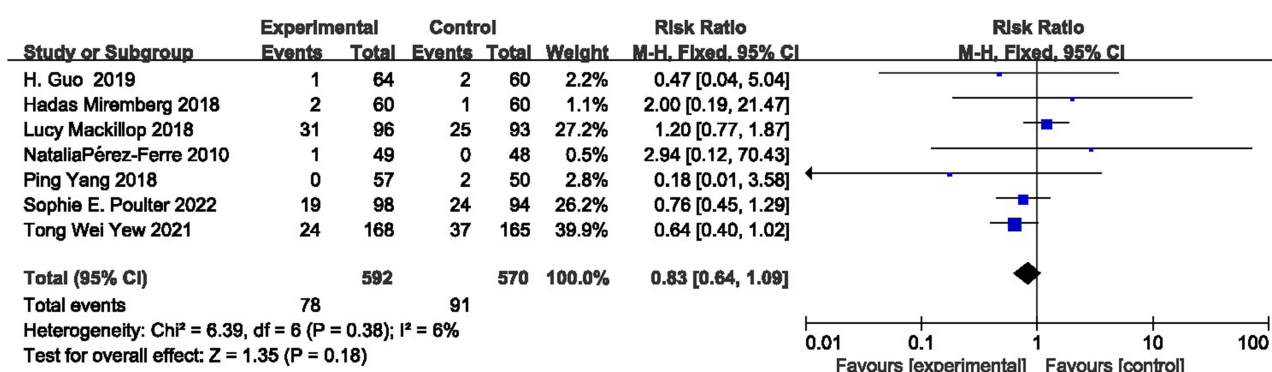


Figure 9 Forest plot of neonatal hypoglycemia.

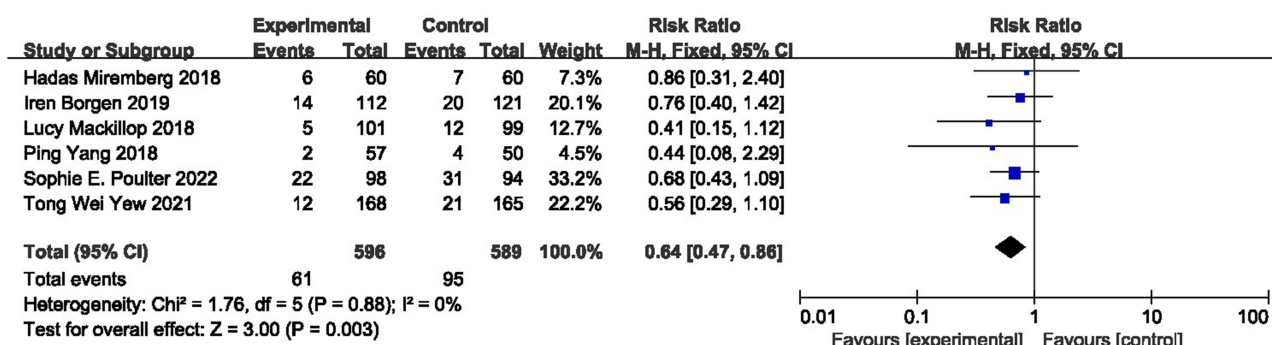


Figure 10 Forest plot of NICU admission.

Satisfaction Evaluation

Two studies evaluated satisfaction^{43,44} with the structured semiquantitative Oxford Maternity Diabetes Treatment Satisfaction Questionnaire (a 7-point Likert scale). Participants showed overall high satisfactions on smartphone based, due to the special focus on reducing contact and perceived time.

Cost Effectiveness

In terms of cost-effectiveness, two out of 10 studies reported the conflicting results. One⁴³ indicated a significant reduction in resource use on the total cost during study period after smartphone-based intervention ($P = 0.023$) compared

Table 5 Effect Sizes for Primary and Secondary Outcomes from RCTs

Outcome	Studies	Participants	Statistical Method	Effect Estimate	I^2	Z	P
1. Compliance	3	584	Std. Mean Difference (IV, Random, 95% CI)	7.36 [4.05, 10.68]	99	4.35	< 0.0001**
2. HbA1c	2	221	Std. Mean Difference (IV, Random, 95% CI)	-1.30 [-3.36, 0.77]	98	1.23	0.22
3. Gestational weight gain	6	905	Std. Mean Difference (IV, Random, 95% CI)	-0.47 [-1.05, 0.11]	94	1.59	0.11
4. Gestational age at delivery	7	1001	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.21, 0.24]	65	0.15	0.88
5. Normal vaginal delivery	8	1409	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.98, 1.16]	35	1.51	0.13
6. Cesarean delivery	8	1409	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.77, 1.03]	43	1.58	0.11
7. Infant birth weight	7	1072	Mean Difference (IV, Fixed, 95% CI)	9.98 [-46.75, 66.71]	0	0.34	0.73
8. Neonatal hypoglycemia	7	1162	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.64, 1.09]	6	1.35	0.18
9. NICU admission	6	1185	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.47, 0.86]	0	3.00	0.003*

Notes: *Statistically significant at $P < 0.05$ level; **Statistically significant at $P < 0.0001$ level.

Abbreviations: HbA1c, Hemoglobin A1c; NICU, Neonatal Intensive Care Unit.

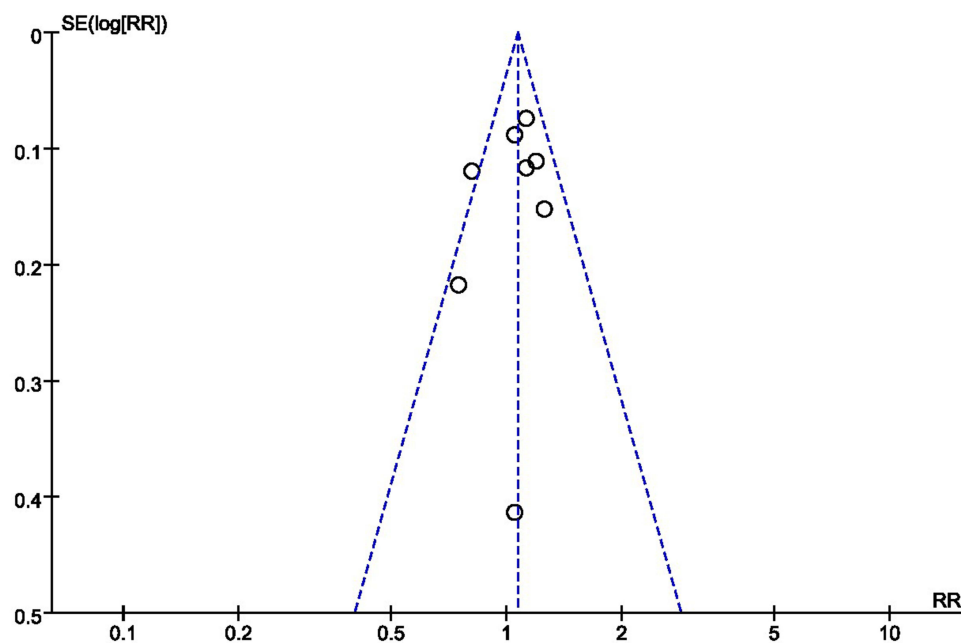


Figure 11 Funnel plot.

to the control group. Another study⁴⁴ demonstrated no statistically significant cost differences between the two groups over the study period.

Publication Bias and Sensitivity Analyses

Visual inspection of the funnel plot did not find evidence of potential publication bias (see Figure 11). A sensitivity analysis was conducted to examine how the results changed with the removal studies and assessed the stability of the results. When we removed the study from the model and recalculated the combination estimate on the remaining studies, heterogeneity disappeared or decreased, and the pooled results were consistent, which indicated the robustness of our findings.

Discussion

This meta-analysis systematically evaluated the effectiveness of smartphone-based lifestyle interventions compared with the standard care on compliance, HbA1C, maternal and infant outcomes, psychological status, satisfaction, and cost effectiveness for women with GDM. This review indicated that smartphone-based lifestyle interventions can contribute to favorable impacts on compliance, and the incidences of NICU admission. Contrastingly, we did not observe significant improvements in HbA1c, neonatal hypoglycemia, infant birth weight, maternal outcomes, psychological status, and cost effectiveness. Moreover, participants' satisfaction reported in the two studies was high, and higher level of satisfaction is conducive to obtain better outcomes.

Regarding compliance, the current meta-analysis showed that smartphone-based lifestyle interventions can improve compliance significantly ($I^2 = 99\%$). The heterogeneity did not disappear by sensitivity analysis when each study was deleted from the model one by one. This heterogeneity might have been due to different devices available to measure compliance from different countries. Guo's study was conducted in a developing country (China),⁴⁸ whereas Yew's study⁴¹ and Mirembert's study⁴⁷ were implemented in Singapore. Additionally, a high heterogeneity may be due to the different measurement criteria of compliance. Moreover, our finding is consistent with the effects of technology-based lifestyle interventions on patients by providing real-time reminders and guidance, which can improve participants' compliance and increase positive health behaviors.^{50,51} Interestingly, although the compliance was improved, smartphone-based lifestyle interventions on HbA1C levels were non significant. The intervention effects observed in our analysis should be interpreted with caution due to the small number of studies and the high heterogeneity.

We observed no significant improvements of maternal outcomes. Regarding gestational weight gain, the current study observed no statistically significant difference between the two groups. Several reasons possibly explain the non significant effect of the smartphone-based lifestyle interventions on gestational weight gain. First, those studies that demonstrated that lifestyle interventions reduced gestational weight gain or improved other maternal outcome mainly targeted women with BMI of at least 31.3 kg/m².⁴⁴ We included women with GDM with the average BMI at recruitment of roughly 26.53 kg/m². Second, a recent study revealed that gestation week at baseline was associated with maternal outcomes.⁵² Mean gestation at recruitment of 25 weeks showed decreased gestational weight gain⁴⁸ possibly because there was a longer intervention time from recruitment to. In our meta-analysis, the mean gestational week at baseline was 27.4 in included studies. Therefore, it was not surprising that our review did not identify improvements in the gestational weight gain.

Our finding is consistent with the current available evidence ($n = 11$ trials including 5658 participants, MD = 0.05 weeks, 95% CI: -0.05 to 0.15),⁵³ which has reported that no evidence of a difference in the gestational age at delivery exists between the lifestyle intervention and standard care groups. As for the rate of normal vaginal delivery and cesarean birth, the available literature has reported different results.^{29,30,33} A recent review ($n = 32$ trial including 5108 participants)²⁹ reported that telemedicine interventions on women with GDM showed a significant improvement in incidences of caesarean section [relative risk (RR) = 0.82, $P = 0.02$] compared to the control group. Another review ($n = 6$ trials including 408 participants)³³ reported that mHealth-apps might improve vaginal deliveries showing improving trends. However, a recent meta-analysis in 2020 evaluated technology-supported lifestyle interventions for GDM covering 10 studies, demonstrated that no differences in normal vaginal delivery and cesarean birth were found in the two groups.³⁰

Our meta-analysis showed that smartphone-based lifestyle interventions were associated with lower incidences of NICU admission, which is in line with one systematic review demonstrating that lifestyle interventions were beneficial for NICU admission mainly due to a reduced risk of being born preterm (<37 weeks) (RR = 0.71, 95% CI = 0.53, 0.96) and of shoulder dystocia (RR = 0.38, 95% CI = 0.21, 0.66).⁵⁴ However, as for the infant birth weight and rate of neonatal hypoglycemia, the current study did not observe statistically significant differences between the two groups. These findings were consistent with two reviews of technology-based interventions that found no significant differences in infant outcomes between the two groups.^{30,33} The possible reason is that gestational weight gain and gestational age delivery were not improved. Higher quality and more adequately powered studies are warranted to investigate the effects of smartphone-based lifestyle interventions on maternal and fetal outcomes among women with GDM.

In our included studies, the psychological status of GDM receives little attention. One of 10 studies reported depression and anxiety, showing non significant improvements in psychological status. The psychological burden is also common in GDM.⁵⁵ The prevalence of anxiety was highest (39.9%), followed by depression (12.5%), among women with GDM.⁵⁶ Prior studies suggested that depression and anxiety can directly affect patients' behavior and ability to self-management and indirectly affect HbA1c.⁵⁷ Moreover, the psychological status of pregnant women also has a certain impact on maternal and offspring outcomes.^{55,58,59} Evidence suggests that strategies to tailor psychological interventions modules based on smartphone help adults with diabetes cope positively and achieve diabetes treatment goals.⁶⁰ Therefore, psychological intervention elements must be integrated into smartphone-based lifestyle interventions to investigate the effects on psychological status among women with GDM in future studies.

Strength and Limitations

The principal strength of this review is its inclusion of various outcomes that evaluated the effectiveness of smartphone-based lifestyle interventions on compliance, HbA1C, maternal and neonatal outcomes and psychological status, satisfaction, and cost effectiveness. In addition, we did not limit our systematic review to smartphones for developing/developed countries. The search strategy was comprehensive and inclusive, and this review reported outcomes according to PRISMA guidelines. Finally, the attrition of this review included studies in the intervention group was low, approximately 0% to 7.7%, especially in the WeChat group, which was 0%.

However, this study also has some limitations that must be considered while interpreting our findings. First, the lack of standardized intervention time and assessment time points prevented a direct comparison between trials due to the

different GDM diagnosis criteria. Meanwhile, the insufficiency of existing data (eg, compliance, HbA1c) in included studies prevented us from drawing a solid conclusion about the effects of smartphone-based lifestyle interventions on women with GDM. Second, the included studies had suboptimal quality, and methodological weakness may decrease the internal validity of the results and increase the heterogeneity, which may have led to a biased estimate of the overall effect. Third, all studies for women with GDM were conducted during gestation; however, the effects of smartphone-based behavior intervention on women with GDM after postpartum remain unknown. Fourth, participants' psychological outcomes ($n = 1$), satisfaction ($n = 3$), and cost effectiveness ($n = 2$) were reported in limited studies, making data synthesis extremely difficult.

Implications for Practice and Research

Implications for Practice

In clinical practice, smartphone-based lifestyle interventions are routinely under-recognized. This review found that smartphone-based lifestyle interventions affects the compliance and the incidences of NICU admission. Smartphone-based lifestyle interventions are promising for women with GDM during gestation and can be applied in clinical practice. According to the evidence in this systematic review, multidisciplinary collaboration involving dietitians, diabetes educators, obstetricians, and endocrinologists will help women with GDM improve their health outcomes.

Implications for Research

Considering the methodological weakness of some included studies, future RCTs must follow the guidelines of the Consolidated Standards of Reporting Trials statement to enhance the standard of reports.⁶¹ In this review, most studies were conducted in developed countries; more research is warranted in developing and low-income countries. Most of the trials in the included studies were conducted during gestation, more research is required before pregnancy or postpartum or all-round. The effects of smartphone-based lifestyle intervention on HbA1c, maternal-fetal, and infant outcomes, as well as psychological status, are warranted in multi-center designs guided by a framework to investigate effects and possible intervention mechanisms. Thus far, APP/smart phone-based interventions have not performed well, and participants are unsure how to use the technology effectively. It would be preferable to involve participants more in the content development for smartphone-based interventions. Future researchers must try new strategies for using technology to promote healthy lifestyles. More rigorous cost-effective analyses of smartphone-based interventions are warranted to demonstrate the impact on public health. Future meta-analyses with a larger sample of RCT studies can perform subgroup analysis on the basis of the type of country, gestation or postpartum, and App, WeChat, or SMS.

Conclusion

The current systematic review fills the research gap regarding the effectiveness of smartphone-based lifestyle interventions among women with GDM. It provides further evidence to help elucidate future research directions and guide clinical practice. Smartphone-based lifestyle interventions as a practical strategy improve compliance and the incidences of NICU admission among women with GDM. However, the effectiveness appears to be non significant with respect to HbA1c, maternal outcomes, infant birth weight, and neonatal hypoglycemia. Future studies at larger scales are warranted to examine the long-term effects and cost effectiveness of smartphone-based lifestyle interventions.

Disclosure

The authors report no conflicts of interest in this work.

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