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Digital therapeutics-based lifestyle intervention for gestational diabetes mellitus prevention of high-risk pregnant women: a study protocol for a non-randomised controlled trial

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ABSTRACT

Introduction Digital therapeutics have been approved as a treatment aid for various medical conditions and are increasingly prevalent. Despite numerous studies on the potential of digital therapeutic interventions in preventing gestational diabetes mellitus (GDM), there is a critical need for more high-quality, large-scale studies to validate their effectiveness. This need arises from the inconsistencies in results and variations in the quality of previous research.

Methods and analysis We propose a non-randomised controlled trial involving 800 high-risk pregnant women in 6 maternity and child health hospitals in Fujian, China. This study aims to investigate the role and effectiveness of digital therapeutics-based lifestyle intervention in managing the health of pregnant women at high risk for GDM. The study will compare the differences in GDM prevalence, pregnancy weight management and other pregnancy-related health outcomes between pregnant women who received digital therapeutics-based lifestyle intervention and those in the control group. The intervention includes dietary guidance, a personalised physical activity programme and lifestyle improvement strategies delivered through a smartphone app. Primary outcomes include the incidence of GDM at 24–28 weeks gestation and gestational weight gain (GWG). Secondary outcomes comprise improvements in individual lifestyle and risk factors, nutritional issues, implementation outcomes and other pregnancy-related outcomes.

Ethics and dissemination section The trial was approved by the Ethics Committee of Fujian Maternity and Child Health Hospital (approval number: 2023KY046), Jianyang Maternity and Child Health Hospital (approval number: A202401), Fuqing Maternity and Child Health Hospital (approval number: FY2024003), Changting Maternity and Child Health Hospital (approval number: 202401), Datian Maternity and Child Health Hospital (approval number: dtfy202401) and Quanzhou Maternity and Child Health Hospital (approval number: 2024(50)). We will disseminate our findings by publishing articles in leading peer-reviewed journals.

Trial registration number ChiCTR2300071496.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The non-randomised controlled trial can better reflect the actual effects of the intervention in real medical practice.
⇒ All participants have an equal opportunity to receive the intervention that is more likely to be beneficial to them.
⇒ Limitations of this study include the impossibility of blinding participants and researchers.
⇒ The participants choose the type of intervention, which may increase their satisfaction and adherence to the intervention.
⇒ Differences in baseline characteristics which might influence the effect of intervention and adjustment for baseline data is needed.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as abnormal glucose metabolism that is first recognised during pregnancy, accounting for 5%–25% of all pregnancies.[1] In 2021, the International Diabetes Federation reported that 16.7% of women had hyperglycaemia during pregnancy, 80.3% of whom had GDM, and the prevalence of GDM increased from 4% in 2010 to 21% in 2020.[2] GDM not only increases the risk of preeclampsia, preterm birth, miscarriage, type 2 DM and cardiovascular disease in mothers but also may lead to fetal macrosomia, intrauterine growth retardation and future obesity, cardiovascular disease in the adulthood of infants.[3–5] The increase in GDM brings a huge burden on the global economy.[6 7] For example, in China, the prevalence of GDM in 2015 was 17.5%, with an economic burden of 19.36 billion yuan, accounting for 0.5% of public health spending.[8] GDM is not covered by maternity insurance, and 60% of births are paid for

out-of-pocket by the family, putting great financial pressure on the family.[9]

Risk factors for GDM include genetic predisposition and environmental factors.[10] Genetic factors are strongly associated with GDM, including variants in the prolactin and melatonin receptor genes.[11 12] Lifestyle in early pregnancy, including nutritional factors, has become a key element driving the development of GDM.[13] Additionally, prepregnancy overweight or obesity is one of the major risk factors,[14 15] along with excessive gestational weight gain, advanced maternal age, a history of GDM, family history of DM, polycystic ovary syndrome, low literacy level and low healthcare knowledge.[16–18]

Previous research mainly focused on glycaemic control and complications prevention after the diagnosis of GDM. However, domestic and international scholars have also begun to explore early pregnancy interventions aimed at delaying or preventing the onset of GDM in recent years, with lifestyle intervention being the primary method. Lifestyle intervention, encompassing dietary adjustment and physical exercise, have been shown to effectively mitigate the progression of GDM among high-risk pregnant women. The Gestational Diabetes Prevention Study indicated that a combination of moderate physical activity and dietary intervention reduced the incidence of GDM by 39% in high-risk pregnant women.[19] A systematic review and meta-analysis involving 30 871 pregnant women demonstrated that dietary patterns such as the Mediterranean diet, dietary approaches to discourage hypertension and the Healthy Eating Index diet decreased the relative risk of GDM by 18%–35%.[20] Furthermore, evidence from prospective cohort studies also suggested that a diet rich in vegetables, fruits and rice-based foods reduced the occurrence of GDM in Chinese pregnant women.[21] Physical exercise has been recognised as an effective method to manage weight gain during pregnancy and enhance insulin sensitivity.[22] A prospective randomised clinical trial conducted in China revealed that engaging in physical activity for at least 30 min three times a week, commencing in early pregnancy, reduced the incidence of GDM in overweight pregnant women by 45.8%.[23 24] Additionally, two meta-analyses indicated that the intervention group following an aerobic, low-intensity to moderate-intensity exercise programme had a 28%–31% lower risk of GDM compared with the control group, with a discrepancy in gestational weight gain of approximately 1.1 kg.[25 26] Therefore, personalised lifestyle intervention should be implemented in early pregnancy for high-risk women and sustained throughout the duration of pregnancy.

Although lifestyle intervention was commonly used in clinical practice, the prevalence of GDM in China continues rising, indicating a need for more targeted intervention among high-risk women. Traditional maternal and child healthcare heavily relies on face-to-face counselling, which faces challenges such as lack of standardisation and poor patient compliance with behaviour intervention. This makes it difficult to provide effective feedback and support. Therefore, there is an urgent need to shift from a 'one-size-fits-all' pattern to individualised intervention strategies that consider individual differences, including behavioural and socioeconomic factors.

With the increasing popularity and advancement of mobile internet, digital products are transforming various aspects of our lives. In the healthcare sector, digital technology is revolutionising the treatment, prevention and management of health conditions. Currently, 'digital therapeutics' have emerged as a highly promising field in the healthcare industry. These therapies are evidence-based treatment or intervention delivered to patients through high-quality software programmes. They primarily aim to prevent, manage or treat diseases effectively.

In particular, lifestyle intervention based on digital therapies has emerged as an important research direction for the prevention of GDM. However, despite the widespread interest in this research field, inconsistencies and qualitative differences in the results of existing studies revealed that key questions remain unanswered. These issues include how to develop efficient and feasible digital intervention strategies to minimise the risk of GDM and how to assess the applicability and effectiveness of these intervention in different population. These challenges point to the urgent need to validate and optimise the effectiveness of digital therapeutics-based lifestyle intervention programme for practical application through more rigorous study designs, larger sample size and more nuanced interventions. Based on this background, this study aims to evaluate in depth the effectiveness of an innovative digital therapeutics-based lifestyle intervention programme in the prevention of GDM in high-risk pregnant women through a multicentre, large sample size, non-randomised controlled trial to address the key issues in current research.

Digital therapy is not only complementary to traditional medical treatments but also addresses deficiencies that exist in patients, providers, and the healthcare system by automating the clinical process through artificial intelligence learning to integrate clinical knowledge graphs and expert experience. For patients, digital therapies increase accessibility and adherence to healthcare, reduce the cost of accessing care and enable patients to receive services at their homes and interact one-on-one with healthcare professionals if necessary. For healthcare providers, digital therapies save precious time by automating operations, increasing service capacity, reducing service costs and improving service efficiency. Based on these advantages, we have developed a digital therapeutics-based lifestyle intervention aimed to reducing the risk of GDM through lifestyle changes, thus providing new strategies and perspectives on the prevention of GDM in high-risk pregnant women.

Table 1 The eligibility and exclusion criteria of the trial

Inclusion criteria	Singleton pregnancy
	Before 16 week's gestation
	GDM high risk: a history of GDM; prepregnancy overweight or obesity (prepregnancy body mass index ≥24 kg/m^2; a history of macrosomia; family history of type 2 diabetes mellitus; polycystic ovary syndrome; fasting blood glucose ≥5.1 mmol/L during early pregnancy; maternal age ≥30 years. (Any point can be met is the GDM high risk).
	Maternal age <45 years
	Access to a smartphone
	Chinese speaking
	Volunteered to participate, and were able to follow-up on time
Exclusion criteria	Fasting blood glucose ≥7.0 mmol/L during early pregnancy
	With severe liver or kidney disease, heart disease, immune disease, diabetes or hypertension before pregnancy
	Unable to take care of themselves
	Cannot cooperate

GDM, gestational diabetes mellitus.

METHODS

Study design

This non-randomised controlled trial based on digital therapeutics is a multicentre, prospective, open-label endpoint trial with a 7-month intervention and follow-up period. The primary focus of this study is to assess the effectiveness and implementation outcomes.

Study population and recruitment

The study population will consist of early pregnant women giving birth in six maternity and child health hospitals in Fujian, China. Eligible participants are pregnant women with risk factors for GDM who own a smartphone. The recruitment will take place in six maternity and child health hospitals located in Fuzhou, Quanzhou, Sanming, Nanping and Longyan cities in Fujian, China. Participants meeting the criteria will be recruited directly by nurses, nutritionists and physicians. The eligibility criteria are outlined in table 1. All participants will be informed about the study objectives, procedures and will choose their desired intervention type, either digital therapeutic support intervention or standard health management. This trial does not involve the collection of biological specimens.

Intervention and control conditions

The intelligent medical portal used in our study consists of a smart medical portal, a participant smartphone app and wearable devices (figure 1). The smart medical portal aids in collecting baseline data, conducting intelligent assessments, making diagnoses and managing prescriptions for intervention participants. The participant smartphone app enables self-management, facilitates the collection of home monitoring information, and sends notifications and education materials. Home behaviour monitoring information data are captured using wearable devices. Researchers can extract data from the smart medical portal, participant smartphone app and wearable devices and store it in a central database. The digital therapeutics platform was developed in collaboration with software developers and researchers from Fuzhou

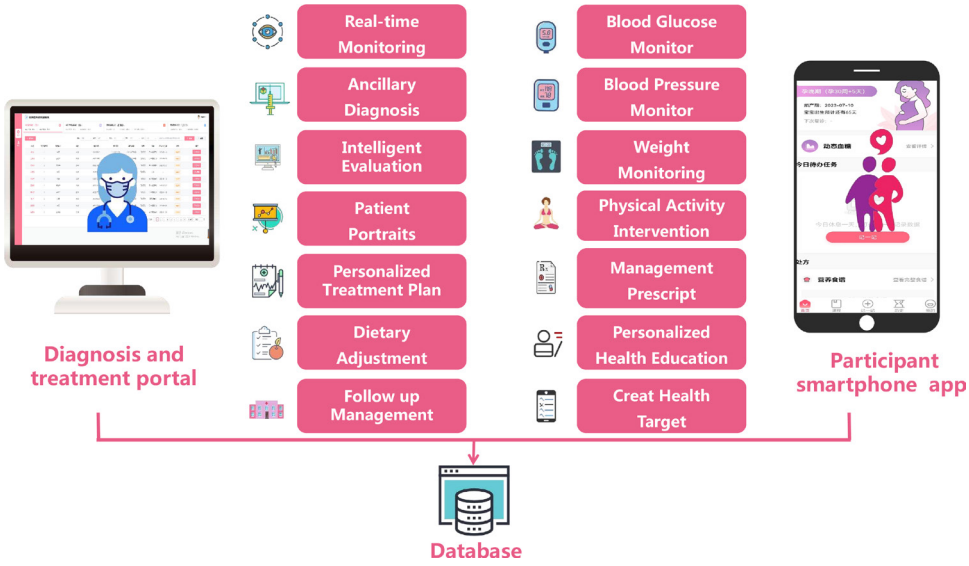

Figure 1 Overview of the intelligent medical portal consisting of smart medical portal, the participant smartphone app and wearable devices.

Comvee Network & Technology, Fuzhou, China, as well as team members with expertise in nutrition, obstetrics, endocrinologist and physical activity. The development process is continuously updated and iterative to align with the needs and preferences of researchers and users. The participant smartphone app delivers a comprehensive programme comprising recommendations, goals, planing, monitoring, feedback and push notifications related to a healthy diet, physical activity, weight management, blood glucose level and blood pressure. The intervention content provided by the app is evidence based on guidelines and high-quality literature. Two versions of the participant app were developed, with participants having access to only one of the versions. Both versions facilitate the collection of baseline and outcome assessments for all participants through questionnaires.

Participants expressing interest in the programme will undergo eligibility screening by research team members using the smart medical portal. Written informed consent (online supplemental file 1) including information on the use and sharing of participant data with relevant regulatory authorities will be obtained. Standard procedures will be followed by trained researchers and team members in the nutrition room for measurements such as blood pressure, maternal weight, height and waist circumference. All participants are required to complete self-assessment questionnaires in the app. These questionnaires include the baseline information questionnaire, the The International Federation of Gynecology and Obstetrics (FIGO) nutrition checklist,[27] the International Physical Activity Questionnaire-Short Form (IPAQ-SF),[28] the Chinese Dietary Guidelines Compliance Index Questionnaire,[29] the Pittsburgh Sleep Quality Index (PSQI),[30] the Edinburgh Postnatal Depression Scale (EPDS)[31] and the Generalised Anxiety Disorder-7 (GAD-7).[32] These assessments will be used to evaluate secondary outcomes related to diet, physical activity, sleep quality, depression and anxiety, as well as to gather baseline information.

Blinding strategy

Due to the non-randomised controlled trial, blinding of both participants and researchers was impossible. However, the individuals conducting the trial for participants are different from those responsible for the assessment and data analysis. To prevent contamination between groups, a unique passcode is provided for each intervention participant. During the follow-up visit, participants are instructed not to use other digital health devices.

Intervention group

Participants in the digital therapeutics-based lifestyle intervention group will have access to the interactive application. This application aims to assist pregnant women in managing their lifestyle by promoting adequate weight gain, increased physical activity, optimal glycaemia level and sufficient nutrition for pregnancy. It provides education, self-monitoring and timely feedback to support behaviour modification. Participants can set personal goals for lifestyle changes and receive automated reminders to enter measurements. The application would then provide intelligent feedback. In addition, it can send push notifications, deliver education material and assist with follow-up management based on data calculations. All data are transmitted in real time to the hospital's smart medical portal, where doctors can view goals and measurements and send management prescriptions to the application to promote sustainable behaviour change. The integration of the smart medical portal and the interactive application form a closed-loop management system within and outside the hospital, enhancing participants' compliance with recommended behaviour and lifestyle changes. Subsequently, participants are asked to complete additional questionnaires in the second and third trimesters, as detailed in table 2. All measurements conducted during the follow-up visits are repeated in the second and third trimesters.

Intervention content

Before enrolment, each participant will receive health education sessions from a nurse, focusing mainly on nutrition and physical activity advice. Following this, a nutritionist will prescribe a personalised dietary intervention, explaining food substitution and encouraging the replacement of high glycaemic index foods with low glycaemic index alternatives. Women without contraindications to exercise will be advised to engage in moderate-intensity exercise lasting 30 min for 5 days per week. Obstetricians will conduct a nutritional evaluation and book the next follow-up appointment within 2–4 weeks. Women will be required to track their weight, blood glucose, blood pressure, diet and physical activity during pregnancy. When these indicators reach critical levels, the app will issue a warning, helping to prevent emergencies. All intervention content used in the app is based on evidence-based guidelines and literature.

Control group

Participants in this group will receive standard medical care offline throughout the trial, including screening, check-ups, counselling and guidance on healthy lifestyles such as a balanced diet, appropriate physical activity and weight management until childbirth. They will be informed of the recommended weight gain range during pregnancy based on different prepregnancy body mass index (BMI) and the risks associated with nutritional metabolic disorders during pregnancy and childbirth and will be advised to attend regular antenatal visits at medical institutions. Depending on the risk of nutritional metabolic disease specific to pregnant women, tailored interventions for nutritional healthcare during pregnancy will be provided. Some pregnant women will be taught how and when to measure their blood glucose levels if abnormalities occur. Healthcare providers will offer standard medical care every 2~4 weeks. Participants will have access to the control app, which only includes recording

Table 2 Questionnaires and measured time points

Domain	Questionnaire/measurement	Time point measured
Diet	International Federation of Gynecology and Obstetrics(FIGO) nutrition checklist	Before 16 weeks gestation
	Chinese Dietary Guidelines Compliance Index Questionnaire	Before 16 weeks gestation 24–28 weeks gestation 34–36 weeks gestation
Physical activity	International Physical Activity Questionnaire-Short Form	Before 16 weeks gestation 24–28 weeks gestation 34–36 weeks gestation
Sleep	Pittsburgh Sleep Quality Index	Before 16 weeks gestation 24–28 weeks gestation 34–36 weeks gestation
Depression	Edinburgh Postnatal Depression Scale	Before 16 weeks gestation 24–28 weeks gestation 34–36 weeks gestation
Anxiety	Generalised Anxiety Disorder-7	Before 16 weeks gestation 24–28 weeks gestation 34–36 weeks gestation

FIGO, The International Federation of Gynecology and Obstetrics.

functions for baseline information and reviews nutrition and physical activity, lacking interactive features and intelligent support.

Primary and secondary outcomes

The primary effectiveness outcomes of the trial include the incidence of GDM and GWG. GDM is typically diagnosed between 24 and 28 weeks gestation using the criteria established by the International Association of the Diabetes and Pregnancy Study Group.[33] Participants are required to undergo a 75 g oral glucose tolerance test, with GDM being diagnosed if any of the following values are exceeded: fasting glucose ≥5.10 mmol/L, 1 hour glucose ≥10.0 mmol/L or 2 hour glucose ≥8.5 mmol/L. GWG is assessed through changes in maternal weight (in kilograms) and is categorised as inadequate, appropriate or excessive based on the Chinese gestational weight gain recommendation according to different Chinese prepregnancy BMI.[34 35]

Maternal and neonatal outcomes

The main secondary outcomes involve assessing improvement in individual lifestyle changes, nutritional diseases, implementation outcomes and other pregnancy-related outcomes. Maternal outcomes encompass changes in individual lifestyle factors such as dietary intake, physical activity, sleep quality, depression and anxiety as well as changes in measurement including blood pressure, body composition, haemoglobin A1c and blood glucose levels. Additional maternal adverse perinatal outcomes consist of gestational hypertension, preeclampsia, preterm delivery, induction of labour and caesarean delivery. Adverse outcomes among infants include macrosomia, being large or small for gestational age, having a full-term birth weight, admission to the intensive care unit, hyperbilirubinaemia, birth trauma and respiratory distress syndrome. Other nutritional diseases to be considered are anaemia, vitamin D deficiency, hyperlipidaemia and so on.

Implementation outcomes

Implementation outcomes specifically refer to the adherence of participants to the intervention. User statistics will be analysed to evaluate adherence to the application.

Self-monitor adherence

The frequency of participant logins and recordings in the app, including food diaries, weight, blood glucose and other records, is used to evaluate self-monitoring adherence to the smartphone app. The recorded days up to 24–28 weeks gestation are categorised as follows: <7 days, 8–30 days, 31–60 days and >60 days or <1 month, 1–2 months, 3–4 months and 5–6 months until delivery. Participants who use the application for more than 60 days at 24–28 weeks gestation or 5–6 months until delivery are considered to have sufficient adherence.

Diet adherence

Diet adherence among participants is assessed using the Chinese Dietary Guidelines Compliance Index questionnaire.[36] This questionnaire was developed based on the Chinese Dietary Guidelines (2016) for pregnant women and the Chinese Balanced Dietary Pagoda for pregnant women. The index comprises 13 scoring components, ranging from 0 to 100 points, with scores allocated for each trimester of pregnancy. A higher index score indicates a greater, proportion of pregnant women who have reported food intake in line with recommendations. This straightforward screening tool for dietary status can effectively identify participants in need of dietary guidance

and evaluate the impact of interventions on improving diet adherence in the second and third trimesters of pregnancy.[37]

Physical activity adherence

Physical activity adherence is defined as completing exercise at least 3 days per week.[38] For pregnant women who did not have exercise habits before pregnancy, adherence is assessed by achieving physical activity goals, including meeting set goals and changing levels of physical activity. Daily point wins are reported when participants reach their daily goals to meet set goals.[39 40] Evaluating changes in physical activity levels involves comparing the duration of exercise performed vs planned, such as average daily step count or physical activity time,[41–44] self-reported walking and sitting time,[45] and exercise time.[46]

Other outcome measures

1. Change in dietary intake measured by the Chinese dietary guidelines compliance index questionnaire from baseline to the second trimester and third trimester.
2. Change in physical activity measured by IPAQ-SF from baseline to the second trimester and third trimester.
3. Change in sleep quality measured by the PSQI from baseline to the second trimester and third trimester.
4. Change in depression measured by the EPDS from baseline to the second trimester and third trimester.
5. Change in anxiety measured by GAD-7, from baseline to second trimester and third trimester.

Sample size

The incidence of GDM will be used as the primary effectiveness outcome. In previous studies, the incidence of GDM was reduced by 25%–44% as a result of dietary intervention, physical activity intervention and combined lifestyle intervention.[19 47–49] The background rate of GDM in Fujian Province is nearly 20%, and we assume a 20% decrease in the incidence of GDM. A total of 622 participants (311 in each group) are required with 80% power to detect the difference at a significance level of 0.05. Considering that approximately 15%–20% of the participants would drop out of the study, we needed to recruit 800 women (400 in each group) to participate in the study.

Data collection and management

All research data are collected through an electronic medical record system and an application designed specifically for the study. The system, including the user-side application and the physician-side diagnostic treatment system, is set up to assess accuracy and completeness of the data and to alert the researcher or participant to complement missing and incomplete data. An electronic data capture system is used for data storage and management, with multiple levels of access and password protection to safeguard data security and confidentiality. Given that participants chose the intervention group based on their personal preference, this study has a special focus on collecting detailed baseline data (eg, age, weight, BMI, medical history, lifestyle habits and mental health status) in order to compare or adjust for potential differences between groups. When analysing the intervention effect, statistical methods will be used to control for differences in baseline characteristics, such as analysis of covariance or multivariate regression modelling, to ensure the accuracy of the assessment of the intervention effect.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Statistical methods

The independent-sample t-test, χ^2 test and/or Wilcoxon rank-sum test will be used to verify the homogeneity between the groups by comparing baseline characteristics, as appropriate. Any significant differences will be regarded as confounding factors in the subsequent analyses. Paired Student's t-test or McNemar's test was applied to test the (change in the same group). Binary logistic regression was used to analyse the effectiveness of the digital therapeutic-based lifestyle intervention adjusted for confounding variables, including parity, age, education, income, BMI, family history of DM, previous GDM and other confounders. A linear mixed model with fixed effects will be conducted to examine the intervention on gestational weight gain, diary, physical activity, nutrition status, adherence, physiological outcomes and pregnancy outcomes at different intervention times and trimesters of pregnancy. Subanalysis of the intervention effect on the primary and secondary outcomes stratified by advanced age, parity and educational level will be performed with multivariate analysis. A $p<0.05$ was considered statistically significant. Analyses will be performed by using IBM SPSS software (V.20.0 or later; IBM), STATA V.15 or later (Stata), SAS software (version 9.3 SAS Institute, Cary, NC, US)) or R software (V.4.1.0 or later), as appropriate for analysis type.

Ethics and dissemination

The trial was approved by the Ethics Committee of Fujian Maternity and Child Health Hospital (approval number: 2023KY046), the Ethics Committee of Jianyang Maternity and Child Health Hospital (approval number: A202401), the Ethics Committee of Fuqing Maternity and Child Health Hospital (approval number: FY2024003), the Ethics Committee of Changting Maternity and Child Health Hospital(approval number: 202401), the Ethics Committee of Datian Maternity and Child Health Hospital (approval number: dtfy202401) and the Ethics Committee of Quanzhou Maternity and Child Health Hospital (approval number:2024(50)). All women will provide written informed consent before entering the study. This trial is registered with Chinese Clinical Trial Registry (www.chictr.org.cn) on 16 May 2023, registration number: ChiCTR2300071496. We will disseminate our findings by publishing articles in leading peer-reviewed

journals. In addition, we plan to use social media and online platforms within China, such as Weibo, WeChat and Zhihu, to expand the impact of our research and to engage in dialogue with health policy-makers with the aim of translating the research findings into concrete health policies and prevention strategies.

DISCUSSION

This article presents a detailed description of a non-randomised controlled trial, designed to evaluate the effectiveness of a digital therapeutics-based lifestyle intervention on the incidence of GDM in high-risk pregnant women. The digital therapeutics-based lifestyle intervention aims to change the health behaviour of GDM high-risk pregnant women by providing health information and lifestyle intervention through the development of a smart medical portal and smartphone app. Lifestyle intervention plays an important role in preventing GDM and a smartphone app supports a safe and convenient way for pregnant women to access health information and can be used by anywhere and anyone, especially for those who live in remote areas or have limited access to healthcare resources.

The non-randomised controlled trial will allow participants to choose interventions to their wishes that are more meaningful to them, taking into account individual differences and specific health needs. In addition, the non-randomised controlled trial can be conducted in conditions that are more closely aligned with real medical conditions, which can better reflect the actual effects of the intervention in routine medical practice. Therefore, if the digital therapeutics-based lifestyle intervention significantly helps high-risk pregnant women in preventing GDM, this method is expected to play a very useful role for both pregnant women and medical staff.

However, there are limitations to this study. First, due to the nature of a non-randomised trial, the poor comparability of the baseline characteristics needs to be adjusted through well-designed statistical analyses to assess the effectiveness of the intervention. Second, poor compliance might occur owing to the cumbersomeness of the intervention process in the intervention group. Additionally, while the smart medical technology can provide personalised advice, this personalisation may be limited and may not fully address the unique health conditions and needs of each pregnant woman.

TRIAL STATUS

Protocol version 1.0; 20 March 2023. This trial has not yet started and is anticipated to start on 15 July 2023. According to the approval of the ethical institution, this study will end on 31 December 2025.

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Contributors CM and JL conceived and designed the study. LL, JD, LS, XY and XC participated in the design and development of the intervention. YW has been responsible for interpretation and analysis of data and modified the manuscript. LL and JD helped draft the manuscript. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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REFERENCES

1 Zhu Y, Zhang C. Prevalence of gestational diabetes and risk of progression to type 2 diabetes: a global perspective. *Curr Diab Rep* 2016;16:7.
2 Zhu H, Zhao Z, Xu J, *et al*. The prevalence of gestational diabetes mellitus before and after the implementation of the universal two-child policy in China. *Front Endocrinol* 2022;13:960877.
3 Kanguru L, Bezawada N, Hussein J, *et al*. The burden of diabetes mellitus during pregnancy in low- and middle-income countries: a systematic review. *Glob Health Action* 2014;7:23987.
4 Poomalar GK. Changing trends in management of gestational diabetes mellitus. *World J Diabetes* 2015;6:284–95.
5 Boney CM, Verma A, Tucker R, *et al*. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. *Pediatrics* 2005;115:e290–6.
6 Johns EC, Denison FC, Norman JE, *et al*. Gestational diabetes mellitus: mechanisms, treatment, and complications. *Trends Endocrinol Metab* 2018;29:743–54.
7 Ferrara A. Increasing prevalence of gestational diabetes mellitus: a public health perspective. *Diabetes Care* 2007;30 Suppl 2:S141–6.
8 Xu T, Dainelli L, Yu K, *et al*. The short-term health and economic burden of gestational diabetes mellitus in China: a modelling study. *BMJ Open* 2017;7:e018893.
9 You H, Gu H, Ning W, *et al*. Comparing maternal services utilization and expense reimbursement before and after the adjustment of the new rural cooperative medical scheme policy in rural China. *PLoS One* 2016;11:e0158473.
10 Plows JF, Stanley JL, Baker PN, *et al*. The pathophysiology of gestational diabetes mellitus. *IJMS* 2018;19:3342.
11 Le TN, Elsea SH, Romero R, *et al*. Prolactin receptor gene Polymorphisms are associated with gestational diabetes. *Genet Test Mol Biomarkers* 2013;17:567–71.
12 Kim JY, Cheong HS, Park B-L, *et al*. Melatonin receptor 1 B Polymorphisms associated with the risk of gestational diabetes mellitus. *BMC Med Genet* 2011;12:82.

13 Ruiz-Gracia T, Duran A, Fuentes M, *et al*. Lifestyle patterns in early pregnancy linked to gestational diabetes mellitus diagnoses when using IADPSG criteria. *Clin Nutr* 2016;35:699–705.
14 Hanson MA, Gluckman PD, Ma RCW, *et al*. Early life opportunities for prevention of diabetes in low and middle income countries. *BMC Public Health* 2012;12:1025.
15 Graves E, Hill DJ, Evers S, *et al*. The impact of abnormal glucose tolerance and obesity on fetal growth. *J Diabetes Res* 2015;2015:847674.
16 Gibson KS, Waters TP, Catalano PM. Maternal weight gain in women who develop gestational diabetes mellitus. *Obstet Gynecol* 2012;119:560–5.
17 Schwartz N, Nachum Z, Green MS. The prevalence of gestational diabetes mellitus recurrence--effect of ethnicity and parity: a metaanalysis. *Am J Obstet Gynecol* 2015;213:310–7.
18 Ashrafi M, Sheikhan F, Arabipoor A, *et al*. Gestational diabetes mellitus risk factors in women with polycystic ovary syndrome (PCOS). *Eur J Obstet Gynecol Reprod Biol* 2014;181:195–9.
19 Koivusalo SB, Rönö K, Klemetti MM, *et al*. Gestational diabetes mellitus can be prevented by lifestyle intervention: the Finnish gestational diabetes prevention study (RADIEL): a randomized controlled trial. *Diabetes Care* 2016;39:24–30.
20 Wang Y-Y, Liu Y, Li C, *et al*. Frequency and risk factors for recurrent gestational diabetes mellitus in Primiparous women: a case control study. *BMC Endocr Disord* 2019;19:22.
21 Azziz R, Carmina E, Chen Z, *et al*. Polycystic ovary syndrome. *Nat Rev Dis Primers* 2016;2:16057.
22 Keshel TE, Coker RH. Exercise training and insulin resistance: a current review. *J Obes Weight Loss Ther* 2015;5.
23 Wang C, Wei Y, Zhang X, *et al*. Effect of regular exercise commenced in early pregnancy on the incidence of gestational diabetes mellitus in overweight and obese pregnant women: a randomized controlled trial. *Diabetes Care* 2016;39:e163–4.
24 Wang C, Wei Y, Zhang X, *et al*. A randomized clinical trial of exercise during pregnancy to prevent gestational diabetes mellitus and improve pregnancy outcome in overweight and obese pregnant women. *Am J Obstet Gynecol* 2017;216:340–51.
25 Russo LM, Nobles C, Ertel KA, *et al*. Physical activity interventions in pregnancy and risk of gestational diabetes mellitus: a systematic review and meta-analysis. *Obstet Gynecol* 2015;125:576–82.
26 Sanabria-Martínez G, García-Hermoso A, Poyatos-León R, *et al*. Effectiveness of physical activity interventions on preventing gestational diabetes mellitus and excessive maternal weight gain: a meta-analysis. *BJOG* 2015;122:1167–74.
27 Hanson MA, Bardsley A, De-Regil LM, *et al*. The International Federation of Gynecology and obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: 'think nutrition first'. *Int J Gynaecol Obstet* 2015;131 Suppl 4:S213–53.
28 Craig CL, Marshall AL, Sjöström M, *et al*. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003;35:1381–95.
29 Ding Y, Xu F, Zhong C, *et al*. Association between Chinese dietary guidelines compliance index for pregnant women and risks of pregnancy complications in the Tongji maternal and child health cohort. *Nutrients* 2021;13:829.
30 Sedov ID, Cameron EE, Madigan S, *et al*. Sleep quality during pregnancy: a meta-analysis. *Sleep Med Rev* 2018;38:168–76.
31 Chan AW, Reid C, Skeffington P, *et al*. Experiences of using the Edinburgh postnatal depression scale in the context of antenatal care for aboriginal mothers: women and midwives' perspectives. *Women Birth* 2022;35:367–77.
32 Gong Y, Zhou H, Zhang Y, *et al*. Validation of the 7-item generalized anxiety disorder scale (GAD-7) as a screening tool for anxiety among pregnant Chinese women. *J Affect Disord* 2021;282:98–103.
33 International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, *et al*. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010;33:676–82.
34 Zhou B, Coorperative Meta-Analysis Group Of China Obesity Task Force. Predictive values of body mass index and waist circumference to risk factors of related diseases in Chinese adult population. *Zhonghua Liu Xing Bing Xue Za Zhi* 2002;23:5–10.
35 Chinese Nutrition Society. Weight monitoring and evaluation during pregnancy period of Chinese women. T/CNSS 009-2021. 2021.
36 Fangping Xu ZW, Ding Y, Yang N, *et al*. Establishment and application of the Chinese dietary guidelines compliance index for pregnancy women. *J Nutr* 2021;43:7.
37 Lin L, Huang Y, Chen L, *et al*. Gestational weight trajectory and risk of adverse pregnancy outcomes among women with gestational diabetes mellitus: a retrospective cohort study. *Matern Child Nutr* 2024;20:e13645.
38 Hopkins SA, Artal R. The role of exercise in reducing the risks of gestational diabetes mellitus. *Womens Health (Lond Engl)* 2013;9:569–81.
39 Dugas M, Crowley K, Gao GG, *et al*. Individual differences in regulatory mode moderate the effectiveness of a pilot mHealth trial for diabetes management among older veterans. *PLoS One* 2018;13:e0192807.
40 Ryan J, Edney S, Maher C. Engagement, compliance and retention with a Gamified online social networking physical activity intervention. *Transl Behav Med* 2017;7:702–8.
41 Cai C, Bao Z, Wu N, *et al*. A novel model of home-based, patient-tailored and mobile application-guided cardiac telerehabilitation in patients with atrial fibrillation: a randomised controlled trial. *Clin Rehabil* 2022;36:40–50.
42 Jiwani R, Wang J, Li C, *et al*. A behavioral lifestyle intervention to improve frailty in overweight or obese older adults with type 2 diabetes: a feasibility study. *J Frailty Aging* 2022;11:1–9.
43 Rayward AT, Vandelanotte C, Corry K, *et al*. Impact of a social media campaign on reach, uptake, and engagement with a free web- and app-based physical activity intervention: the 10,000 steps Australia program. *Int J Environ Res Public Health* 2019;16:5076.
44 Valentiner LS, Thorsen IK, Kongstad MB, *et al*. Effect of ecological momentary assessment, goal-setting and personalized phone-calls on adherence to interval walking training using the Interwalk application among patients with type 2 diabetes-A pilot randomized controlled trial. *PLoS One* 2019;14:e0208181.
45 Grau-Pellicer M, Lalanza JF, Jovell-Fernández E, *et al*. Impact of mHealth technology on adherence to healthy PA after stroke: a randomized study. *Top Stroke Rehabil* 2020;27:354–68.
46 Salvi D, Ottaviano M, Muuraiskangas S, *et al*. An M-health system for education and motivation in cardiac rehabilitation: the experience of Heartcycle guided exercise. *J Telemed Telecare* 2018;24:303–16.
47 Al Wattar BH, Dodds J, Placzek A, *et al*. Mediterranean-style diet in pregnant women with metabolic risk factors (ESTEEM): a pragmatic multicentre randomised trial. *PLoS Med* 2019;16:e1002857.
48 Assaf-Balut C, García de la Torre N, Durán A, *et al*. A Mediterranean diet with additional extra virgin olive oil and Pistachios reduces the incidence of gestational diabetes mellitus (GDM): a randomized controlled trial: the St. Carlos GDM prevention study. *PLoS ONE* 2017;12:e0185873.
49 Bennett CJ, Walker RE, Blumfield ML, *et al*. Interventions designed to reduce excessive gestational weight gain can reduce the incidence of gestational diabetes mellitus: a systematic review and meta-analysis of randomised controlled trials. *Diabetes Res Clin Pract* 2018;141:69–79.

Informed Consent

Trial Title: Digital therapeutics-based lifestyle intervention for gestational diabetes mellitus prevention of high-risk pregnant women

Informed Consent Form Version No.: 1.1, Version Date: 4/18/2023

Institution: Fujian Maternity and Child Health Hospital

Principal Investigator: Lihua Lin

Patient's name:

Dear Ms:

We hereby invite you to participate in a medical research study. This informed consent form provides you with information to help you decide whether or not to participate in this study. Please take some time to read the following carefully and discuss any unclear questions or terms with the appropriate physician. You can discuss your decision to participate in this study with your family and friends before making it. If you are taking part in another study, please let us know.

I. Background

1. Nature of the project: This study is sponsored by Fujian Maternity and Child Health Hospital (FMCHH) as a "Digital therapeutics-based lifestyle intervention for gestational diabetes mellitus prevention of high-risk pregnant women", which is led by FMCHH in conjunction with six medical institutions in the Fujian province, and the principal researcher is Li-Hua Lin, and the project will start and end from October 2023 to September 2026.

2.Background significance: Gestational diabetes mellitus is one of the most common comorbidities in pregnancy, often leading to an increased risk of short- and long-term complications for the pregnant woman herself and her offspring, including type II diabetes mellitus and cardiovascular disease in the distant future in the mother, as well as an increased risk of metabolic disorders, such as obesity and type II diabetes mellitus, in her offspring. Several studies have demonstrated that following a healthy lifestyle during pregnancy can reduce the incidence of gestational diabetes by about 40%.

3. This study was reviewed and approved by the Ethics Committee of Fujian Maternity and

Child Health Hospital.

II. Research Process

In this study, pregnant women with high risk factors for gestational diabetes mellitus were enrolled in the obstetrics clinic after filing and were assigned to the intervention group and the standardized management group in the regular nutrition clinic based on their voluntary choice of whether to receive the digital therapy management program by the doctor's detailed explanation of the digital therapy intervention program. The intervention group provides data-driven personalized diagnosis and treatment services for the subjects based on remote monitoring and intelligent feedback to pregnant women through APP. This study is expected to involve 800 participants in this research program with a follow-up period starting from early pregnancy until oral glucose tolerance measurement at 24-28 weeks.

This study requires the combination of routine clinical data to generate a personalized prescription for the management of people at risk for gestational diabetes mellitus. Your information and personal data will be kept strictly confidential and will not be shared with anyone outside the group without the consent of the principal investigator.

III.Risks and discomforts of participating in the study

In addition to the regular medical treatment, this study will conduct additional questionnaires for you, the content of the survey does not involve sensitive issues, if there is discomfort in the questionnaire, you can refuse to answer. During the study period, pregnant women will be required to use the sports bracelet at home to collect home health data. The sports bracelet is branded by Huawei, and according to Huawei's quality inspection report, it will not be harmful to pregnant women.

IV. Benefits of participating in the study

If you agree to participate in this study, you can receive timely feedback and better answers to your questions about nutritional care during pregnancy and other areas.

V. Costs associated with participation in the study

You do not need to pay any additional fees to participate in this study.

VI.Right to refuse to participate or withdraw from the study

Participation in this study is completely voluntary. You may choose not to participate in this study, or you have the right to withdraw from the study at any stage of the trial without any reason, and none of your medical treatment or rights will be affected as a result. However, the investigator's processing of your data prior to withdrawal is lawful, and it is unlikely that the data prior to withdrawal will be erased or processed if it has been integrated into the research program, and it may continue to be used in this study, provided that your privacy is protected. Once you have decided to participate in this study, please sign this informed consent form to indicate your agreement. Prior to entering the study, you will be screened by your physician to confirm that you are a suitable candidate.

VII.Privacy and Confidentiality

During the study, your name, gender and other personally identifiable information will be replaced with codes or numbers, and will be kept strictly confidential. Only the physician concerned will know your personal information, and your privacy will be well protected. The results of the study may be published in journals, but will not reveal any of your personally identifiable information.

If you agree to participate in this study, all of your medical information will be accessed by the investigator, the research authority, and the ethics committee to check the appropriateness of the operation of the study. If you sign the informed consent form, it also means that you agree to be accessed by the above people. Your medical records will be kept at the hospital, and any public reporting of the results of this study will not disclose the subject's personal identity. The investigator will make every effort to protect the privacy of subjects' personal medical information to the extent permitted by law.

VIII.How to get help in the study

You can keep yourself informed of information materials and research progress related to this study. If you have questions related to this study, please contact Leah Lin at 0591-87279153.

If you need to know about the rights and interests of the participants in this study, you can

contact the Ethics Committee of Fujian Maternity and Child Health Hospital at 0591-88312052.

Consent Signature Page

If you fully understand the content of this research project and agree to participate in this study, you will sign this informed consent form in duplicate, with one copy to be retained by the researcher and one copy to be retained by the subject or delegate.

Signed by the subject himself/herself or his/her legal representative:

Statement of Consent:

1. I acknowledge that I have read and understood the informed consent form for this study, that problems and solutions that may arise during the course of the study have been explained to me, and that I have had the opportunity to ask my own questions.

2. I have made it clear that participation in the study is voluntary and that refusal to participate will not jeopardize any benefits to which I am entitled.

3. I have been informed that the team members involved in this study and the Ethics Committee of Fujian Provincial Maternal and Child Health Hospital have the right to review the study records and case information, and I agree to the direct access to my study records by the abovementioned personnel, with the understanding that the abovementioned information will be treated in a confidential manner.

4. I agree to participate in this study

Your full name: Date:

The following will be completed by the physician performing the informed consent process:

INVESTIGATOR'S DECLARATION: I confirm that the nature, purpose, requirements, and possible risks of this study have been explained and discussed with the patient, and that other available treatment options have been explored at the same time, and I ensure that a copy of this Subject Informed Consent Form has been given to the subject for safekeeping.

Full name of researcher: Date:

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